Evaluation of Clinical Data
For
FERTI·LILY Conception Cup

Manufacturer: Rosesta Medical BV
Mr. Treublaan 7
1097 DP, Amsterdam
The Netherlands
http://www.fertilily.com

Product: FERTI·LILY Conception Cup
Product category: Device for the aid of conception
Product description: Silicone device to help in conceiving and fertility
Classification: **Class I**
Assessment procedure: Annex VII
Notified body: Not Applicable

ER Checklist	Name	Function	Date	Signature
Established by	Robert Stal	CEO		
Reviewed and approved by	Maarten Wiegerinck	Senior Scientific Advisor		

Description of change		
Version	**Date**	**Reason for change**
1.0	04 April 2018	First Draft
2.0	07 January 2019	Update with usability testing
3.0	19 June 2019	Update pre-launch using latest data and IFU
4.0	12 Jan 2021	Update material specifications and Clinical Data

CONTENTS

1. Summary

FERTI·LILY Conception Cup is a Medical Device Class I to help with the conception of a child. The FERTI·LILY provides users with a comfortable and effective tool to insert vaginally after intercourse to help increase the number of spermatozoa swimming into the cervical mucus. This can increase the chances of becoming pregnant and will help mechanically with a number of practical issues after intercourse (such as being able to urinate after).

2. Introduction and Scope

This document concerns the overall clinical evaluation of the FERTI·LILY Conception Cup. Clinical evaluation is regarded as an ongoing process conducted throughout the product life cycle of a Medical Device. The evaluation of clinical data is first performed during the conformity assessment process leading to the launch of a medical device and is repeated periodically as new information about the safety and performance of the device are received during the post market phase.

2.1. Manufacturer

Rosesta Medical BV
Mr. Treublaan 7
1097DP Amsterdam
The Netherlands

www.FertiLily.com

2.2. Device Identification FERTI·LILY Conception Cup

The FERTI·LILY Conception Cup (FLCC) is a unique cup designed to insert after intercourse to help physically push the ejaculate close to the cervix and keep it there for extended periods of time. The mode of action is purely physical. The cup is made of medical grade silicone.

2.3. Applicable regulations, standards, and guidelines.

This clinical evaluation was performed according to the requirements and guidelines of:

- MDR 2017/745/EC Annex I and Annex XIV
- ISO 14155:2020 Clinical investigation of medical devices for human subjects — Good clinical practice.
- EN ISO 10993-1:2009/C01:2010 Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process.
- FDA guidance: Use of International Standard ISO 10993-1, Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process, 2016.
- EN ISO 14971:2019 “Medical devices - Application of risk management to medical devices”

- MEDDEV 2.7.1 rev.4, June 2016: Evaluation of clinical data: A guide for the manufacturers and notified body

2.4. Device Description

The FERTI·LILY Conception Cup is a device made of medical grade silicone intended to be inserted vaginally after intercourse to physically transport the ejaculate towards the cervix. The device has a cord attached to it that can be pulled to help remove the device as well as indentations for the fingers to help position the device at the cervix.

The FERTI·LILY cup is invasive with respect to body orifices and has been classified as Medical Device Class I.

For the description of the manufacturing process reference is made to DHF 5.2.9.

Product and process risks are identified in the risk management report DFH 6.1.3.

2.4.1. Packaging Materials

FERTI·LILY Conception Cup:

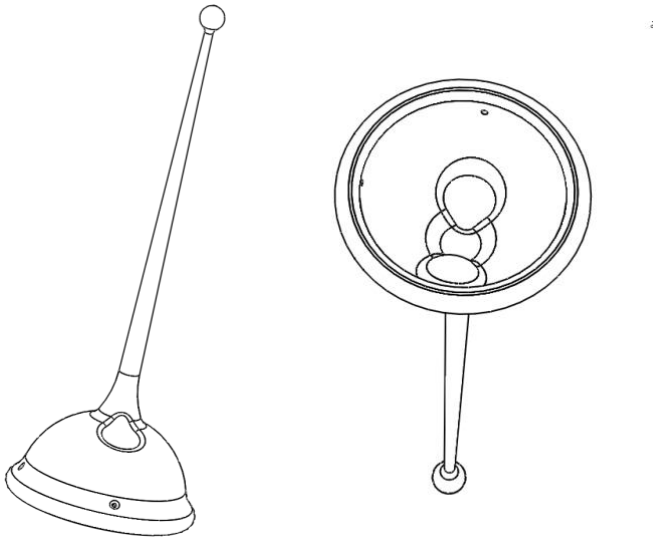


Figure 1: Side View and Top View of FERTI·LILY Conception Cup

Device is made of: Medical Silicone: Wacker Chemie

2.4.2. Mode of Action

The FERTI·LILY Cup's mode of action is based on the physical action of pushing the ejaculate towards the cervix and keeping it there for a period of time. This action has been shown to increase the amount of semen deposited in the Cervical Mucus.

The device is also designed to be inserted and removed comfortably. The use of the device allows couples trying to conceive to carry on with their normal routine and use of the product is as non-invasive on this routine as possible.

2.4.3. Claims

- Transports the ejaculate towards the cervix/Delivers more sperm to the cervix.
- Helps to increase the number of spermatozoa deposited in the cervical mucus.
- Increases the chances of conception by 48%*
- 1.5x higher chances of conception*
- Helps to conceive at home
- Supports/helps natural conception
- Helps to conceive faster; get pregnant quicker
- Clinically Proven
- Protects semen from the harsh environment of the vagina.
- Comfortable and easy to insert, wear, and remove.
- Intended to be inserted after intercourse.
- No negative impact on intimacy
- No need for uncomfortable condoms and applicators.
- 100% Medical Grade, sperm friendly Silicone.
- Re-usable for up to 6 cycles/months

* In a clinical study, women using the FERTI·LILY Conception Cup as intended for 3 cycles were found to be 48% more likely to conceive. Find out more at www.fertilily.com

2.4.4. Application and Warnings

The FERTI·LILY Cup acts as a protective cradle for sperm, encouraging more sperm to swim through the cervical mucus and thereby increasing the chances of one of the sperm cells reaching your egg. FERTI·LILY gives a little help, making your little miracle.

A. FERTI·LILY Conception Cup

The FERTI·LILY Conception Cup is a tested and approved medical device developed by fertility specialists who want couples to fulfil their dream of starting a family. The FERTI·LILY Cup will not interfere with romance or spontaneity because it's designed for use comfortably after sex. At FERTI·LILY, our mission is to help you increase the odds of conceiving, without getting in the way of the intimacy.

The cup is designed to bring as much of his sperm as possible right to the cervix, the opening of your uterus. Using the FERTI·LILY Cup increases the number of sperm delivered to the protective environment of your cervical mucus, which acts as a reservoir for extended sperm survival

The FERTI·LILY Cup is easily placed in the vagina after intercourse, using your fingers. It's made of soft, flexible silicone and is proven to be comfortable to insert, wear and remove.

Benefits of using the FERTI·LILY Conception Cup:

- The FERTI·LILY Cup brings more sperm cells directly to the cervix.
- Sperm safeguarded within the FERTI·LILY Cup is exposed to less contact time in the vagina, which typically has a pH level toxic to sperm.
- The FERTI·LILY Cup can remain in place for up to 1 hour, increasing the amount of time individual sperm cells have to swim into the fertile cervical mucus.
- You can urinate, shower, sleep, or go about your business after inserting the FERTI·LILY Cup without worrying about losing any of his sperm.
- Cuddle afterwards for as long as you like. There's no need to keep your legs in the air if you're using the FERTI·LILY Cup.

Did you know?

- Normally up to 60% of the sperm can flow out of the vagina after sex.
- The low pH of your vagina actually kills off sperm. The less time in the vagina that the sperm spends, the better for its survival.
- Stress reduces your chances of conceiving. Relax, don't worry and try to have some fun.
- Urinating after sex helps to reduce the chances of bladder infections (UTI).
- You can tell by the colour and consistency of your cervical mucus when you are most fertile.
- For more tips and tricks visit www.FertiLily.com.

B. How to use the FERTI·LILY Cup

IMPORTANT PRODUCT SAFETY INFORMATION
DO NOT USE the FERTI·LILY Cup before you read and understand these instructions.

RETAIN FOR FUTURE REFERENCE.
This User Guide is for information only and should not be considered as medical advice, nor does it substitute for a consultation with your doctor. If you have any medical concerns or conditions, please consult your doctor prior to using the Cup.
For a handy video on how to use the FERTI·LILY Cup have a look on www.FertiLily.com

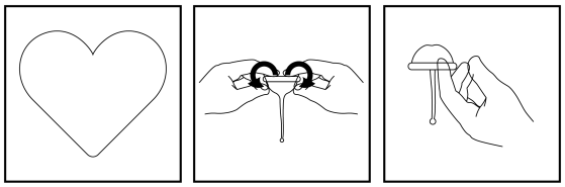
Before first use, boil the FERTI·LILY Cup in an open pot of boiling water for 5-10 minutes. Dry the FERTI·LILY Cup and store it in the cotton pouch provided.

For first-time users, it is recommended the FERTI·LILY Cup be inserted, positioned, and removed a number of times before intercourse until you're familiar with insertion and removal. The first few times may be a bit tricky, but practicing will help make it easier to use after intercourse. Using a lubricant may increase the comfort of use during practice. Use caution when inserting and removing the FERTI·LILY Cup if you have long fingernails.

Use the FERTI·LILY Cup during the ovulatory phase of your menstrual cycle. Using ovulation predictors may help you to determine the days of your monthly cycles with the highest fertility.

Step 1:
Prior to insertion, thoroughly wash the FERTI·LILY Cup for 15-20 seconds with warm water. Remember to keep the FERTI·LILY Cup close to the bed, so you will not have to get up after intercourse.

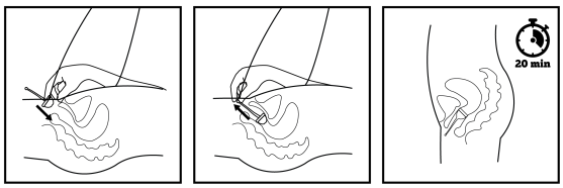
Step 2:
Have intercourse (Pictogram A). After your partner has ejaculated inside you, get the cup without sitting or standing up, to avoid semen flowing back out of your vagina. Turn the cup inside-out to look like an umbrella (Pictogram B). Hold the FERTI·LILY Cup with the stem pointing toward your feet and one finger inside the umbrella shape (Pictogram C).



Pictogram A Pictogram B Pictogram C

Step 3:
Gently push the cup up inside your vagina (Pictogram D). If you are having trouble inserting the cup, you can also fold it over to make it smaller for insertion. This will push the semen towards the cervix. Once you reach the top of your vaginal canal, gently pull on the cord to pop the FERTI·LILY Cup back into its original shape while holding the cup in place with the inserted finger (Pictogram E). How to tell if you've done it right? You can actually feel the indents when the cup is in its correct shape, and you can barely feel them when it's in the umbrella shape. (Try this a few times when holding the cup in your hands prior to use, if you like.) If you really can't tell if the cup is in its original shape or its umbrella shape, don't worry too much. You've got the sperm up there and the cup will prevent it from flowing back. Just leave the cup in place for now. Practice makes perfect, so next time it should go smoothly.

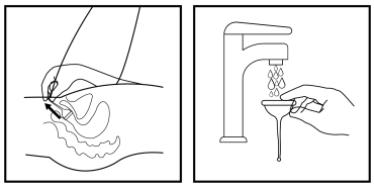
The FERTI·LILY Cup can be worn for 20 minutes up to a maximum of 1 hour (Pictogram F). See removal instructions below.



Pictogram D Pictogram E Pictogram F

C. How to remove the FERTI·LILY Cup

Wash your hands with soap and water. In a comfortable position, either standing up or sitting on the toilet, bear down in a series of gentle downward pushes with your abdominal/pelvic floor muscles (as if you are having a bowel movement). Since the vagina is only about 8-10 cm long, you can insert your index finger up slowly until you reach the removal stem if it's not already accessible (Pictogram G). Gently and slowly pull the stem horizontally until you can feel the base of the FERTI·LILY Cup at the opening of your vagina (be gentle, pulling on the stem too hard can cause irritation and discomfort and ultimately the stem can break). Gradually pull the cup out little by little instead of pulling with force on the ball. Firmly pinch the base of the cup with the two indents or use your finger to pull one edge of the cup down to release the seal and pull it gently out of your vagina. Once removed, simply empty the contents into the toilet. Wash the FERTI·LILY Cup thoroughly and store as directed (Pictogram H).



Pictogram G Pictogram H

REMINDER: It is not necessary to remove the FERTI·LILY Cup before urinating or having a bowel movement.

D. How to clean the FERTI·LILY Cup

Clean the FERTI·LILY Cup with warm water. Do NOT use vinegar, tea tree oil, scented soap, castile/peppermint soap, oil-based soap, rubbing alcohol, antibacterial soap, hand sanitizer, pre-moistened wipes, dish soap, hydrogen peroxide, bleach or harsh chemicals, as these may damage the silicone and cause irritation.

The FERTI·LILY Cup may naturally discolor slightly over time. This does not impair its functionality. As needed, it may be boiled for 5-10 minutes in an open pot with plenty of water. Do not leave the boiling pot unattended. If you accidentally burn your cup because the pot boiled dry, your cup may be ruined and should be replaced.

The small holes located below the rim are meant to avoid a vacuum when removing the cup and must be kept clear and clean at all times. Gently stretch each hole under warm running water to remove any debris. At the end of your fertile period, it is recommended to wash and then boil the FERTI·LILY as instructed above and dry the FERTI·LILY Cup completely. Store it in the cotton bag provided, NOT in a plastic bag or air tight container.

If you are unable to wash the FERTI·LILY Cup directly after removal (for instance, when using a public restroom), wash your hands thoroughly before entering the cubicle,

empty the contents in the toilet and simply use a dry or damp tissue to clean the cup. At the next convenient time, clean as instructed. When traveling, always wash the cup using potable (safe to drink) water.

KEEP DRY. KEEP AWAY FROM SUNLIGHT. KEEP AWAY FROM CHILDREN. Store at room temperature between uses.

E. How often to replace the FERTI·LILY Cup

Medical silicone is very durable, but the lifespan of the FERTI·LILY Cup varies, depending on factors unique to each user. Inspect your cup before each use for signs of deterioration, such as a sticky or powdery residue, breaks in the silicone, severe discoloration or odor. A general guideline is to replace it after 6 months of use, or sooner if the cup shows signs of deterioration.

F. Precautionary Warnings

- Use according to the directions provided.
- You may experience light cramping during the first use.
- Never pull the FERTI·LILY cup out using force. If you experience a vacuum or resistance it may help to insert a finger and fold over the edge of the cup to break the seal before gently pulling at the stem. It helps to relax and squat down to bring the cup closer to the opening of the vagina.
- Do not pull on the stem of the cup with force. The stem can break with excessive force and while it can be used to remove the cup slowly, one should not pull on the ball of the stem with force, but use the stem to remove the cup little by little.
- The FERTI·LILY Cup is not a contraceptive device and will not protect you against sexually transmitted infections.
- The FERTI·LILY Cup and TSS: There is no known link between Toxic Shock Syndrome (TSS) and cups such as the FERTI·LILY Cup. Consult your physician prior to using the FERTI·LILY Cup if you have previously been diagnosed with TSS. TSS is a rare condition, usually associated with the use of tampons, whose symptoms must be taken seriously. Remove the FERTI·LILY Cup and contact your doctor immediately if you experience any of the following symptoms: sudden vomiting, diarrhea, high fever, headache, a sunburn-like rash, muscle aches, confusion or seizures.
- Do not use the FERTI·LILY Cup if you have a yeast or bacterial infection. Resume use once the infection has completely cleared. If you have used the FERTI·LILY Cup while you have had an infection, it is recommended that you replace your cup with a new one to ensure against repeat infection.
- Dispose in trash. Do not flush the FERTI·LILY Cup down the toilet.
- If you experience any adverse effects, discontinue use and consult with your physician.

FERTI·LILY helps to increase the amount of sperm that swims into the cervix. There are many factors that could influence fertility on which FERTI·LILY cannot have any

influence. If you are still not pregnant after 12 months of trying or are worried about your fertility, please consult with your doctor.

This device is intended as an aid in conception and does not guarantee pregnancy.

G. Contact and Consumer Care

Carefully follow these instructions for best results. Visit FertiLily.com for more information. For other questions, contact our consumer care team by phone [XXXXX-XXX-XXXX] or email at [email address local customer support].

The FERTI·LILY Cup is a registered trademark of FERTI·LILY. This is the official User Guide for the FERTI·LILY Cup and content may change without prior notice. Visit FertiLily.com for up-to-date information.

CE
The FERTI·LILY Conception Cup is a MEDICAL DEVICE Class I

Manufacturer:
FERTI·LILY
Mr Treublaan 7
1097DP Amsterdam
The Netherlands

Distributor:
[NAME AND ADDRESS DISTRIBUTOR]

Date of latest Revision:Jan 2020

3. Clinical Background

The FERTI·LILY Conception Cup has been developed to help couples that are trying to conceive to improve their chances in a comfortable, discreet, and safe manner in the comfort of one's home. The product is manufactured by Rosesta Medical BV. The product is based on a Medical Silicone cervical cup that is inserted after intercourse to push the ejaculation of the male partner towards the cervix. Once inside the vagina it opens up and is pushed manually up the vaginal canal towards the cervix pushing the ejaculate and seminal load.

A literature investigation has been carried out to identify the available data on the indication, clinical background, current treatments and state of the art, and to identify risks involved. Special attention has been placed on identifying:

- Causes and prevalence of infertility, subfertility and delayed fertility.
- Risk factors of infertility, subfertility and delayed fertility.
- Physiology of infertility, subfertility and delayed fertility.
- Current treatment methods of infertility, subfertility and delayed fertility.

A basic background of the knowledge of (in)fertility, cervical cups and related fertility treatments was obtained from a systematic review by computerized literature searches to identify all published articles on the subject. The following databases were used: the Cochrane Library, MEDLINE, EMBASE, PubMed, all from 1980 – 2020.

In addition to this, a literature search was carried out on PUBMED, and with the assistance of Google Scholar with the criteria date of publishing set above using the following search terms (or a combination thereof):

- Cervical Cap/Cup
- (In)fertility treatment
- Subfertility
- Fecundability Odds Ratio (FOR)
- Stress
- Fertility device
- Insemination
- Menstrual Cup
- Vagina
- Vaginal environment
- Sperm Survival
- Vaginal Anatomy
- (Medical) Silicone

Criteria for literature and data therein is that they should be the most comprehensive and up-to-date data possible. Studies were included if they contained original data describing clinical investigations or outcomes from a recognized, scientific, independent, peer-reviewed journal, preferably in the field of the indication. Investigations were included irrespective of focus region to allow a global picture of the indication and treatment thereof. Publications were considered relevant if they included information on any aspect of the indication.

See the report on literature research result 5.3.1a and 5.3.1b for the list of publications considered and their contribution to the clinical background.

3.1. What is Fertility

3.1.1. The Menstrual Cycle and conception

The menstrual cycle consists is controlled by many hormones in our bodies and consists of three phases; the follicular phase, the ovulation day and the luteal phase.

Follicular phase

The period

The menstrual cycle starts on the first day of menstrual bleeding and the total cycle lasts an average of 28 days. The period lasts 5 days on average but can be anywhere from 3 to 8 days, with bleeding being the heaviest on the first 2 days.

Once the bleeding stops the uterine lining (endometrium) starts building up again for the possibility of a pregnancy. In this time, it becomes thicker and is filled with nutrients and blood.

The fertile window

You are actually most fertile in days 11-15 of your cycle. These are the days just before ovulation and shortly after ovulation has happened. That's because sperm can survive for quite a while inside the fallopian tubes (up to 5 days!). It gives the sperm the time to swim into the fallopian tubes and wait there for the egg to pass. So best timing: have sex every other day from day 10 or 11 of your cycle.

Ovulation

Ovulation occurs around day 14 of the menstrual cycle when an egg is released from one of the ovaries (usually alternating each month). The egg starts it journey along the fallopian tubes towards the uterus. This is also where fertilization can take place if there are sperm cells waiting in the fallopian tubes.

When the egg reaches the uterus implantation may occur. If the egg is not fertilized it will not implant in the lining. If the egg is fertilized it will try to implant into the lining, but unfortunately it doesn't always happen. If the fertilized egg manages to implant in the lining, conception is complete, and the pregnancy will begin.

Luteal phase

If the egg is not implanted in the lining, hormonal changes will signal the uterus to start shedding its lining. The egg will break down and is shed together with the lining in the menstruation. Then the cycle begins again on day 1 of the menstruation.

3.1.2. Fertility and chances of incremental conception rates

Humans are not very fertile beings. Even during our most fertile stages our peak probability of conception lies around 33% per successful attempt. While on its own this is not a high number, there are numerous factors that may further reduce the chances of couples to become pregnant.

The estimated cumulative probability of conceiving at one, three, six and 12 cycle(s) were 38, 68, 81 and 92% respectively[1]. This means that 32% of couples have been trying for more than 3 months before conceiving. This study of German women is also supported in the study by Axmon et al (figure 2), showing similar outcomes in the Swedish population[2]. 10–15% of couples have difficulties conceiving at all, or conceiving the number of children they want, and seek specialist fertility care at least once during their reproductive lifetime.

[1] C. Gnoth, D. Godehardt, E. Godehardt, P. Frank-Herrmann, G. Freundl; Time to pregnancy: results of the German prospective study and impact on the management of infertility, *Human Reproduction*, Volume 18, Issue 9, 1 September 2003, Pages 1959–1966,
[2] Axmon, Anna & Rylander, Lars & Albin, M & Hagmar, L. (2006). Factors affecting time to pregnancy. Human reproduction (Oxford, England). 21. 1279-84.

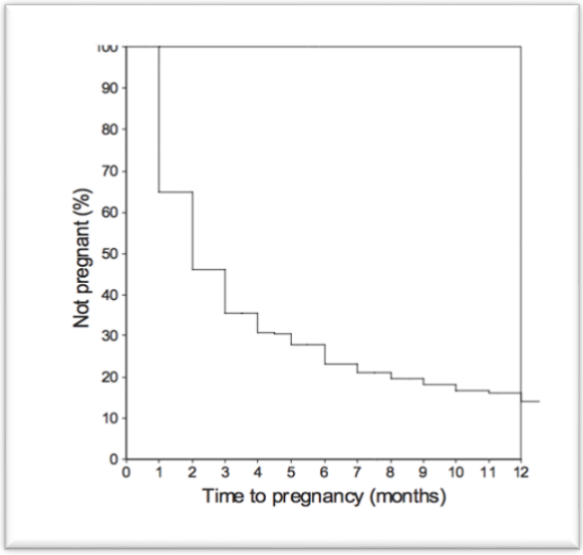
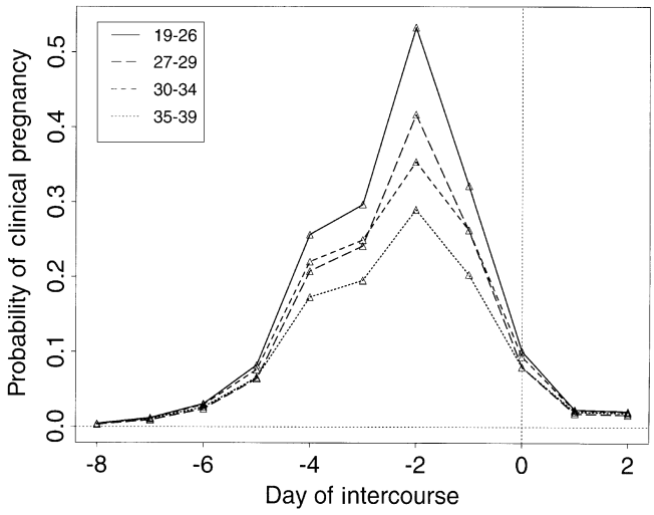


Figure 2: Time to Pregnancy. Axmon, A. (2006)

The general trend globally is that couples are waiting longer to try to get pregnant. From 2000 to 2014, the proportion of first births to women aged 30–34 rose 28% (from 16.5% to 21.1%), and first births to women aged 35 and over rose 23% (from 7.4% to 9.1%)[3]. Furthermore, the mean age of women at childbirth has increased from 29 to 30.5[4]. This also leads to a lower probability of fertility as the chances of conception decline significantly after the age of 30. Nearly a 50% drop occurred between women in their late 20s and women in their late 30s[5] as shown in figure 3 below.



[3] T.J. Mathews, M.S.; and Brady E. Hamilton, Ph.D. Mean Age of Mothers is on the Rise: United States, 2000–2014 *Center for Disease Control and Prevention*. January 2016 NCHS Data Brief No. 232.
[4] Mean age of women at childbirth across EU regions - Product - Eurostat_13Aug2018
[5] Dunson DB, Colombo B, Baird DD. Changes with age in the level and duration of fertility in the menstrual cycle. Hum Reprod 2002;17-1399–403

Figure 3: Probability of clinical pregnancy following intercourse on a given day relative to ovulation for women of average fertility aged 19–26, 27–29, 30–34 and 35–39 years (European Study of Daily Fecundability, 433 pregnancies), adjusted for male partner's age. Dunson, DB. (2002)[6]

It is clear that age and time trying to conceive are factors that are highly influencial in the prediction of successful pregnancies in couples trying to conceive. There are a number of prognostic models that are available to help predict the pregnancy rate for couples trying to conceive. These models are based on several input criteria to be able to predict conception rates in individuals. Two widely used models have been described below and can help to further put the chances of conception into perspective.

The computational model by Sozou has been selected because this model is able to predict the chances of conception for most couples[7]. The input criteriae used by Sozou are only age and time trying to conceive. This model shows that age can play a large role in chances of conception showing that a woman aged 25 that is just starting to try to conceive has as chance of 22.3% to conceive in the next cycle and 87.2% likelihood of conceiving within the next 12 cycles. A woman aged 35, on the other hand has a 16.2% chance of conceiving in the next cycle and a 73.3% chance of conceiving in the next 12 cycles. One can see that a high time of trying to conceive also has a negative effect on one's prognosis as a 25 year old that has already been trying to conceive for 12 months without success has a 10.3% chance of conceiving in the next cycle and a 62.6% chance of conceiving within the next 12 cycles.

The model by Hunault incorporates more initial data about couples trying to conceive, also taking account of sperm motility, referral by a specialist, and a Post Coital test[8]. While the Hunault model is only applicable to couples that have been trying to conceive for more than 12 cycles, it has been highly validated[9] and is currently used in determining the mode of treatment of patients suffering from infertility[10].

The two prognostic models discussed above show that estimates of fertility rates by several previous studies can be too generalised. One should always look at the specific situation in order to determine likely conception rates and whether medical intervention should be considered. These prognostic models also show that many couples trying to conceive may be overestimating their chances of conception. A study carried out by ClearBlue showed that: "Women expected pregnancy to happen quickly, "within 3–6 months" was the most common answer to the question on how long on average they thought it would take for a woman like themselves to become pregnant"[11].

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[6] Dunson, D. et al. Changes with age in the level and duration of fertility in the menstrual cycle. Human Reproduction Vol.17, No.5 pp. 1399–1403, 2002

[7] Sozou PD, Hartshorne GM. Time to Pregnancy: A Computational Method for Using the Duration of Non-Conception for Predicting Conception. PLoS One 2012;7.

[8] Hunault CC, Habbema JDF, Eijkemans MJC, Collins JA, Evers JLH, te Velde ER. Two new prediction rules for spontaneous pregnancy leading to live birth among subfertile couple, based on the synthesis of three previous models. Hum Reprod 2004;19:2019–26.

[9] van der Steeg, Jan Willem, et al. "Pregnancy is predictable- a large-scale prospective external validation of the prediction of spontaneous pregnancy in subfertile couples." Human reproduction 22.2 (2007)- 536-542.

[10] https://www.freya.nl/kinderwens/zwangerworden/spontane-zwangerschapskans-2/spontane-zwangerschapskans/ (date viewed 12 January 2020)

[11] Johnson SR., Pion C.. **Multi-national survey of women's knowledge and attitudes towards fertility and pregnancy** *SPD Development Company Ltd., Bedford, United Kingdom, SPD Swiss Precision Diagnostics GmbH, Geneva, Switzerland*

3.2. Subfertility or Infertility

Infertility is currently defined as 1 year of unwanted non-conception with unprotected intercourse in the fertile phase of the menstrual cycles. Most of the pregnancies occur in the first twelve cycles with intercourse in the fertile phase. After that, serious subfertility must be assumed in every second couple (10%) although—after 12 unsuccessful cycles—untreated live birth rates among them will reach nearly 55% in the next 36 months.

While the large majority of infertility can be explained by sperm defects, ovulation failure or tubal infective damage, up to 25% of infertility causes are unexplained. Sperm defects or dysfunctions account for 30% of infertility and ovulation Failure accounts for 25% of infertility. Whereas the combination of endometriosis, coital failure, and cervical mucus defects account for 13% of infertilities.

Various treatments are available to couples ranging from hormonal treatments to regulate ovulation, to intra-uterine insemination (IUI), in-vitro fertilization (IVF) to intra-cytoplasmic sperm injection (ICSI). These procedures are often very invasive in terms of impact on quality of life as well as on the body when using hormones. In order for couples to receive specialist treatment they must generally try to conceive for at least 12 months in order to show that they are, in fact, clinically considered subfertile and eligible for specialist support. Often the Hunault model is used in order to determine which treatment course shall be followed.

While some forms of subfertility and infertility may indeed require specialist care, 50% of couples still are able to conceive naturally after the time of 12 months. Furthermore, the number of couples trying to conceive for an extended period (3 cycles or more) is significant.

3.3. Delayed Fertility

Delayed fertility (without underlying infertility) is often more difficult to associate directly to any condition. The probabilities alone as stated above can be enough to drive couples to despair after some time of trying to conceive. While the initial probabilities of conceiving a child are quite favourable, the chances of conception associated with trying to become pregnant seem to diminish as couples are trying for longer times.

At this point stress and pressure can pick up, further helping to diminish the probability of conceiving[12]. Studies have shown that delayed fertility and infertility are associated with an increase of stress and anxiety. Increased levels of stress and anxiety have further been associated with diminishing the Fecundability Odds Ratio (FOR), an indicator of the probability that conception will occur at a given time period. Figure 4 below shows the decrease in probability of conceiving as stress increases (measured by salivary amylase).

[12] Germaine, MBL. Et al. Stress reduces conception probabilities across the fertile window: evidence in support of relaxation. *Fertility and Sterility.* Vol. 95, No. 7, June 2011

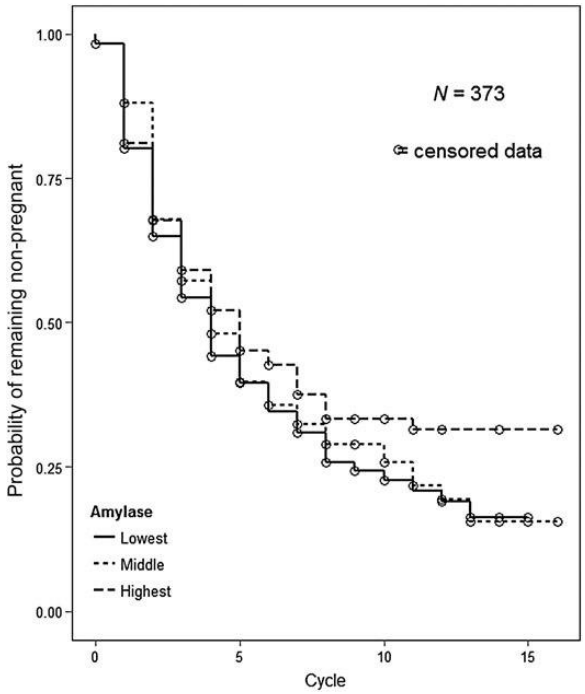

Figure 4 : Adjusted probability of remaining not pregnant by tertile of salivary alpha-amylase.*Adjusted for age of female, difference in age between male and female, income of female (dichotomized), race of female (dichotomized), female's cigarette use, female's caffeine use, and female's alcohol use. Louis, GMB. (2014)*[13]

As discussed in the section above, roughly one third of couples trying to conceive have not succeeded after 6 months. While experts advise 12-18 months of trying to conceive before seeing a specialist, this can be a long and anxious wait without any guidance or help. This has led to a number of solutions becoming available to people trying to conceive without medical intervention.

Various solutions are available to couple trying to conceive to increase their chances of conception. The most well-known consumer solution would likely be to use ovulation tests to help predict the day of ovulation. These solutions are all designed around optimizing the chances of conception. The Clear Blue Fertility Monitor, for example, has shown that couples using this monitor to estimate and plan their fertile days can increase the chances of conception from 14.4% to 22.7%. While the previously mentioned ovulation test is based on hormones found in the urine, other testers measure body temperature to estimate ovulation.

Other solutions include physical aids in the achievement of conception such as cervical caps and conception kits involving cervical caps and applicators to help 'present' the ejaculate to the cervical os. These aids were initially developed to aid in artificial inseminations increasing the chances of frozen semen to result in successful pregnancy, but in recent years various alterations of this technology have brought some solutions to the market to help couples that are looking for help in conceiving. Most of these products include a semen-friendly condom or receptacle. The ejaculate is then inserted into the cervical cap and placed at the cervix with or without an applicator[14,15]. These cervical caps have been shown to significantly increase the amount of semen entering the cervical mucus by 323% in the 85% of

[13] Louis, GMB. 2014. Preconception stress increases the risk of infertility- results from a couple-based prospective cohort study—the LIFE study. *Human Reproduction.* Vol. 29. No. 5. Pp. 1067-1074. 2014.
[14] Artwork-IFU-Stork-OTC_Rev.6
[15] https://www.conceptionkit.com/at-home-cervical-cap-insemination/. Visited June 2018.

couples that showed an increase of seminal deposit[16]. A big downside to these solutions is that they are quite mechanical and invasive. A condom is required to be worn during intercourse, the ejaculate is deposited in a cervical cap and this is inserted vaginally using a rigid, hard applicator.

3.4. Other Factors influencing Fertility

As highlighted in the previous sections, there are some factors that can influence fertility in a negative way. These include stress, age, weight (as previously discussed), but also diets including alcohol, cigarette and drug (ab)use by both partners, and even activities like going to the sauna, biking for extended periods can influence male fertility.

There are a number of factors that can also affect the ability of sperm cells to effectively swim towards and fertilise the egg. In the vaginal canal the pH of the vagina is hostile to sperm survival[17]. While female arousal does stimulate mucus production which does help to increase the pH of the vaginal canal during intercourse, the pH levels remain sub-optimal for sperm survival and motility[18]. Another factor that can negatively influence fertility is the presence of anti-sperm antibodies in the male or female. antisperm antibodies were detected in 31.1% of infertile couples in one or both partners, whereas immobilizing antibody activity has not been reported in the sera of fertile individuals. The presence of circulating antisperm antibodies is directly related to decreased fertility[19].

4. Device Under Evaluation

The device under evaluation is made of medical silicone, its dimensions are developed to bring and hold the ejaculate in the proximity of the cervix when the device is physically inserted into the vagina. Where the FERTI·LILY Conception Cup differs from the previous devices is that it is inserted following natural intercourse and does not require use of a condom or recepticle. The device is soft and comfortable and allows consumers to follow their intimate routine in trying to conceive which will have a positive impact on factors such as stress and anxiety, female orgasm, comfort during application, and ease of general use.

In this section all available data used in the clinical evaluation procedure is listed and appraised. When data from an equivalent device has been used in the evaluation, the equivalence will be demonstrated. Using this data together with all essential requirements on product safety, acceptability of benefit/risk profile and the performance and acceptability of side-effects the FERTI·LILY Conception Cup product will be evaluated.

4.1. Product Description

[16] Pelekanos, MICHAEL J. Postcoital Sperm Assessment Comparative Study. *Surgical technology international* 27 (2015): 184-190.

[17] Zhou, Ji, et al. "The semen pH affects sperm motility and capacitation." *PloS one* 10.7 (2015): e0132974.
[18] Wagner, Gorm, and Roy Levin. "Human vaginal pH and sexual arousal." *Fertility and Sterility* 41.3 (1984): 389-394.
[19] Naz, Rajesh K., and Alan C. Menge. "Antisperm antibodies: origin, regulation, and sperm reactivity in human infertility." *Fertility and sterility* 61.6 (1994): 1001-1013.

The FERTI·LILY Conception Cup is a new design of an existing technology. The aim of this cup is to lower the entry barrier of consumers to use a cervical cup when trying to improve their chances of conception. The added benefits of the cup include:

- Ease of use
- Comfortable to insert, wear and remove
- Allows for natural intercourse and romance
- Reduces distance semen has to swim to reach the cervix
- Reduces amount of time semen spends in hostile environment of the vagina
- Increases the amount of semen entering the cervical mucus
- Increases the chances of conception
- Allows for post-intercourse activities such as using the toilet, showering, travelling without worrying about 'seminal loss'.

The clinical data supporting the FERTI·LILY Conception Cup comes from 3 main requirements. The first requirement focusses on the physical attributes of the product. These include for example the ability of women to use and understand the product, the physical fit of the product, and the comfort of the product. The second requirement for clinical data concern the safety of the material used in the device for its intended purpose and safety of its intended use. Finally, clinical data has been gathered to support the clinical performance of the product as a cervical cup to be able to influence the chances of conception favourably.

The sections below will list the clinical data evaluated and the conclusions will highlight the way in which these data support the FERTI·LILY clinical performance.

4.2. Usability

The usability of the FERTI·LILY cup is supported by a myriad of usability data from existing vaginal devices and is substantiated by usability studies carried out with the FERTI·LILY Conception Cup. Most of the products listed here are devices for the collection of menstrual blood (Menstrual Cups). Several different designs and dimensions of menstrual cups have been placed on the market in recent years and there is significant data available regarding the use, usability, comfort, and safety of these products.

Menstrual cups come in many sizes and made of various types of materials. Most menstrual cups are made of medical grade silicone and have a diameter of 40-47mm. One of the most well-known and frequently used cup is the DivaCup®. The Diva Cup is available in size one and 2 having the sizes 43mm and 46mm available[20]. This cup has been tested extensively in comparison with Tampons in a study including 94 women using the products. In this study the DivaCup was preferred to use of Tampons and 91% of the women using the DivaCup would continue using the product[21]. This result was supported in various other studies showing acceptability of menstrual cups. Even menstrual cups such as the SoftCup,

[20] https://menstrualcupreviews.net/comparison/?diameter=ASC
[21] Howard, Courtney et al. FLOW (finding Lasting Options for Women): Multicentre Randomized Controlled Trial Comparing Tampons with Menstrual Cups. *Canadian Family Physician* 57.6 (2011): e208-e215.

which have a significantly higher diameter (70mm), and are made of the tougher proprietary material, find high acceptability and comfort among users[22].

The FERTI·LILY Conception Cup has been designed to be equivalent to menstrual cups in all ways except for indication of use. The FERTI·LILY Conception Cup is made of a Medical Silicone with a shore-30 elasticity, similar to many marketed Menstrual cups. It has a diameter of 40mm. The diameter has been chosen to remain towards the lower end of menstrual cups as leakage is not a significant worry when using this product in comparison to menstrual cups. Furthermore, the anatomical data available show that 40mm will remain near the cervical OS even for women with a wider flexure without creating discomfort among women with a narrower fornix, as shown by the studies on various menstrual cups[23]. Other differences in the design of the FLCC is that the cup is smaller as the volume presented to the cervix is lower than that needed to collect menstrual flow. This also allows flipping back for the cup for easier insertion and allows the shape of the cup to fit snuggly against the cervix to present the sperm. The FLCC also has an elongated tail to allow easy removal.

The final product was tested by a user group according to its intended use and within the home setting. This study was overseen by marketing research company MWM2. 13 couples received the FERTI·LILY Conception Cup with minimal instructions and were asked to use it. The ladies using the product all practiced with the cup (as instructed in the IFU) and then used the cup after intercourse in order to transport the ejaculate close to the cervix[24]. The purpose of this study was to support the usability of the product and the adequacy of the IFU as well as any unforeseen adverse events or risks to the user. This study showed that 85% of consumers found the current cup easy to use to move the ejaculate towards the cervix after intercourse. **92% of users found no significant negative impact on the intimacy of conceiving by using the cup**. Only 1 user found it difficult to manipulate the cup and also found it uncomfortable.

The results above show that the product adequate for consumer use in its current form with its current IFU. While more practice with the product will surely increase the ease of use and comfort, the current design is sufficiently usable to warrant successful use and to allow couples to continue using the product.

4.3. Clinical Safety

Intravaginal silicone devices have been used for numerous applications. As highlighted in the previous section, medical silicone is being used at a large scale for menstrual cups. These are classified in the EU as “hygiene products”, but in the USA they are registered as Medical Devices. As such, these devices have been tested according to the ISO 10993 biocompatibility norms and fall under the scrutiny of post-market surveillance as medical devices.

In the European union, other comparable intravaginal medical silicone products are currently being used as medical devices. Examples of these products include

[22] North, Barbara B., and Michael J. Oldham. Preclinical, Clinical, and Over-the-Counter Postmarketing Experience with a New Vaginal Cup: Menstrual Collection. *Journal of Women's Health* 20.2 (2011): 303–311. *PMC*. Web. 13 June 2018.
[23] Bernhart, KT. Et al. Baseline dimensions of the human vagina. Human Reproduction Vol.21, No.6 pp. 1618–1622, 2006 doi:10.1093/humrep/del022 Advance Access publication February 14, 2006.
[24] 6.1.8.5 Usability validation report FERTI·LILY Conception Cup. Internal Document

diaphragms (anti-conception pessaries), pessaries for incontinence and prolapse. These indications are all relatively long-term indications and often require long-term use of the product. Most intravaginal pessaries are currently manufactured from medical grade silicone because the material is flexible, pliable, long-lasting, non-absorbent, biologically inert, non-allergenic, non-carcinogenic, washable and can generally be sterilized using boiling water[25].

The material used for the FERTI·LILY Conception Cup has been used extensively for comparable indications. Both menstrual cups and pessaries have longer term applications than the FERTI·LILY and are made of Medical grade silicone. The medical silicone used in FERTI·LILY has safety data supplied specifically for this material which is further discussed in the Biological Safety Evaluation (DHF 5.1.8.).

During the usability study and the PMCF (see section 4.4) of the FERTI·LILY Conception Cup no unexpected adverse events or risks were uncovered. While some ladies feel a light cramping during first use (as is also common when using a menstrual cup), these cramps did not manifest during subsequent uses or during use after intercourse[26].

Women using the FLCC are able to place the ejaculate in proximity of the cervix (only 8% did not manage to do so on the first try). The study also shows that there was **minimal impact on the intimacy of conceiving** (only 8% noted a negative impact on intimacy). The majority of users found the device comfortable to insert, wear and remove and would recommend it to other couples trying to conceive.

Post Market Questionnaire

An extensive Post Market Clinical Follow-up questionnaire has also been initiated and finalised in 2020. More than 2000 customers of FERTI·LILY were asked to share their experience of using FERTI·LILY and roughly 10% of those approached were happy to share their thoughts, showing a good brand engagement.

205 consumers entered the questionnaire, sharing their experience with the FERTI·LILY Conception Cup. The results of the questionnaire show that the **FERTI·LILY Conception Cup is easy to use** (86.34%) and **comfortable to use (87.80%).** Users of the cup were in general very satisfied with the product (88.78%), giving an average of 4.4 out of 5 stars, and would in general recommend it to others (81.95%). 47.32% of those filling in the questionnaire managed to conceive since purchasing the FLCC, of which 89.58% were using the FLCC in the cycle of conception.

Rooms for improvement identified related to the ease of flipping the cup back after insertion and confusion about liquid still remaining in the cup after use. Some adverse events reported by customers using the cup include mild cramping and mild pain, and light irritations after use. There were no unexpected adverse events reported.

The full results of the questionnaire can be found in the PMS data.

The FCC is a safe, comfortable, and easy to use medical device.

[25] Atnip, S., & O'Dell, K. Vaginal support pessaries: Indications for use and fitting strategies. Urologic Nursing, 2012, 32(3), 114-125.
[26] 6.1.8.5 Usability validation report FERTI·LILY Conception Cup. Internal Document

4.4. Clinical Performance

4.4.1. Post Market Clinical Follow-up

A post market clinical follow up study was also conducted to evaluate the safety and performance of the cup. The aim of the PMCF study was to evaluate the safety, efficacy, and user feasibility of the FLCC. 85 female volunteers trying to conceive entered the study using the FLCC and were followed-up for maximally 3 months or until pregnancy was established. The pregnancy rate observed in the study was compared to the pregnancy expectation based on 2 prognostic models to determine its efficacy. The prognostic models by Suzou and Hunault, previously discussed in section 3.3 of this evaluation of clinical data were used for the basis of this prediction.

Through questionnaires, information about safety, pregnancy, and user feasibility was collected. Of the 85 study participants, 65 used the product as instructed throughout the study. No Adverse Events (AEs) were reported. The current study demonstrates that **35.4% of the women using the medical device during every menstrual cycle were pregnant after 3 months, which is significantly more than the 23.9% pregnancy prediction rate in such general population ($p < 0.05$)**. The FLCC thus **increases the likelihood of pregnancy with 48%, or by 1.5x** when used as instructed. **Results obtained for a subpopulation that has been trying to conceive for at least 1 year were even more pronounced.** In this infertile population the calculated pregnancy probability of 8.3% in the total study population and 9.4% in the population that completed the study according to protocol, was statistically significant outweighed by the observed pregnancy rates of 23.3% and 30.3%, respectively ($p < 0.05$). In other words, use of the FLCC in the infertile subpopulation increased the pregnancy efficacy with 180% to 222%. These results show that more pregnancies were observed in the 3 months observation window than expected, showing that couples using the FLCC according to the intended use **conceive faster** than would be expected. It shall be noted that in implementing the Hunault model for the purpose of this analysis, Dr. Jan Willem van Steeg, also known for his validation of the Hunault model, was consulted and found the use of the model fit for purpose as used.

User of the FLCC is even progressing toward pregnancy rates induced by IUI as demonstrated by a retrospective study where this technique results in 39% clinical pregnancies in couples with unexplained infertility[27].

Overall, the use of the FLCC was indicated as easy and comfortable while no device-related AEs were reported throughout the study, indicating that the device can be safely used.

Apart from the demonstrated clinical benefits, there are equally important emotional advantages associated with the use of the FCC device. This class I medical device consists of 100% soft and flexible medical silicone that are easy to use to limit disruptions of the natural conceiving process as much as possible, while avoiding additional distress. Thanks to its design, the FCC is significantly less

[27] Michau A, El Hachem H, Galey J, Le Parco S, Perdigao S, Guthauser B, et al. Predictive factors for pregnancy after controlled ovarian stimulation and intrauterine insemination: A retrospective analysis of 4146 cycles. J Gynecol Obstet Hum Reprod 2019;48:811–5. https://doi.org/10.1016/j.jogoh.2019.05.006.

invasive, does not include rigid applicators or complicated procedures, and carries lower residual risks than other products available with the same purpose. In addition, the FLCC is used in the comfort of a couple's home without the need of specialized support, allowing women to urinate, shower, or walk around while avoiding seminal backflow after intercourse. The low study drop-out rate and high recommendation rate to other couples trying to conceive supports a high user's satisfaction.

The FLCC is a safe, comfortable, and easy to use medical device that significantly increases pregnancy rates, even in couples with fertility issues.

4.4.2. Equivalence

Cervical Caps and Cervical Cups have been used for the enhancement and support of fertility. The primary purpose for these cups is to physically place the ejaculate as close as possible to the Cervical Os in order to maximise the chance of the semen to swim through the cervical mucus into the uterus. Once near the Cervical Os the cervical cup also protects the semen from the harsh environment of the vagina, assuring maximum survival of the spermatozoa. It has been shown in various clinical studies that the proximity of the spermatozoa to the cervix and protection of the spermatozoa from the vaginal environment results in an increase of spermatozoa reaching into the cervical mucus28.

It has furthermore been established in-vitro that an increased penetration of spermatozoa in the cervical mucus is associated with a beneficial effect on the chances of conception. This was noted when the increase in pregnancy rates were linked to higher cervical mucus penetration29. These findings were further validated by Eggert-Kruse et al who found that couples with a high Sperm-Cervical Mucus penetration had a significantly higher chance of conceiving after 6 months than couples with a low penetration rate (29.1% vs. 2.3%). Eggert-Kruse notes that "Even in couples with normal sperm quality of the male, markedly more pregnancies were achieved when penetration of [the cervical mucus] was good30.

Two medical devices have been identified as currently available on the market for the facilitation of Fertility. The Stork OTC, a fertility kit including a condom/receptacle, a cervical cup, and an applicator to insert the cup; and the conceivex conception kit, a kit of several (3) condoms and cervical cups which can be used for 3 months.

4.4.3. Stork OTC

The Stork OTC is a device used to collect the semen in a cervical cup that is attached to the end of a rigid applicator. The semen is collected via a special silicone condom containing a cervical cup that covers the penis during intercourse. The cervical cup including the ejaculate is removed from the condom after ejaculation and clamped into the applicator. The applicator is then inserted vaginally and placed near the cervix. The applicator has a function to release the cervical cup and be removed from the vagina subsequently. The cervical cup stays in place for 4-6 hours. The cervical cup can then be removed with a string that is protruding from the vagina.

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[28] Whitelaw, JW. The cervical cap self-applied in the treatment of severe oligospermia. *Fertility and sterility*, 1979, 31(1), 86-87.
[29] Alexander, NJ. Evaluation of male infertility with an in vitro cervical mucus penetration test. *Fertility and Sterility*. 1981, 36(2), 201-209
[30] Eggert-Kruse, W. et al. Prognostic value of in vitro sperm penetration into hormonally standardized human cervical mucus. *Fertility and Sterility.* 1989, 51(2) 317 - 314

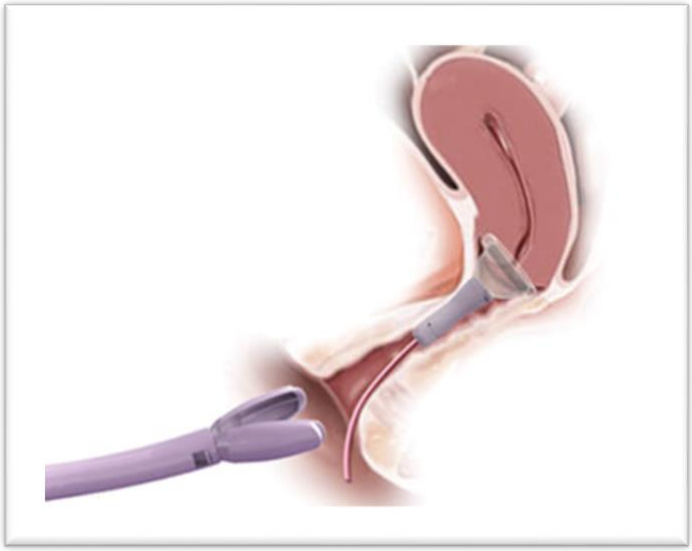

Figure 5: Diagram showing release of the Stork OTC Cervical Cup

Use of the Stork OTC device has been shown to increase the number of sperm cells present in the cervical mucus by 323%[31]. This substantial increase in the seminal load within the cervical mucus increases the number of sperm cells that can swim through into the uterus and, thereby, can help improve the chances of conception.

The use of a cervical cup or cap can prevent semen flowing back into the vagina and can reduce prolonged exposure of spermatozoa to the vaginal environment, reducing the risk of sperm loss[32]. Cervical cups ensure to prolong exposure to the cervical mucus which has been shown to increase the number of spermatozoa that swim into the cervical mucus. While these chances are comparable with the probabilities of pregnancy shown in methods such as In-Uterine Insemination, the use of a Cervical cup is much less invasive and can be done in the privacy of one's home[33].

4.4.4. The Conceivex Conception Kit

The Conceivex Conception Kit has a silicone condom/semen collector that collects the ejaculate during intercourse. The ejaculate is then manually transferred from the semen collector to the cervical cap. The cervical cap is then inserted vaginally and positioned at the cervix for 4-6 hours. The kit also contains sperm friendly lubricant as well as a number of ovulation tests and pregnancy tests.

[31] Pelekanos, MJ. Postcoital Sperm Assessment Comparative Study. *Surgical Technology International*, XXVII, December 2015.
[32] Flierman, Hendrikus, et al. A Prospective, randomized, cross-over comparison of two methods of artificial insemination by donor on the incidence of conception: Intracervical insemination by straw versus cervical cap, Human Reproduction, Vol. 12, no.9 1945-1948, 1997
[33] Corsono SL, Batzar FR, Otis C, Fee D. The cervical cap for home artificial insemination. J. Reprod. Med., 1986, May; 31 (5): 349-52

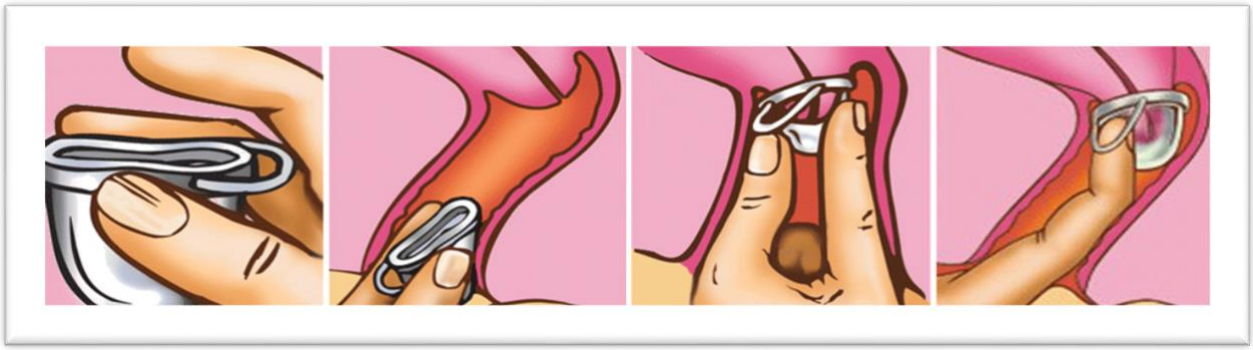

Figure 6: Diagram showing how to insert the conceivex conception kit

4.4.5. Equivalence with the Cup

The FERTI·LILY Conception Cup has been designed to function like the cervical cups already on the market while focussing on the comfort of use. The cup has been developed to minimise invasiveness during use. As such, the product is inserted after regular intercourse and there is no need for use of a condom or a receptacle. The FERTI·LILY Conception Cup is simply inserted after intercourse and pushes the ejaculate towards the cervix. The material used in the FERTI·LILY Conception Cup is soft silicone to allow comfortable wear and allow the user to continue her regular routine after inserting it (including urinating, showering, etc) but also to allow the highest chance of the female partner to climax before or after inserting the device.

The FERTI·LILY Conception Cup is furthermore not specifically indicated for couples with known fertility issues. It is a minimally invasive aid to help primarily in the comfort of conceiving. In this capacity the FERTI·LILY Conception Cup is inserted after natural intercourse and remains in place for up to 20 minutes in order to assure that as much ejaculate as possible has reached the cervix for as long as possible. In this manner the FERTI·LILY Conception Cup increases the amount of semen reaching the cervix and reduces the amount of exposure of the semen to the harsh vaginal environment. The FERTI·LILY Conception Cup will help to avoid semen from flowing out of the vagina during urination or getting up. The FERTI·LILY Conception Cup will also protect the semen at the site of the cervical Os.

FERTI·LILY is a conception aid that focusses on the Human body's abilities. While making use of the advantages shown by other cervical caps and cups, FERTI·LILY allows for the natural course of conceiving. There may be importance of the male ejaculation to deposit the semen near the cervical Os and allowing the semen to swim into the cervical mucus directly after ejaculation. Motile living sperm have been measured in the fallopian tubes within minutes after intercourse[34]. This shows that sperm deposit and motility through the cervix and the uterus happens very quickly and may be impaired by manipulating the sperm unnecessarily by using condoms and depositing the sperm in a receptacle. For this reason, the FERTI·LILY is designed to be inserted after natural intercourse so as not to interfere with the plausibly advantageous mechanics of natural copulation. For example, the male ejaculation deposits the sperm close to the cervix and allows them to swim naturally into the cervical mucus very quickly. The FERTI·LILY Conception Cup allows the natural course of conception to take place, and helps to increase the chances by pushing as much semen as possible towards the cervix and allows it to remain there for longer times.

[34] S.S. Suarez, A. A. Pacey; Sperm transport in the female reproductive tract, *Human Reproduction Update*, Volume 12, Issue 1, 1 January 2006, Pages 23–37

4.5. Conclusion

The FCC is a safe, comfortable, and easy to use medical device that significantly increases pregnancy rates, even in couples with fertility issues. Clinical data collected shows that the FERTI·LILY Conception cup significantly increases the chances of conception without adding any significant risk.

The FERTI·LILY Conception Cup can furthermore be considered as equivalent in terms of its biological, technical, and clinical characteristics to existing technologies with an established safety and performance profile.

4.5.1. Biological Equivalence:

The FERTI·LILY Conception Cup is made of the same material as other cervical caps/cups. Furthermore, this material has been used in pessaries and other medical devices as well as in Menstruation cups.

4.5.2. Technical Equivalence:

The technical characteristics of the FERTI·LILY Conception Cup are equivalent to products already on the market such as menstruation cups. It has been designed to be inserted and removed in the same manner as menstruation cups, while it has the internal volume and general shape as other cervical caps used for conceiving. While the StorkOTC prevents any contact of the ejaculate with the vagina, depositing the ejaculate directly at the cervix, the Conceivex Conception kit works in a similar fashion as the FERTI·LILY Conception Cup in that it pushes the sperm towards the cervix in an open cup, thereby allowing contact with vaginal fluids.

4.5.3. Clinical Equivalence:

The FERTI·LILY Conception Cup is clinically equivalent to other cervical caps/cups used to enhance fertility. The FERTI·LILY Conception Cup is used during the same time in the cycle, inserted vaginally, and comes in contact with the same bodily fluids and mucus membranes as other cervical caps. The product is also used to physically push the ejaculate close to the cervical Os. Approval has been requested and received from the manufacturer of the StorkOTC, Rinovum, to use the clinical data received from them.

4.5.4. Differences:

The FERTI·LILY differs from other cervical cups in that it is manually inserted in a different manner than the existing cervical cups. On the other hand, the manual insertion of this type of silicone cup has been supported by use of menstrual cups with equivalent dimension. Furthermore, the usability of the FERTI·LILY has been substantiated in a dedicated usability study showing satisfactory ease of use. The FERTI·LILY is also different from existing cervical cups/caps in that it allows seminal deposit within the vagina and moves the entire fluid up the vaginal canal towards the cervix. This differs from the OTC Stork which allows no contact with the vaginal canal (while reasonably there will be vaginal mucus present even at the site of the cervix where the cervical cap is deposited). It differs more slightly from the Conceivex Conception Kit in that, while the semen is deposited directly into the

cervical cap, while the insertion of the cap will allow vaginal mucus to mix with the ejaculate during insertion.

Due to these differences, while the cup will be indicated for the facilitation of fertility, direct claims of equivalence to the Stork OTC claims as to the amount of increase seminal deposit in the cervical mucus (323%) shall not apply, while it is substantiated the use of the FERTI·LILY will, like the Conceivex Conception Kit, increase the number of spermatozoa deposited in the cervical mucus.

Studies carried out with the FLCC device have to beeen carried out in vivo to substantiate its performance in increasing the chances of conception (Section 4.4.1).

4.6. Biological Safety:

Based on the composition of the materials contacting the body during use as well as their safety data, low risk of leachables, mode of action, performance and safety data it can be concluded that the biological and performance safety risk of the FERTI·LILY Conception Cup device for its intended use and application are low and thereby acceptable.

While further testing shall help to solidify the safety profile of the product, and future evaluations may help to further reduce the risks as far as possible, current residual risks are acceptable. The level of residual risks is estimated to be lower or equal when compared to equivalent products and are thereby deemed acceptable. Information on the residual risks is provided in the information to the user.

5. Analysis of the Clinical Data

The goal of the section below is to determine if the evaluated clinical data sets demonstrate compliance with the essential requirements for the clinical performance and clinical safety of the medical device when used as intended.

5.1. Requirement on the Safety (MDR GR1)

The FERTI·LILY product has been manufactured with medical grade materials that are safe to be in long term contact with vaginal mucus membrane. The biological safety evaluation furthermore concludes that the product has an acceptable biological safety hazard.

The FERTI·LILY Conception Cup product has been designed in a way that is as safe as possible, and at least as safe as the alternative, comparable treatments available to patients. This has been further supported by usability and clinical data.

5.2. Requirement on Acceptable benefit/risk (MDR GR2)

FERTI·LILY Conception Cup has several benefits to its users. The product allows its users to use a fertility aid within the comfort of their home and without interfering with natural intercourse. The product is furthermore designed in a discreet and comfortable manner and is made to be as non-invasive as possible with respect to the body, and the couple's wish to conceive.

There are no conceivable risks involved with the intended use of the FERTI·LILY Conception Cup while the physical and psychological benefit to using this product

can be significant. The benefits include clinical benefits, such as increasing the chances of survival of semen and increasing the amount of semen entering the cervical mucus as well as physical benefits, such as allowing women to urinate or shower after intercourse while avoiding seminal backflow. The clinical data shows a statistically significant effect on pregnancy outcome when using the FLCC. The benefits compared to other available devices are focussed mainly around comfort and minimising the invasiveness.

The likelihood of a clinical benefit to the patient hereby outweighs the minimal risks associated with use of the product. This has been further supported by post market data and clinical data.

5.3. Requirement on Risk Management (MDR GR3)

A risk assessment has been carried out and after risk controlling measures the residual risk associated to the manufacture and use of this product is low. After evaluating the severity and occurrence of the residual risks it is concluded that the overall residual risk level is acceptable. The likelihood of a clinical benefit to the patient hereby outweighs the minimal risks associated with use of the product.

As manufacturer of the finished Medical Device in the sense of the MDR 2017/745/EC Rosesta Medical concludes that, after implementation of mentioned control measures, the FERTI·LILY Conception Cup product is safe and effective in both manufacturing as well as the medical intended use of the product.

5.4. Requirement on performance (MDR GR6)

The literature with respect to the performance claims of the FERTI·LILY Conception Cup product shall be evaluated below in order to determine if these claims can be proven and if the intended purpose of the product can be fulfilled.

The primary claim of the FERTI·LILY Conception Cup product is that the FERTI·LILY is a Medical Device to assist in the chances of getting pregnant (conceiving).

FERTI·LILY Conception Cup helps to increase these chances by providing a device that allows the user to physically move the seminal load closer to the cervix. The device furthermore helps to keep the seminal load at the cervix for an extended period of time while allowing the user to carry on with her life. During this time the FERTI·LILY furthermore protects the seminal load from the harsh vaginal environment. The ability of the FERTI·LILY Conception Cup to carry out these functions have been evaluated in usability studies[35].

The added benefit of cervical caps/cups during conception has been shown in numerous studies. The performance of the FLCC has been established in a clinical study showing statistically significant improvement in the chances of conception when used as intended. Furthermore, the use of medical silicone cups has been established in the use as cervical cups as well as menstruation cups. Finally, the secondary effects of the FERTI·LILY cup, including comfort allowing orgasm, retaining more seminal fluid etc. have been shown to positively affect chances of conception.

[35] 6.1.8.5 Usability validation report FERTI·LILY Conception Cup. Internal Document

This product provides patients with a comfortable and discreet manner to help conceiving at home. It is more practical and comfortable than other products currently available while adding the same benefit.

It has been shown in packaging integrity testing, mechanical performance testing, and clinically supported, that the FLCC is able to perform as intended and is packaged and maintained in such a way as to maintain this performance and safety.

5.5. Requirement on acceptability of side-effects (MDR GR8)

As previously discussed, the benefits of using FERTI·LILY Conception Cup outweigh the risks associated with its use. The medical silicone of which the FERTI·LILY cup is manufactured is tested and known to have a favourable safety profile. Some mild side-effects are expected such as irritation through friction and light cramping due to insertion, but these outweigh the benefit.

Post market data shall continue to be assessed after the continued marketing of this product to monitor side-effects which are not accounted for previously or in the risk assessment. The acceptability of these side-effects shall then be assessed, and the risk/benefit analysis will continue to be updated.

6. Conclusion

Based on the literature data and the clinical data available it can be concluded that the FERTI·LILY Conception Cup product is safe and performs as claimed when used and applied as intended and that the claims presented in the instructions for use are consistent with the outcomes of the provided data.

The clinical study provided evidence of the establishment of the following performance, safety and usability claims:

- Transports the ejaculate towards the cervix/Delivers more sperm to the cervix.
- Helps to increase the number of spermatozoa deposited in the cervical mucus.
- Increases the chances of conception by 48%
- 1.5x higher chances of conception
- Helps to conceive at home
- Supports/helps natural conception
- Helps to conceive faster; get pregnant quicker
- Clinically Proven
- Protects semen from the harsh environment of the vagina.
- Comfortable and easy to insert, wear, and remove.
- Intended to be inserted after intercourse.
- No negative impact on intimacy
- No need for uncomfortable condoms and applicators.
- 100% Medical Grade, sperm friendly Silicone.
- Re-usable for up to 6 cycles/months

After evaluating the severity and occurrence of residual risks in the risk assessment, it has been concluded that the overall level of risk associated with the use of FERTI·LILY Conception Cup is low and acceptable.

Taking into consideration the intended use, application, and indication of the FERTI·LILY Conception Cup product, Rosesta Medical concludes that for all listed

claims the clinical safety and performance data demonstrate conformity with the General safety and performance requirements of Annex 1, MDR 2017/745/EC.

It has been concluded that no clinical investigation or post market clinical follow up is required at this time. A post market clinical follow-up study has been carried out in December of 2018 to test the usability of the FERTI·LILY with favourable results. Furthermore, comprehensive PMCF study has been carried out in 2019 and 2020 which clearly supports the safety and performance of the FERTI·LILY Conception Cup.

An extensive Post Market Clinical Follow-up questionnaire has also been initiated and finalised in 2020. The results of the questionnaire show that the FERTI·LILY Conception Cup is easy to use and comfortable to use.

It shall continue to be of importance to collect post market data for this device. As the clinical performance has been sufficiently supported, the main focus for PMS data should be to gather customer complaints in order to assess the if there are any unforeseen risks associated with use of the product in an at-home setting. This data should be analysed at regular intervals and become part of this clinical evaluation as well as the risk assessment.