HORMONAL IUD

101

METHOD CHARACTERISTICS
QUALITY-ASSURED PRODUCTS
PROCUREMENT CONSIDERATIONS

Agenda

13:00-13:05	**Welcome & Logistics**	Andrée Sosler, FHI 360
13:05-13:12	**Introductory Remarks & Overview of Early Scale-Up Efforts**	Megan Gomes, USAID
13:12-13:20	**Hormonal IUD Characteristics & Key Research Findings**	Dr. Gathari Ndirangu Gichuhi, Jhpiego
13:20-13:50	**Product Roundtable** • Mirena® - Bayer AG • Avibela® - Medicines360 + IMPACT RH360 • LNG IUS – ICA Foundation	Kai Risse & Thomas Faustmann, Bayer Jill Keesbury, Medicines360 Jim Sailer, Population Council
13:50-14:10	**Global Procurement Considerations** • USAID Procurement – GHSC-PSM • UNFPA Procurement	Morgan Simon, GHSC-PSM Stephen Mawa, UNFPA
14:10-14:25	**Q&A**	**Moderator**: Andrée Sosler, FHI 360
14:25-14:30	**Closing Remarks**	Mark Barone, Bill & Melinda Gates Foundation

Introductory Remarks & Overview of Early Scale-Up Efforts

Megan Gomes
-
USAID

Hormonal IUD Access Group Structure & Goals

Steering Committee
Purpose: Develop, monitor and implement global strategy to expand access to hormonal IUD and strengthen hormonal IUD market; identify and mitigate risks in market health; maintain relationships with suppliers; review demand forecasts.

Operations Group	Partners Exchange
Purpose: Forum that supports monitoring of market health, development of communications, identifying and tracking country needs.	**Purpose:** Technical working group to discuss/share lessons learned related to rollout; address country rollout issues; share information to support steering committee

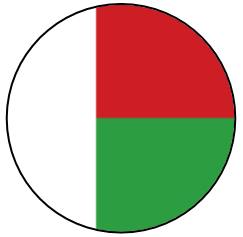
Governments
Donors
Researchers
Suppliers
Procurers
Implementers

Steps Towards **Scale-Up**

- In 2015, a **global learning agenda** for the hormonal intrauterine device (IUD) was developed with priority research questions regarding use of the method in low- and middle-income countries.
- Hormonal IUD Access Group members committed to harmonizing data collection approaches. The same learning agenda questions were ultimately used in **pilot settings** in:

Kenya

Madagascar



Nigeria

Zambia

What we've Learned from Pilot Introductions

In a review of pilot introductions in sub-Saharan Africa, we found:

- **Continuation and satisfaction were high** among hormonal IUD users in pilot settings and generally comparable to those of other long-acting reversible contraceptives.[1]
- Hormonal IUD users reported **positive attributes of the method** including its effectiveness, long duration, convenience, potential for reduced bleeding, and fewer side effects compared to other hormonal methods.[1]
- **Coordination across diverse organizations**, including alignment on a shared learning agenda and access strategy, ultimately contributed to expanded access to the method.[2]

Why this method and why right now?

- With similarities to the copper IUD , the hormonal IUD is a **highly effective, long-acting, reversible** contraceptive with important non-contraceptive health benefits (treatment for menorrhagia, uterine fibroids, and anemia).[2]
- The method was first introduced in Europe in 1990 and in the United States in 2000, and it has been popular in these settings. The method has **not been widely available** in LMICs to date.[2]
- In 2021, the hormonal IUD was **added for the first time** to the United States Agency for International Development (USAID) and United Nations Population Fund (UNFPA) product catalogs.[3]

Section References

1. Danna, K., et al. (2022). Introducing the hormonal Intrauterine Device in Madagascar, Nigeria, and Zambia: results from a pilot study. *Reproductive Health*, 19(1). https://doi.org/10.1186/s12978-021-01300-x
2. Rademacher, K., et al. (2022). What Have We Learned? Implementation of a Shared Learning Agenda and Access Strategy for the Hormonal Intrauterine Device. Global Health, Science and Practice, 10(5), e2100789. https://doi.org/10.9745/ghsp-d-21-00789
3. FHI 360. (2021, July 17). Hormonal IUD added to product catalogs, access expands globally. https://www.fhi360.org/news/hormonal-iud-added-product-catalogs-access-expands-globally

Method History & Key Characteristics

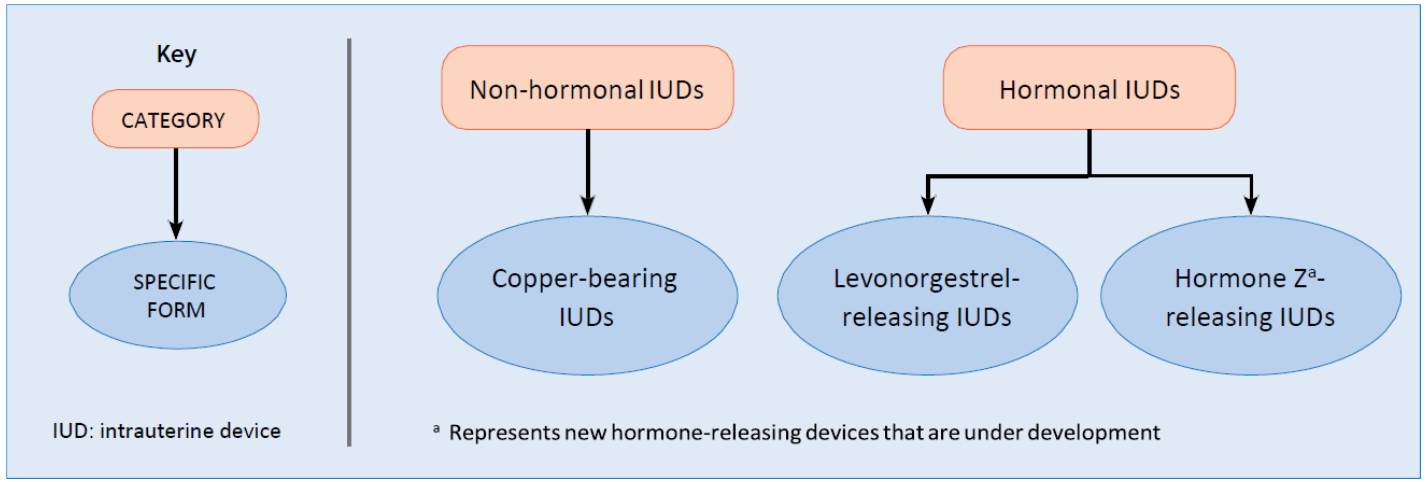
Dr. Gathari Ndirangu Gichuhi
-
Jhpiego

Method Nomenclature

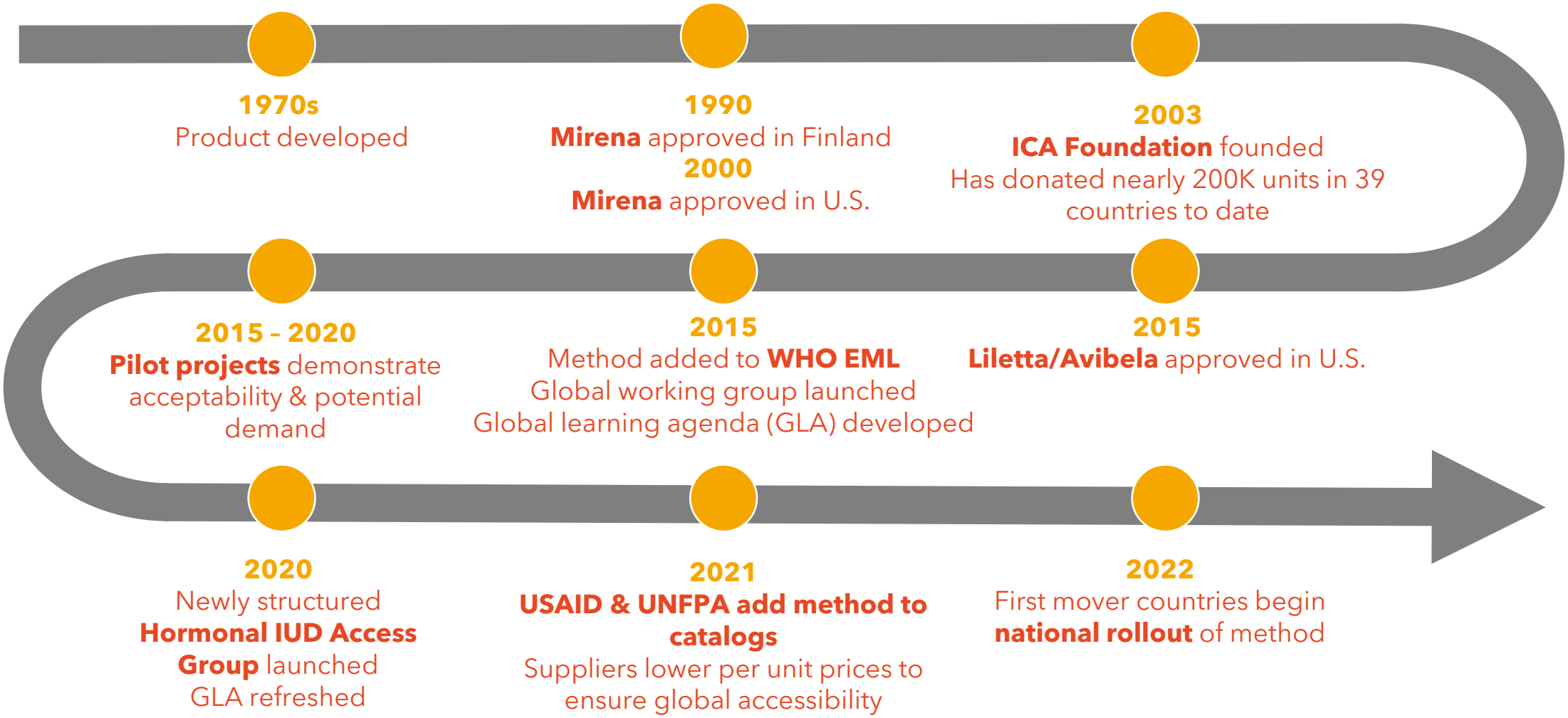
The hormonal intrauterine device (IUD) is sometimes also called:

- Levonorgestrel-releasing intrauterine system (LNG IUS)
- Hormonal IUS
- LNG IUD

The WHO has selected "**hormonal IUD**" as its recommended standard nomenclature, to accommodate all current products and hormone-releasing IUDs under development.[1]

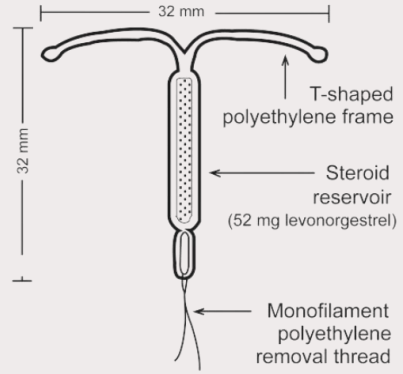


There has been a **30+ year gap** between initial approval of the hormonal IUD and widespread availability in LMICs



What is the **hormonal IUD?**

A highly effective long-acting reversible contraceptive (LARC) with non-contraceptive benefits[2]

Looks Like:	Works By:	Provides:
 Plastic T-frame with 52 mg* of **levonorgestrel**	• Thickening cervical mucus • Inhibiting sperm movement & survival	• **99%** contraceptive efficacy • Potential treatment for heavy menstrual bleeding

Possible side effects include:

Changes in Periods

Cramping During & Right After Insertion

and less commonly

Headaches

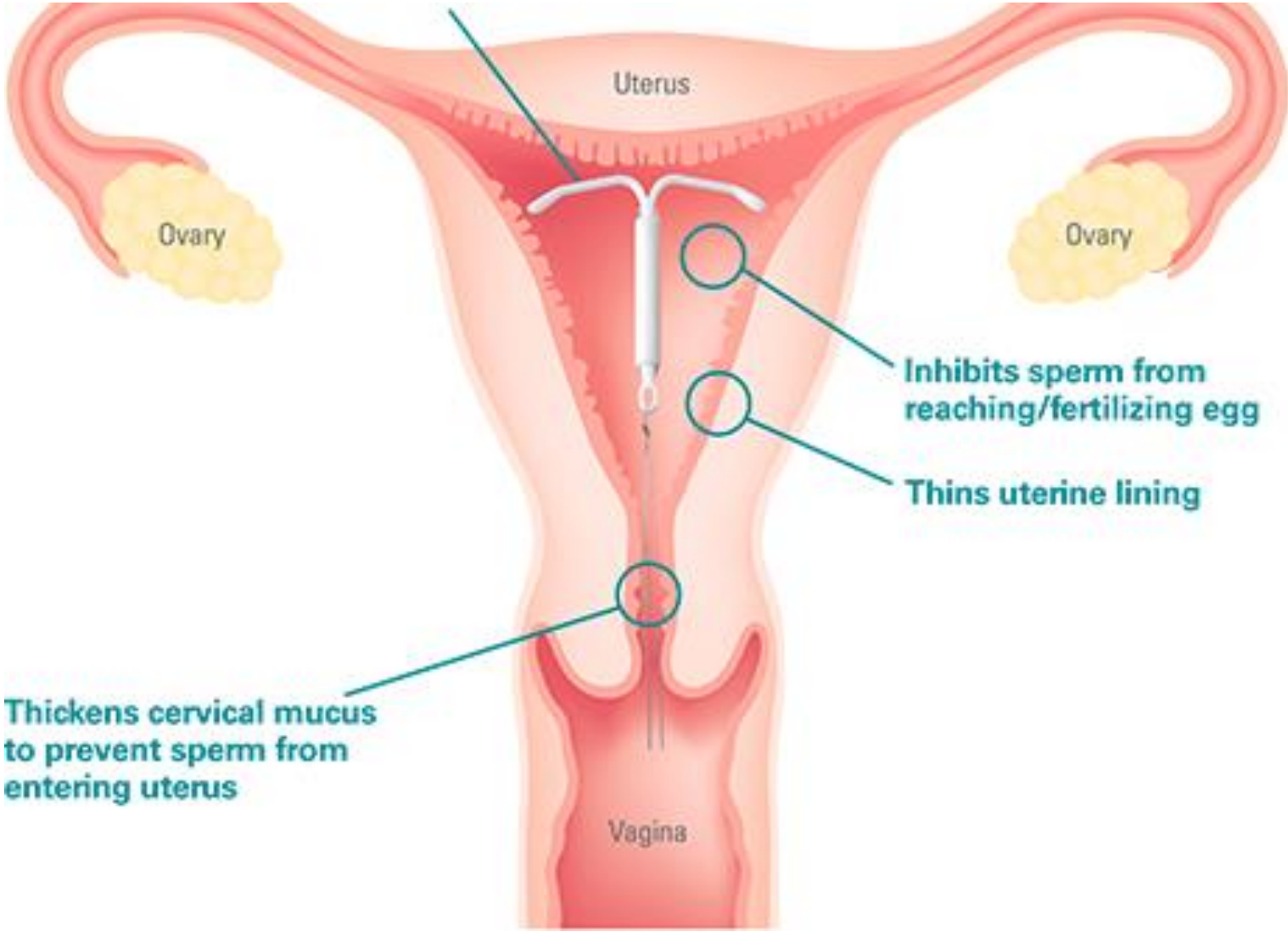
Breast Tenderness

Acne

*13.5 mg and 19.5 mg IUDs available in limited contexts

How does it **work**?

Local Contraceptive Effect [3,4]



Considering Method **Characteristics**[5]

Benefits

- Lasts 3-8 years but can be removed any time
- Doesn't require partner participation
- Return to fertility after removal is typically quick
- Can decrease:
  - Menstrual bleeding
  - Menstrual pain and symptoms associated with endometriosis
  - Risk of pelvic inflammation
  - Risk of endometrial cancer

Challenges

- Requires pelvic exam and insertion/removal by a medical provider
  - Pain management during and after insertion may be needed
- Globally less well known than other LARCs, leading to myths and misconceptions
- Can contribute to unpredictable periods. Amenorrhea may be undesirable to users
- Does not provide protection against STIs

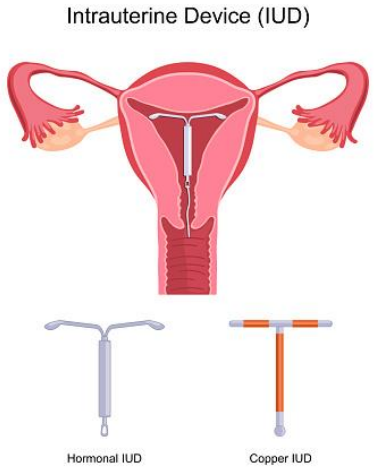
Medical Eligibility

All Women

- Any age, including adolescents and women over 40 years old
- Have or have not had children
- Married or unmarried
- Postpartum (within 48 hours or after 4-6 weeks, breastfeeding or not)
- Have just had an abortion or miscarriage (if no evidence of infection)
- Employed in a highly physical job
- Have previously had an ectopic pregnancy
- Have previously had PID or vaginal infections
- Have anemia
- Have HIV (stages 1 or 2 at initiation), with or without ART
    - Continuation for all stages

Emergency Contraception

Non-inferior to copper IUD for emergency contraception if inserted within 5 days of unprotected sex[6]



Key Learnings in Pilot Settings[7]

Madagascar, Nigeria, Kenya, Zambia

User Demographics

Majority of users were:

- Married with children
- Older than 25 years

In Madagascar and Kenya, large minority of users (30-41%) were younger than 25

Method Switching

- **5%-23%** of adopters were new FP users
- Majority of previous FP users had used a **short-acting method** prior to hormonal IUD

Cost-Effectiveness

Over a 10-year period, the hormonal IUD is **more cost-effective** than implants, but **less cost-effective** than the copper IUD

Non-Contraceptive Attributes

Most users who experienced reduced bleeding and/or amenorrhea reported that it had a **positive impact** on their lives

Continuation

81-95% of users continued to use the method at 12 months

Satisfaction

- **80-98%** of users were satisfied or very satisfied with method use
- **Users liked**: effectiveness, duration, convenience, side effect profile

Section References

1. World Health Organization. (2021). *WHO statement on levonorgestrel-releasing intrauterine device nomenclature*. World Health Organization. https://apps.who.int/iris/handle/10665/340378.
2. ICA Foundation. (2008). *Levonorgestrel Intrauterine System (LNG IUS) Patient Information Sheet* [Leaflet]. ICA Foundation. https://ica-foundation.org/wp-content/uploads/2020/03/LNG_IUS_Patient_Information_Sheet.pdf.
3. Attia, A., Ibrahim, M. A., & Abou-Setta, A. M. (2013). Role of the levonorgestrel intrauterine system in effective contraception. *Patient Preference and Adherence*, 777. https://doi.org/10.2147/ppa.s36948
4. Stanford, JB, & Mikolajczyk, RT. (2002). Mechanisms of action of intrauterine devices: Update and estimation of postfertilization effects. *American Journal of Obstetrics and Gynecology*, 187(6), 1699–1708. https://doi.org/10.1067/mob.2002.128091
5. Rademacher, K., et al. (2018). A Global Learning Agenda for the Levonorgestrel Intrauterine System (LNG IUS): Addressing Challenges and Opportunities to Increase Access. *Global Health, Science and Practice*, 6(4), 635–643. https://doi.org/10.9745/ghsp-d-18-00383
6. Turok, DK., et al. (2021). Levonorgestrel vs. Copper Intrauterine Devices for Emergency Contraception. *The New England Journal of Medicine*, 384(4), 335–344. https://doi.org/10.1056/nejmoa2022141
7. Rademacher, K., et al. (2022). What Have We Learned? Implementation of a Shared Learning Agenda and Access Strategy for the Hormonal Intrauterine Device. *Global Health, Science and Practice*, 10(5), e2100789. https://doi.org/10.9745/ghsp-d-21-00789

Quality-Assured Products

Bayer AG
-
Medicines360
-
ICA
Foundation

The products discussed today are *not* the only hormonal IUD products

Bayer H-IUD

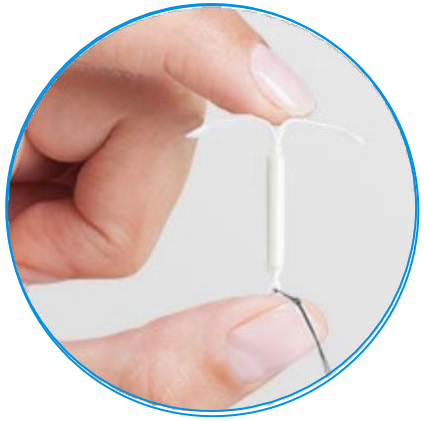
Hormonal IUD 101: Method Basics Mirena

Feb 24th 2023

Kai Risse
Th.Faustmann

Facts about Mirena®

- was first launched in 1990
- is available worldwide with marketing authorization in over 120 countries[1]
- has over 218 million women-years of experience[1]
- more than 6000 publications related to levonorgestrel-releasing intrauterine systems or levonorgestrel in over 20 different languages



Mirena® can offer a number of benefits making it a suitable choice at different stages of a woman's reproductive life

1. Mirena Periodic Safety Update Report 2022

Received: 29 October 2020 | Revised: 14 January 2021 | Accepted: 28 January 2021
DOI: 10.1111/aogs.14110

COMMENTARY

Thirty years of mirena: A story of innovation and change in women's healthcare

Kristina Gemzell-Danielsson[1] | Ali Kubba[2] | Cecilia Caetano[3] | Thomas Faustmann[4] | Eeva Lukkari-Lax[5] | Oskari Heikinheimo[6]

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[2]Guy's and St Thomas' NHS Foundation Trust, London, UK
[3]Bayer Consumer Care AG, Basel, Switzerland
[4]Bayer AG, Berlin, Germany
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Funding information
Bayer.

Abstract

Since its introduction in 1990, the levonorgestrel-releasing intrauterine system (LN
IUS) has played a key role in shaping the healthcare landscape of women. Here we e
plore the development of the first LNG-IUS (Mirena®) and the early clinical trials th
demonstrated its potential. We highlight the contraceptive and therapeutic benef
of Mirena®, and discuss how clinical practice has been changed since the introdu
tion of LNG-IUS and other long-acting reversible contraceptive methods. The histo
of Mirena® is rich in innovation and has also paved the way to the development
smaller intrauterine systems with lower hormone doses. Along with Mirena®, the
newer LNG-IUS contribute to improving contraceptive choices for women, allowi
them to select the option that is right for them and that meets their needs no matt
their age, parity or circumstances.

KEYWORDS
contraception, levonorgestrel-releasing intrauterine system, intrauterine device, women's health issues

1 | INTRODUCTION

Sexual and reproductive health constitute fundamental human rights and play a vital role in the empowerment of women and achievement of gender equality; ensuring universal access to sexual and reproductive health services is essential to achieving this goal.[1] Worldwide, around 40% of pregnancies are unintended,[2] with con-

as safe abortion services and post-abortion care, are importa
empower women, helping them to achieve their goals and ambit
avoid unwanted pregnancy and ensure any pregnancy occurs a
right time for them. The introduction of the first oral contrace
pill in 1960 sparked a movement to put women in control of
sexual and reproductive health through the use of effective mo
methods of contraception. Since then, as attitudes have shifted

Personal view

OPEN ACCESS

More than just contraception: the impact of the levonorgestrel-releasing intrauterine system on public health over 30 years

Kristina Gemzell-Danielsson,[1] Ali Kubba,[2] Cecilia Caetano,[3] Thomas Faustmann,[4] Eeva Lukkari-Lax,[5] Oskari Heikinheimo [6]

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ABSTRACT

Universal access to sexual and reproductive health services is essential to facilitate the empowerment of women and achievement of gender equality. Increasing access to modern methods of contraception can reduce the incidence of unplanned pregnancy and decrease maternal mortality. Long-acting reversible contraceptives (LARCs) offer high contraceptive efficacy as well as cost-efficacy, providing benefits for both women and healthcare systems. The levonorgestrel-releasing intrauterine system (LNG-IUS) first became available in 1990 with the introduction of Mirena (LNG-IUS 20), a highly effective contraceptive which can reduce menstrual blood loss and provide other therapeutic benefits. The impact of the LNG-IUS on society has been wide ranging, including decreasing the need for abortion, reducing the number of surgical sterilisation

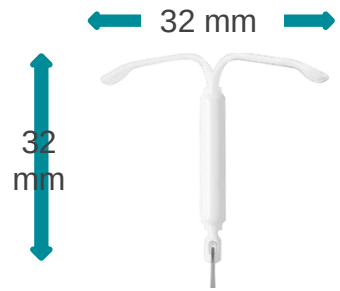
gender equality. Universal access to SRH services is essential to achieving this objective.[1 2] Increasing access to modern, effective methods of contraception can reduce the incidence of unplanned pregnancy, decrease maternal mortality, and can also contribute to fighting poverty.[1 3 4]

Long-acting reversible contraceptives (LARCs), such as implants, and hormonal and non-hormonal intrauterine devices (IUDs), are not only highly effective at preventing unintended pregnancy and subsequent abortion but are also cost-effective options that provide benefits for both women and healthcare systems.

Mirena (Bayer AG, Berlin, Germany) was the first levonorgestrel-releasing intrauterine system (LNG-IUS) of its kind. Developed by the Population Council's International Committee for Contracep-

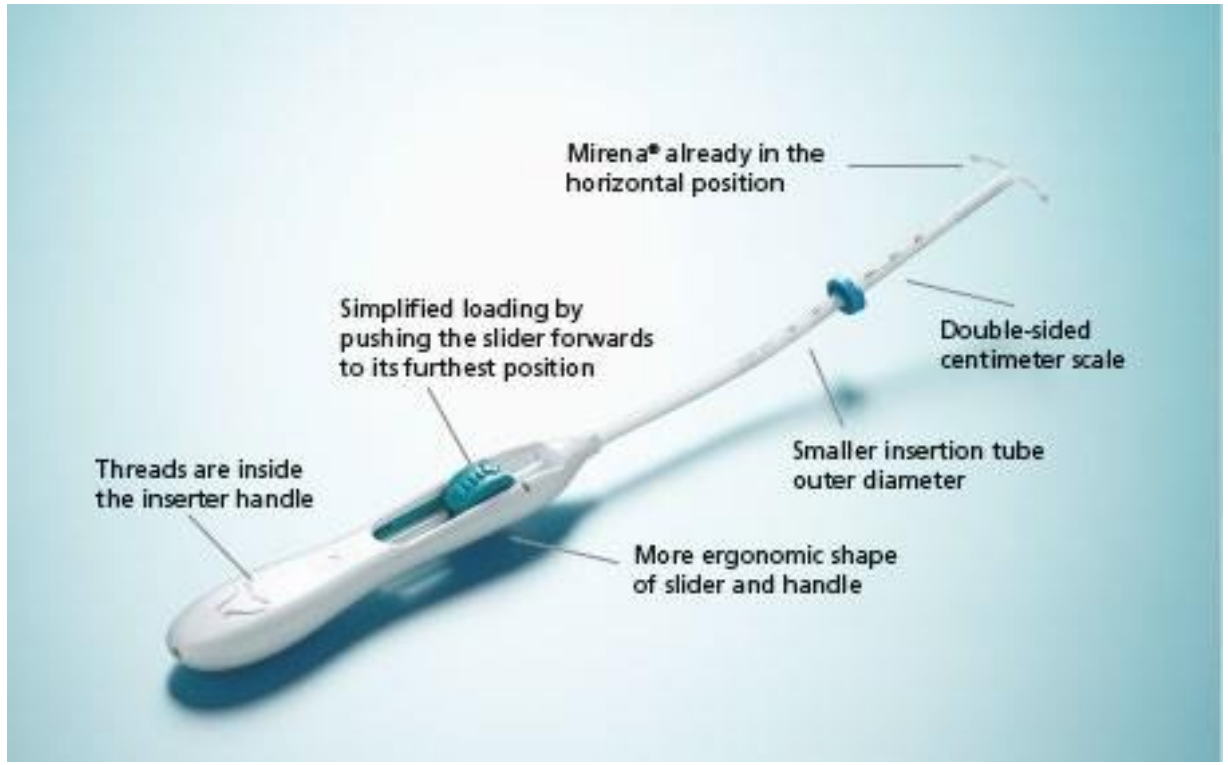
Properties of LNG-IUS 20 (Mirena)

The designation of LNG-IUS 20 is based on the average ***in vivo*** **LNG release rate over the first year**[1]

	
Maximum duration of use (years)	6 (-8)
Efficacy (Pearl Index)	0.35 in Year 6
Average *in vivo* LNG release rate over the first year	20 µg/24 hours
Total LNG content (mg)	52
T-frame dimensions (mm)	32 x 32
Insertion tube diameter (mm)	4.4
Silver ring/ MR compatibility	No Silver Ring/ MR Compatible
Color of the monofilament threads	Brown

1. Mirena Prescibing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021225s040lbl.pdf [accessed November 2020]

The EvoInserter



EvoInserter®

- user-friendly design
- associated with a high placement success rate, ease of placement
- may remove some concerns among HCPs about difficult placement of LNG-IUSs, thereby encouraging increased uptake of an effective contraceptive method

Gemzell et al: Contraception 96 (2017) 426-431

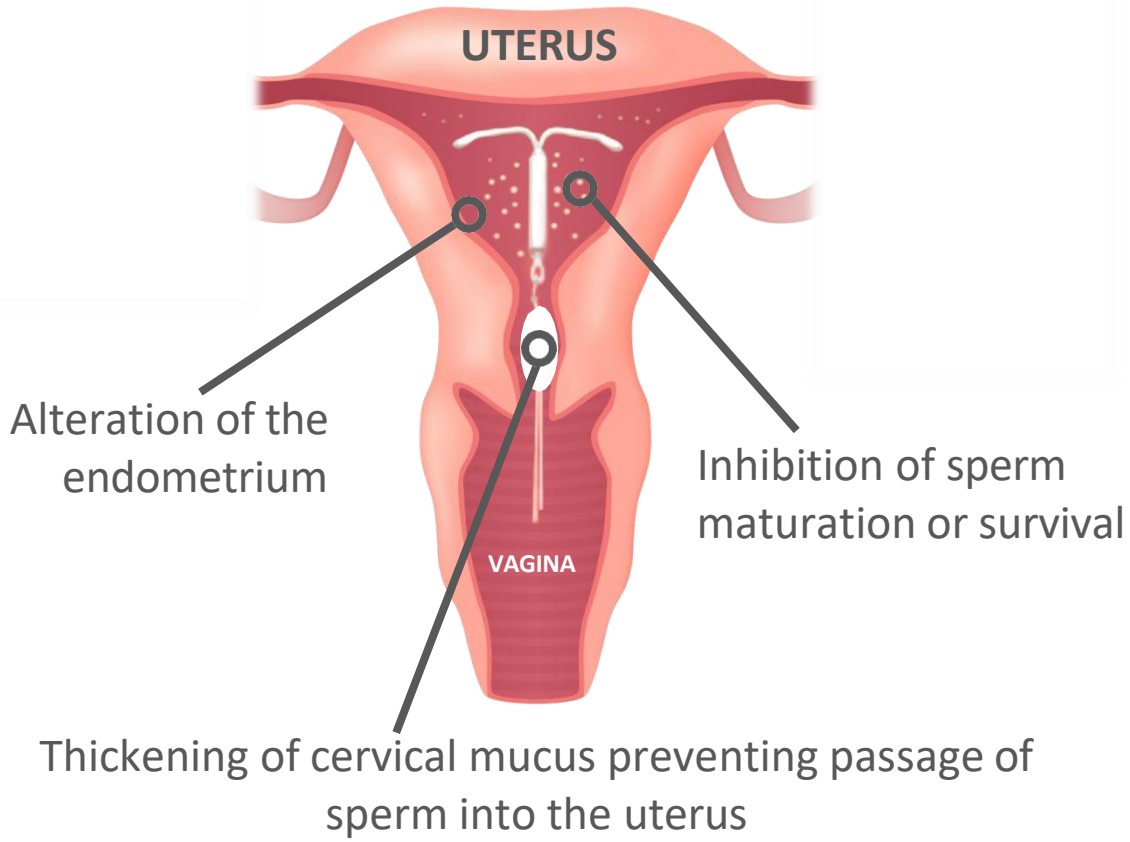
Mechanisms of action

LNG-IUS mainly have a local contraceptive effect[1-,3]

Due to this local effect, plasma levels of LNG are low, meaning that ovulation is not inhibited[1,2]

Studies of Mirena and similar LNG-IUS products have suggested several mechanisms that may prevent pregnancy such as[1-4]:

- Thickening of cervical mucus
- Inhibition of sperm maturation/survival
- Suppressing endometrial maturation



1. Stanford JB, et al. *Am J Obstet Gynecol* 2002;187:1699 –708; 2. Attia AM, et al. *Patient Prefer Adherence* 2013;7:777-85; 3. Rivera R, et al. *Am J Obstet Gynecol* 1999;181(5 Pt 1):1263–9; 4. Sivin I. *Stud Fam Plann* 1989;20:355–9.

Mirena is associated with high satisfation and continuation rates

Over

90%

of Mirena users continue at one year after placement[1]

Around

95%

of Mirena users report they are very satisfied or rather satisfied[2]

Appropriate counseling increases patient satisfaction, avoids unnecessary removals, and improves continuation rates with Mirena[1,3]

1. Backman T, et al. Eur J Contracept Reprod Health Care 2001;6(Suppl 1):23–6; 2. Römer T, Linsberger D. Eur J Contracept Reprod Health Care 2009;14:391–8; 3. Backman T, et al. Obstet Gynecol 2002;99:608–13

Contraceptive efficacy of Mirena

Pregnancy rate at 1 year[1,2]

0 - 0.3%

Cumulative efficacy during years 6-8[3]

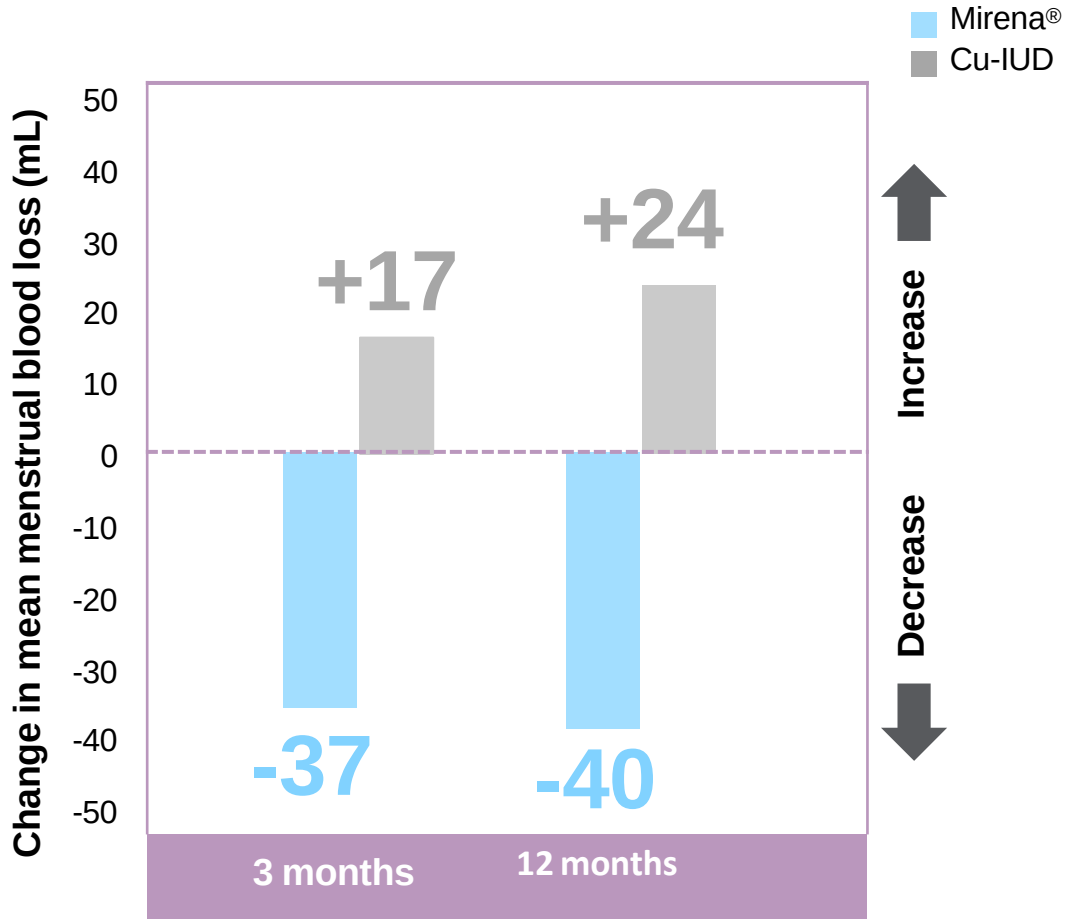
>99%

Mirena provides high contraceptive efficacy for up to 8 years of use[4], with a Pearl Index of 0.35 in Year 6[3]

1. Sivin I, et al. *Contraception* 1984;30:443–56; 2. Indian Council of Medical Research. *Contraception* 1990;42:361-78; 3. Jensen et al, AJOG, 2022, 227 (6), E1 (873)-E124. 4 Mirena Prescibing Information. Available at: FDA Expands Approval of Mirena IUD Device | 2022-08-25 | FDAnews [accessed February 2022]

Mirena has a favorable bleeding profile

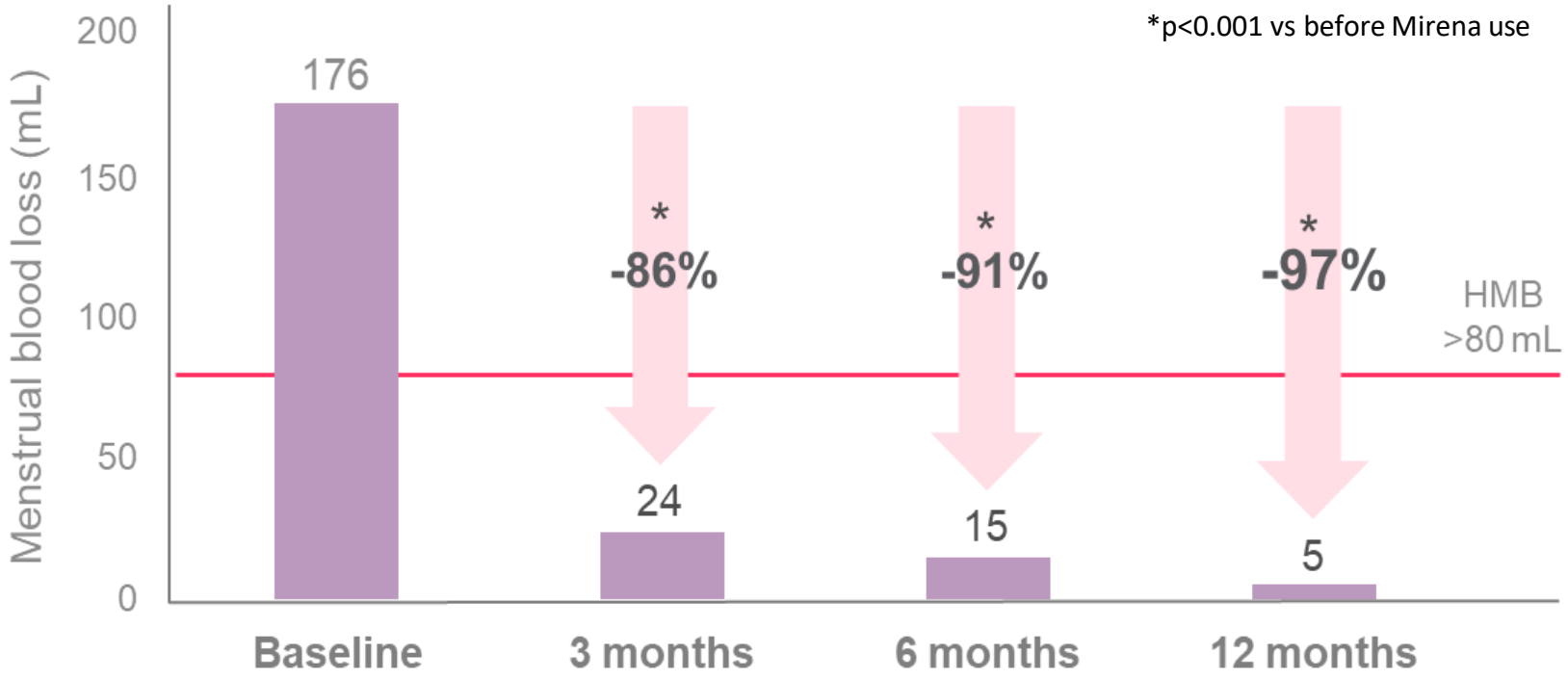
Menstrual blood loss progressively declines with Mirena use, resulting in lighter periods



- Scholten PC. Thesis. The Levonorgestrel IUD: clinical performance and impact on menstruation. University Hospital, Utrecht, 1989

Mirena: very effective treatment for heavy menstrual bleeding

Mirena significantly reduces menstrual blood loss from as early as 3 months after placement[1]



Mirena is recommended as a **first line treatment** option for HMB in multiple guidelines[2-5]

- 1. Andersson JK & Rybo G. *Br J Obstet Gynaecol* 1990; 97: 690–4; 2. NICE Clinical Guidence NG88. Available at: https://www.nice.org.uk/guidance/ng88; 3. FSRH Guidence. Available at: https://www.fsrh.org/standards-and-guidance/documents/ceuguidanceintrauterinecontraception/; 4. Matteson KA *et al*. *Obstet Gynecol* 2013;121:632–643; 5. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2013;122:176–185

Beyond contraception, Mirena can empower women at different stages of their lives

Lighter bleeding and amenorrhea [1,2]

Effective treatment for HMB [3]

Highly effective contraception [6]

Quickly reversible and rapid return to fertility [4]

Discrete, with no need for additional adherence [5,6]

- 1. Suhonen S, et al. Contraception 2004;69:407-412; 2. Andersson K, et al. Contraception 1994;49:56-72 3. Kaunitz AM, et al. Obstet Gynecol 2010;115:625-32; 4. Andersson K, et al. Contraception 1992;46:575-584; 5. ACOG Practice Bulletin 186. Obstet Gynecol 2017;130:e251-e269; 6. Mirena SmPC

Overview of training resources

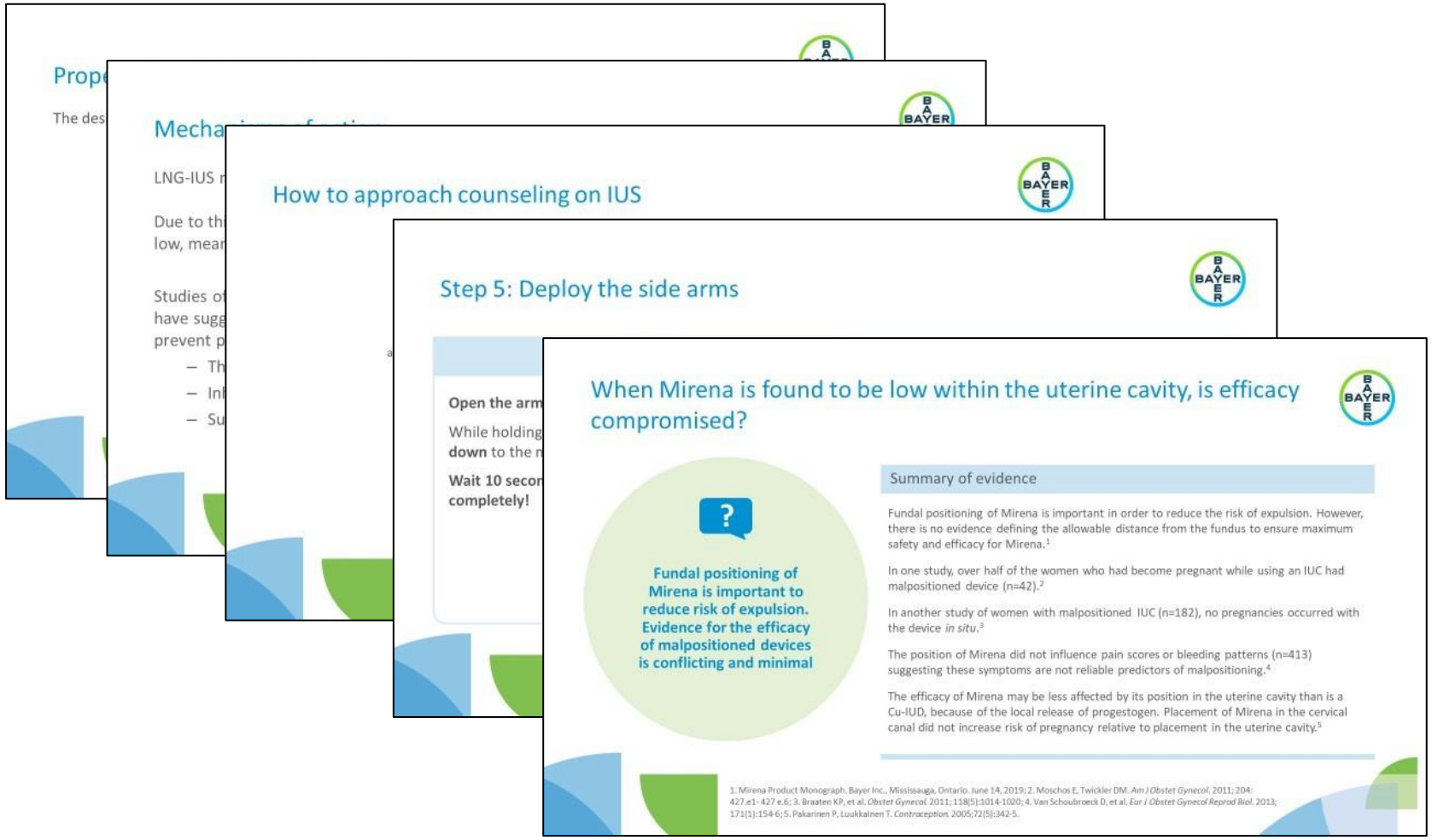
Introduction to training and why it is important

The overall aim of our training materials is to:

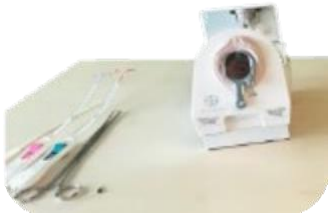
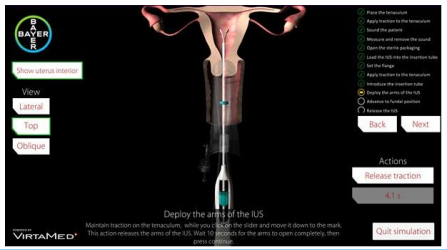
facilitate the **education and empowerment** of all healthcare professionals who are responsible for providing counseling about the LNG-IUS and placing it

IUS, intrauterine system; LNG, low-dose levonorgestrel

Training resources: slide deck



A variety of training models are available

	Uterine disc	Bayer light-up insertion model	"Virtual training" module	PelvicSim™ pelvic simulator
Product				
Benefits	• Quick and easy set-up, no need for power source • General introduction to insertion procedure • Individual practice of insertion technique • Easy to transport	• Quick and easy set up, no need for additional power source • Individual practice of insertion technique • Anatomically correct • Easy to transport	• Can be deployed in any Learning Management (browser window or tablet/mobile) • Bridge between theory and hands-on training • Option to use as a stand-alone component	• Lifelike experience using clinical instruments • Detailed instructions on the insertion procedure • Immediate feedback on procedure as it happens • Possibility of simulating both parous and nulliparous patients
Considerations	• Not lifelike • Experience not representative of clinical practice • No ability to simulate different scenarios, e.g. nulliparous vs parous uterus	• Experience not representative of clinical practice • No ability to simulate different scenarios, e.g. nulliparous vs parous uterus	• Seamless integration between the classical training resources (e-learning) and online simulation • Good solution for situations where access to simulators is not possible	• Time required to ensure appropriate set-up • Sensors and receptors within model are easily damaged • Care and maintenance required to ensure long-term functionality

Thank you

Avibela™

(levonorgestrel-releasing intrauterine system) **52 mg**

IMPACT™ RH360

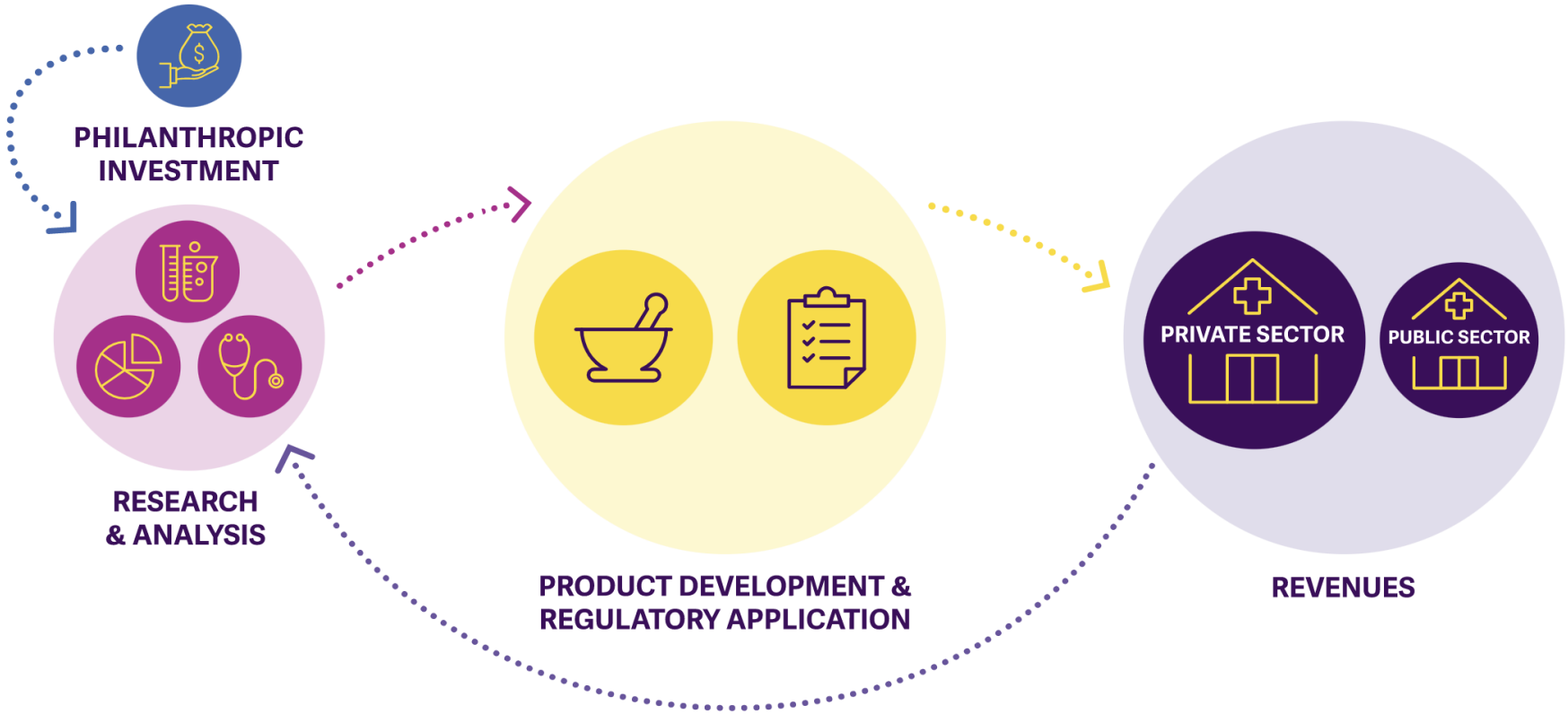
Medicines® 360♀

We believe women should have access to high-quality medicines at a price they can afford

- Medicines360 is a U.S.-based nonprofit pharmaceutical organization with a mission to catalyze equitable access to medicines and devices through product development, policy advocacy, and collaboration with global and U.S. partners
- Medicines360's first product is a 52 mg levonorgestrel-releasing intrauterine system ("hormonal IUD"), sold under the brand name Liletta® in the U.S. and Avibela™ in low- and middle-income countries

- Impact RH360 is a wholly owned subsidiary of Medicines360 that has full rights to make and distribute AVIBELA in 88 low- and middle-income countries
- Impact RH360 works to make AVIBELA available to women around the globe, often in places where the hormonal IUD has historically been inaccessible

Nonprofit pharma model



PRODUCT DESCRPTION

Avibela™ is a hormonal IUD (levonorgestrel-releasing intrauterine system, 52 mg) indicated for contraception and heavy menstrual bleeding.

Avibela™
(levonorgestrel-releasing intrauterine system) **52 mg**

Key clinical characteristics

Highly effective long-acting reversible contraceptive

More than 99% effective at preventing pregnancy for up to six years[1]

Studied in a broad range of women

- 1,751 women ages 16-45[2]
- 58% nulliparous (having never given birth)[2]
- BMI range 16-62 and average 27[2]

Effective at treating heavy menstrual bleeding

Women with heavy menstrual bleeding experience an 88% decrease in the volume of menstrual bleeding by the end of three months of use, and an 82% reduction is sustained for 12 months (based on a 12-month study)[1]

Same-day insertion is possible

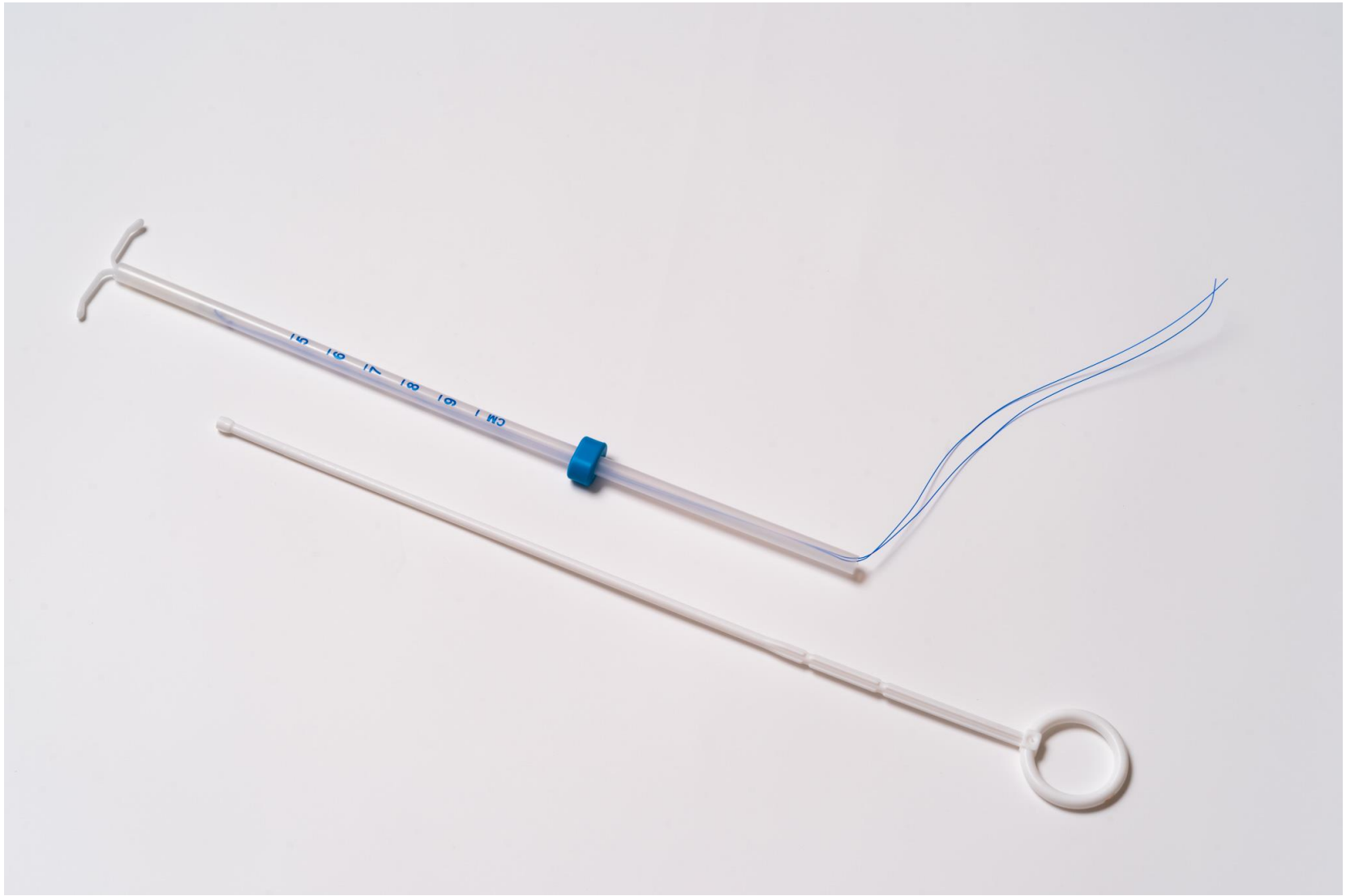
Can be inserted at any time, including the same day as the initial visit to the clinic (if the provider is reasonably certain the woman is not pregnant)[1]

[1]Avibela (levonorgestrel-releasing intrauterine system) 52 mg [Summary of Product Characteristics and Prescribing Information]. Impact RH360; 2022.

[2]Eisenberg, D. et al. Three-year efficacy and safety of a new 52-mg levonorgestrel-releasing intrauterine system. Contraception 92 (2015) 10-16.

Avibela™

AVIBELA is a 52 mg levonorgestrel IUD with an inserter



Avibela™

AVIBELA duration of use and shelf-life

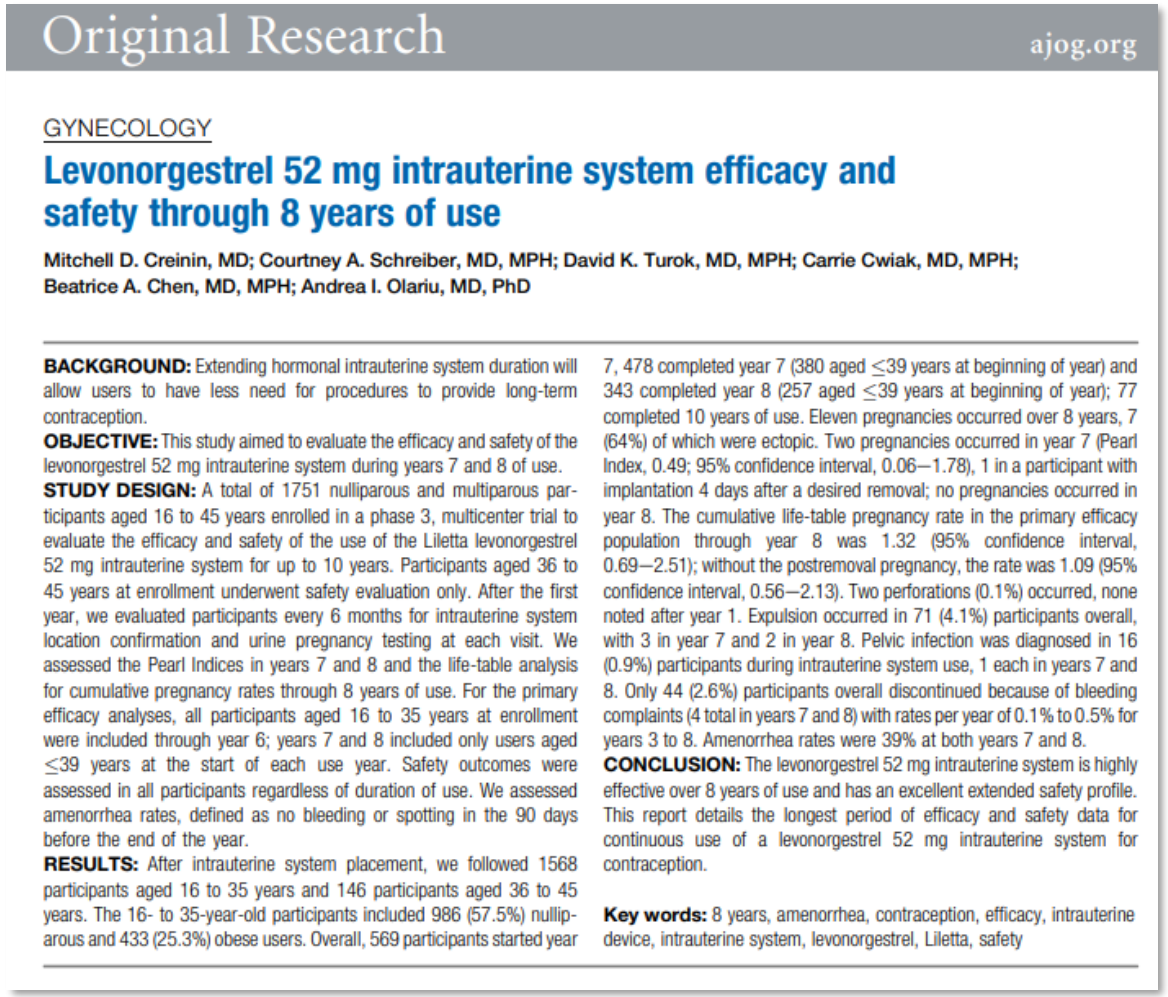
- **Duration of Use:** up to 6 years*
- **Shelf-life:** 60 months (5 years)

* Providers should check local approvals for the approved duration of use in each country

Source: Avibela Summary of Product Characteristics & Prescribing Information, 2022

Avibela™

Medicines360 will seek to extend AVIBELA's duration of use to 8 years



Original Research ajog.org

GYNECOLOGY

Levonorgestrel 52 mg intrauterine system efficacy and safety through 8 years of use

Mitchell D. Creinin, MD; Courtney A. Schreiber, MD, MPH; David K. Turok, MD, MPH; Carrie Cwiak, MD, MPH; Beatrice A. Chen, MD, MPH; Andrea I. Olariu, MD, PhD

BACKGROUND: Extending hormonal intrauterine system duration will allow users to have less need for procedures to provide long-term contraception.

OBJECTIVE: This study aimed to evaluate the efficacy and safety of the levonorgestrel 52 mg intrauterine system during years 7 and 8 of use.

STUDY DESIGN: A total of 1751 nulliparous and multiparous participants aged 16 to 45 years enrolled in a phase 3, multicenter trial to evaluate the efficacy and safety of the use of the Liletta levonorgestrel 52 mg intrauterine system for up to 10 years. Participants aged 36 to 45 years at enrollment underwent safety evaluation only. After the first year, we evaluated participants every 6 months for intrauterine system location confirmation and urine pregnancy testing at each visit. We assessed the Pearl Indices in years 7 and 8 and the life-table analysis for cumulative pregnancy rates through 8 years of use. For the primary efficacy analyses, all participants aged 16 to 35 years at enrollment were included through year 6; years 7 and 8 included only users aged ≤39 years at the start of each use year. Safety outcomes were assessed in all participants regardless of duration of use. We assessed amenorrhea rates, defined as no bleeding or spotting in the 90 days before the end of the year.

RESULTS: After intrauterine system placement, we followed 1568 participants aged 16 to 35 years and 146 participants aged 36 to 45 years. The 16- to 35-year-old participants included 986 (57.5%) nulliparous and 433 (25.3%) obese users. Overall, 569 participants started year 7, 478 completed year 7 (380 aged ≤39 years at beginning of year) and 343 completed year 8 (257 aged ≤39 years at beginning of year); 77 completed 10 years of use. Eleven pregnancies occurred over 8 years, 7 (64%) of which were ectopic. Two pregnancies occurred in year 7 (Pearl Index, 0.49; 95% confidence interval, 0.06–1.78), 1 in a participant with implantation 4 days after a desired removal; no pregnancies occurred in year 8. The cumulative life-table pregnancy rate in the primary efficacy population through year 8 was 1.32 (95% confidence interval, 0.69–2.51); without the postremoval pregnancy, the rate was 1.09 (95% confidence interval, 0.56–2.13). Two perforations (0.1%) occurred, none noted after year 1. Expulsion occurred in 71 (4.1%) participants overall, with 3 in year 7 and 2 in year 8. Pelvic infection was diagnosed in 16 (0.9%) participants during intrauterine system use, 1 each in years 7 and 8. Only 44 (2.6%) participants overall discontinued because of bleeding complaints (4 total in years 7 and 8) with rates per year of 0.1% to 0.5% for years 3 to 8. Amenorrhea rates were 39% at both years 7 and 8.

CONCLUSION: The levonorgestrel 52 mg intrauterine system is highly effective over 8 years of use and has an excellent extended safety profile. This report details the longest period of efficacy and safety data for continuous use of a levonorgestrel 52 mg intrauterine system for contraception.

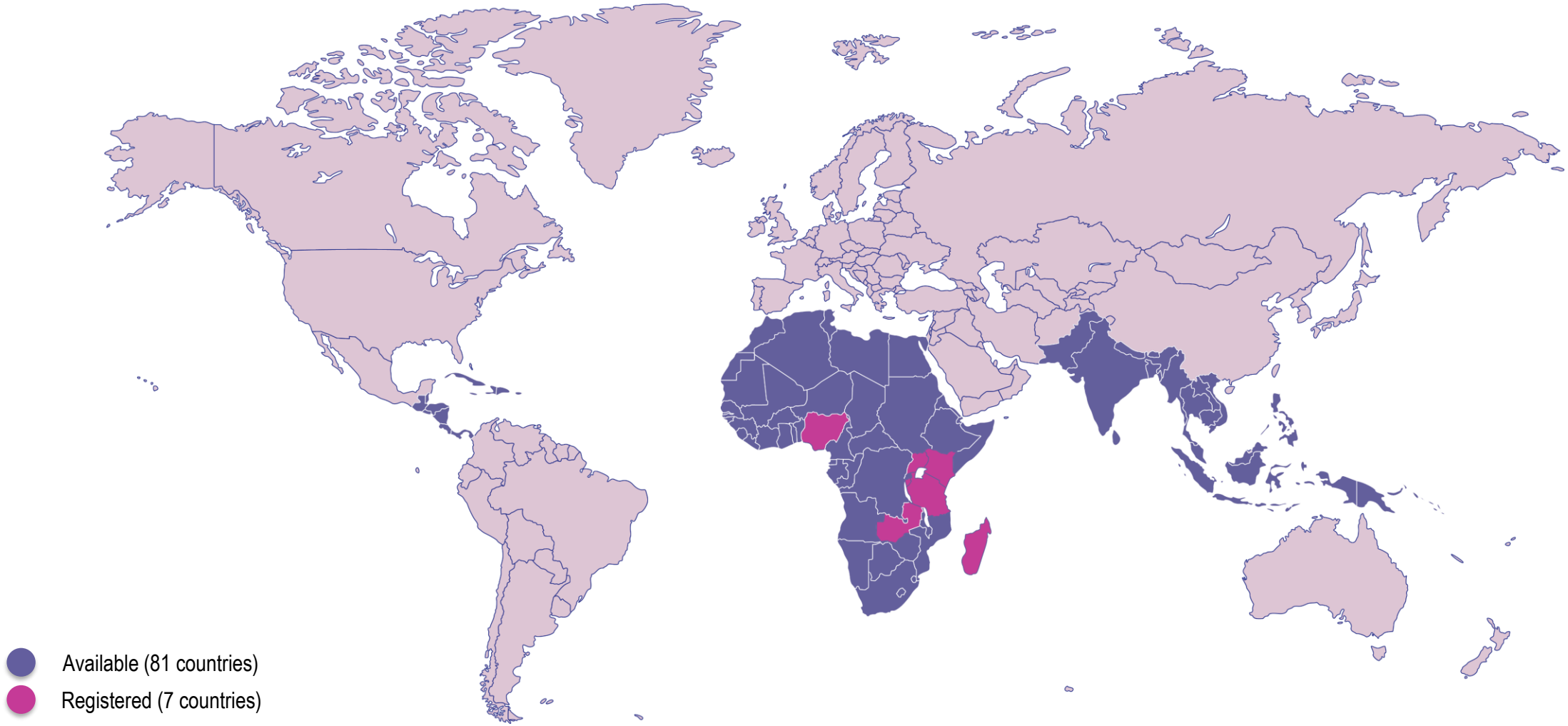
Key words: 8 years, amenorrhea, contraception, efficacy, intrauterine device, intrauterine system, levonorgestrel, Liletta, safety

Source: Creinin, MD, et al. Levonorgestrel 52 mg intrauterine system efficacy and safety through 8 years of use. *AJOG*, May 2022. DOI: https://doi.org/10.1016/j.ajog.2022.05.022

Avibela™

AVIBELA can be made available in 88 countries

AVIBELA is currently registered in Madagascar, Kenya, Nigeria, Rwanda, Tanzania, Uganda, and Zambia



Available (81 countries)

Registered (7 countries)

Medicines360, through its wholly-owned subsidiary Impact RH360, offers a **subsidized access price of $9.50/unit** for AVIBELA through 2024, for all units ordered through international procurement catalogs or on behalf of eligible public sector programs.

Avibela™

To support the introduction of AVIBELA, we provide an insertion and removal training deck, an insertion training video, and a clinical trainer (upon request).

Training Deck

English

French

Spanish

Training Video

English

French

Spanish

IMPORTANT SAFETY INFORMATION

Contraindications to Use of AVIBELA

- Pregnancy
- For use as post-coital contraception (emergency contraception)
- Acute pelvic inflammatory disease (PID) or endometritis or a history of PID unless there has been a subsequent intrauterine pregnancy
- Infected abortion in the past 3 months
- Known or suspected uterine or cervical neoplasia
- Acute liver disease or liver tumor (benign or malignant)
- Conditions associated with increased susceptibility to pelvic infections
- Congenital or acquired uterine anomaly, including fibroids, that distorts the uterine cavity and would be incompatible with correct IUS placement
- Uterine bleeding of unknown etiology
- Untreated acute cervicitis or vaginitis, including bacterial vaginosis, known chlamydial or gonococcal cervical infection, or other lower genital tract infections until infection is controlled
- Known or suspected breast cancer or other hormone-sensitive cancer, now or in the past
- A previously inserted IUS that has not been removed
- A history of hypersensitivity reaction to any component of AVIBELA. Reactions may include rash, urticaria, and angioedema

Special Warnings & Precautions for Use

Medical examination

- Obtain a complete medical and social history, including partner status, to determine conditions that might influence the selection of an IUS for contraception and/or heavy menstrual bleeding
- Exclude underlying endometrial pathology (e.g., polyps or cancer) prior to the insertion of AVIBELA in women with persistent or uncharacteristic bleeding because irregular bleeding/spotting is common during the first months of AVIBELA use and may preclude adequate assessment after insertion. AVIBELA is contraindicated in women with uterine bleeding of unknown etiology
- Exclude underlying congenital or acquired uterine anomalies, including fibroids, that distort the uterine cavity and would be incompatible with correct IUS placement
- Ensure a previously inserted IUS has been removed prior to insertion of AVIBELA
- Assess whether the woman is at increased risk of infection (e.g., leukemia, acquired immune deficiency syndrome [AIDS], IV drug abuse), or has a history of PID unless there has been a subsequent intrauterine pregnancy. AVIBELA does not protect against HIV/STI transmission

Special Warnings & Precautions for Use

Conditions under which AVIBELA can be used by caution

- Use AVIBELA with caution after careful assessment if any of the following conditions exist, and consider removal of the IUS if any of them arise during use:
  - Coagulopathy or use of anticoagulants
  - Migraine, focal migraine with asymmetrical visual loss, or other symptoms indicating transient cerebral ischemia
  - Exceptionally severe or frequent headache
  - Marked increase of blood pressure
  - Severe arterial disease such as stroke or myocardial infarction

- Consider removing AVIBELA if any of the following conditions arise during use:
  - Uterine or cervical malignancy
  - Jaundice

Pregnancy related risks with AVIBELA

- In case of an accidental pregnancy with AVIBELA in place, advise a woman of the increased risks for pregnancy complications, including miscarriage, premature labor, premature delivery, infection and sepsis. Ectopic pregnancy should be excluded, and removal of the system should be considered

- Removal of AVIBELA or probing of the uterus may result in spontaneous abortion. Should these procedures not be possible or if the woman wishes to continue the pregnancy, the woman should be informed about these risks, and accordingly, such pregnancies should be closely monitored. Prenatal care should include counseling about these risks and that she should report immediately any flu-like symptoms, fever, chills, cramping, pain, bleeding, vaginal discharge or leakage of fluid, or any other symptom that suggests complications of the pregnancy

Adverse reactions to AVIBELA

- Undesirable effects are more common during the first months after the insertion and generally subside during prolonged use
- In a large clinical trial of 1751 women using AVIBELA for contraception, very common undesirable effects (occurring in more than 10% of users) include vaginal bacterial infections, vulvovaginal mycotic infections, nausea or vomiting, and acne
- Cases of sepsis (including group A streptococcal sepsis) have been reported following insertions with hormonal IUSs
- The following adverse reactions have been reported in connection with the insertion or removal procedure of AVIBELA: pain, bleeding, and insertion-related vasovagal reaction with dizziness or syncope. The procedure may also precipitate a seizure in patients with epilepsy
- The removal threads may be felt by the partner during intercourse
- Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product
  - Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system or to the supplier

THANK YOU!

FOR MORE INFORMATION, PLEASE VISIT WWW.AVIBELA.COM OR EMAIL US AT GLOBALACCESS@MEDICINES360.ORG

Avibela™
(levonorgestrel-releasing intrauterine system) 52 mg

Medicines360™ | IMPACT™ RH360

THE LEVONORGESTREL INTRAUTERINE SYSTEM (LNG IUS)

Friday, February 24, 2023

Presented by Jim Sailer

On behalf of the ICA Foundation

Founded in December 2003, the International Contraceptive Access (ICA) Foundation is a public-private partnership between Bayer AG, a world-wide specialty pharmaceutical company, and Population Council Inc., an international nonprofit nongovernmental organization, with a mission to provide access to hormonal IUDs at no charge to providers in low- and middle-income countries.

- The hormonal IUD was developed by the Population Council and Bayer and approved by the US FDA in 2000.
- LNG IUS is similar to Mirena® but is exclusively produced for the ICA Foundation and is only distributed in resource-poor settings.

The objective of the Foundation is to provide local service-delivery organizations with LNG IUS contraceptive devices on a not-for-profit basis and ultimately serve the reproductive needs of women in resource-poor settings, primarily in low- and middle-income countries.

In practice, we have always sought:

- To focus on vulnerable populations
- To maximize use of our allocations
- To increase awareness of and access to this method

ICA FOUNDATION
International Contraceptive Access

About the LNG IUS

- The LNG IUS is a plain plastic T-shaped frame with a hormonal reservoir around the vertical stem.
- The steroid hormone reservoir consists of a cylinder, made of LNG and a polydimethylsiloxane mixture, containing 52mg of LNG.
- Minute amounts of LNG (20 µg/day) are released from the cylinder at a constant rate into the uterine cavity.

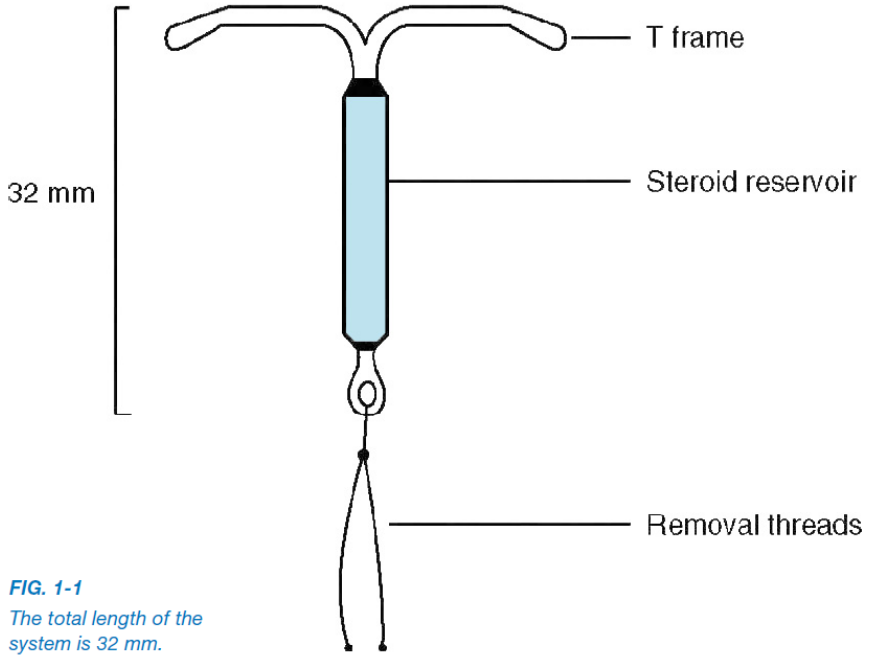
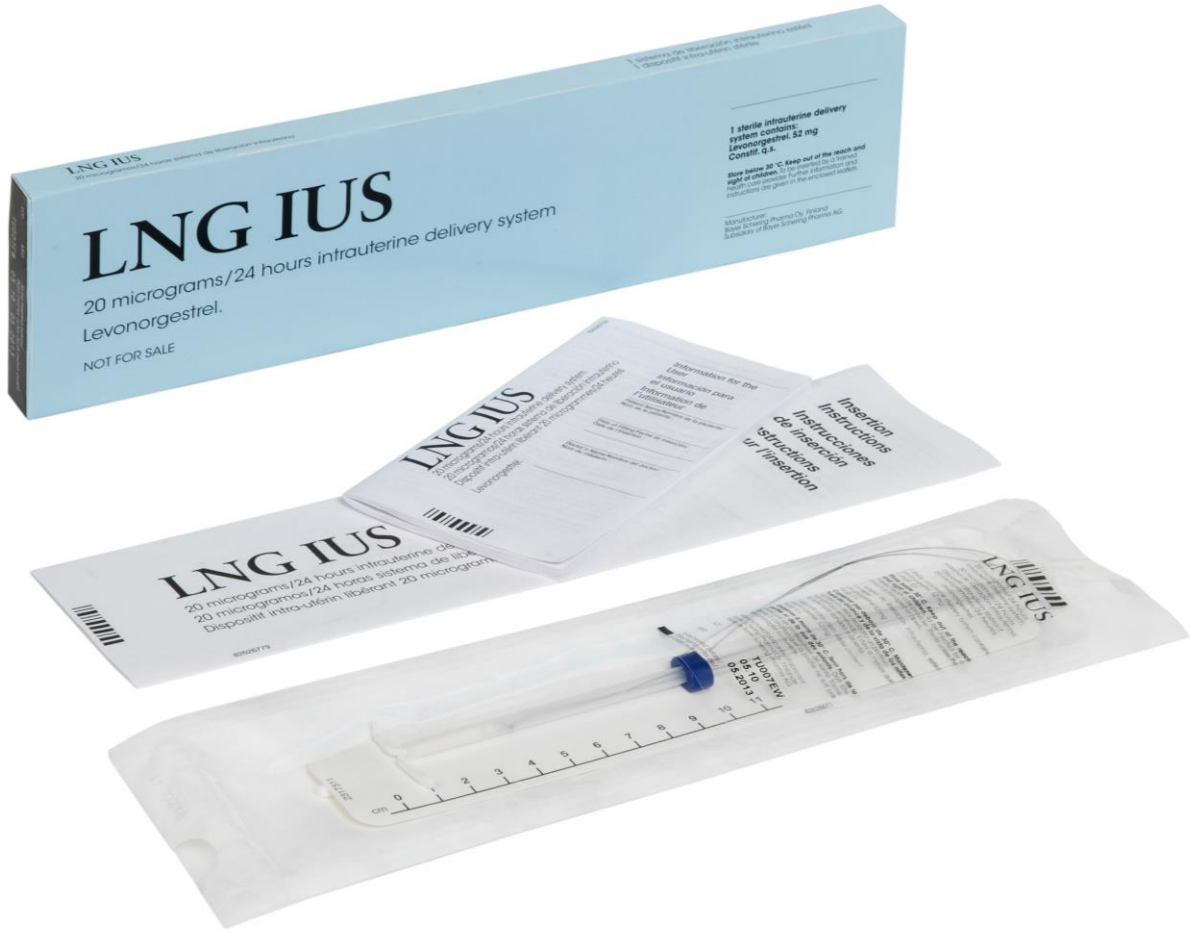


FIG. 1-1
The total length of the system is 32 mm.

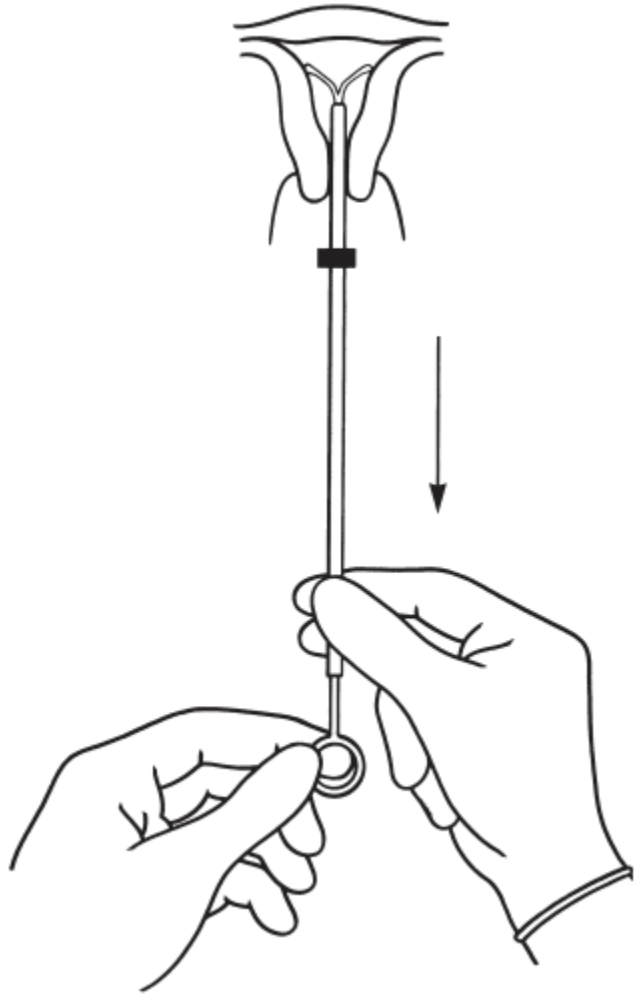
Mechanism of Action

- The LNG IUS functions by suppressing the growth of the uterine wall, reducing fertility, thickening cervical mucus, and inhibiting sperm motility.
- The LNG IUS provides contraception for up to 5 years.



LNG IUS inserter

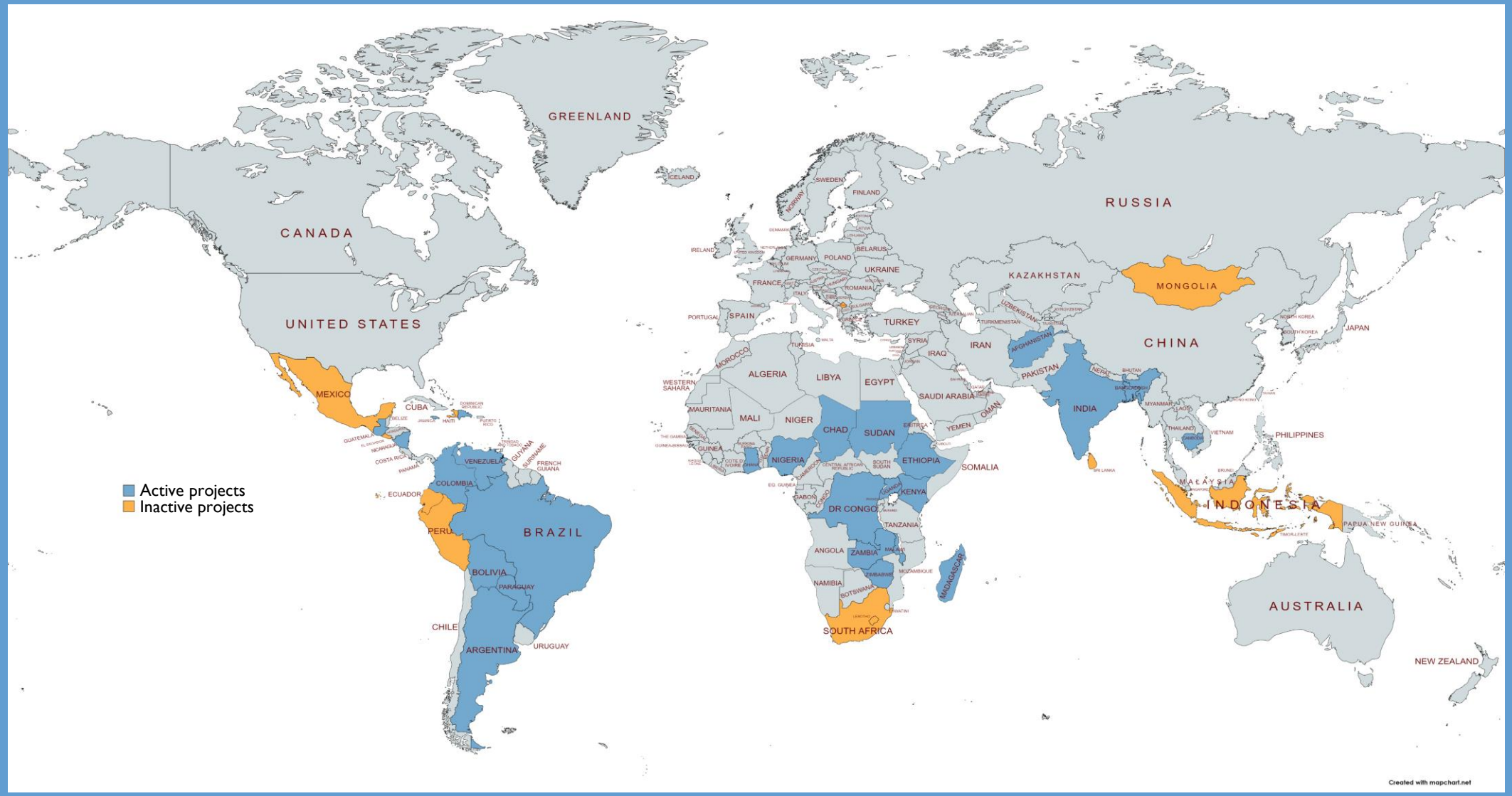
- Biosimilar to Mirena
- Same production line at the Bayer AG factory in Turku, Finland
- 2-handed inserter



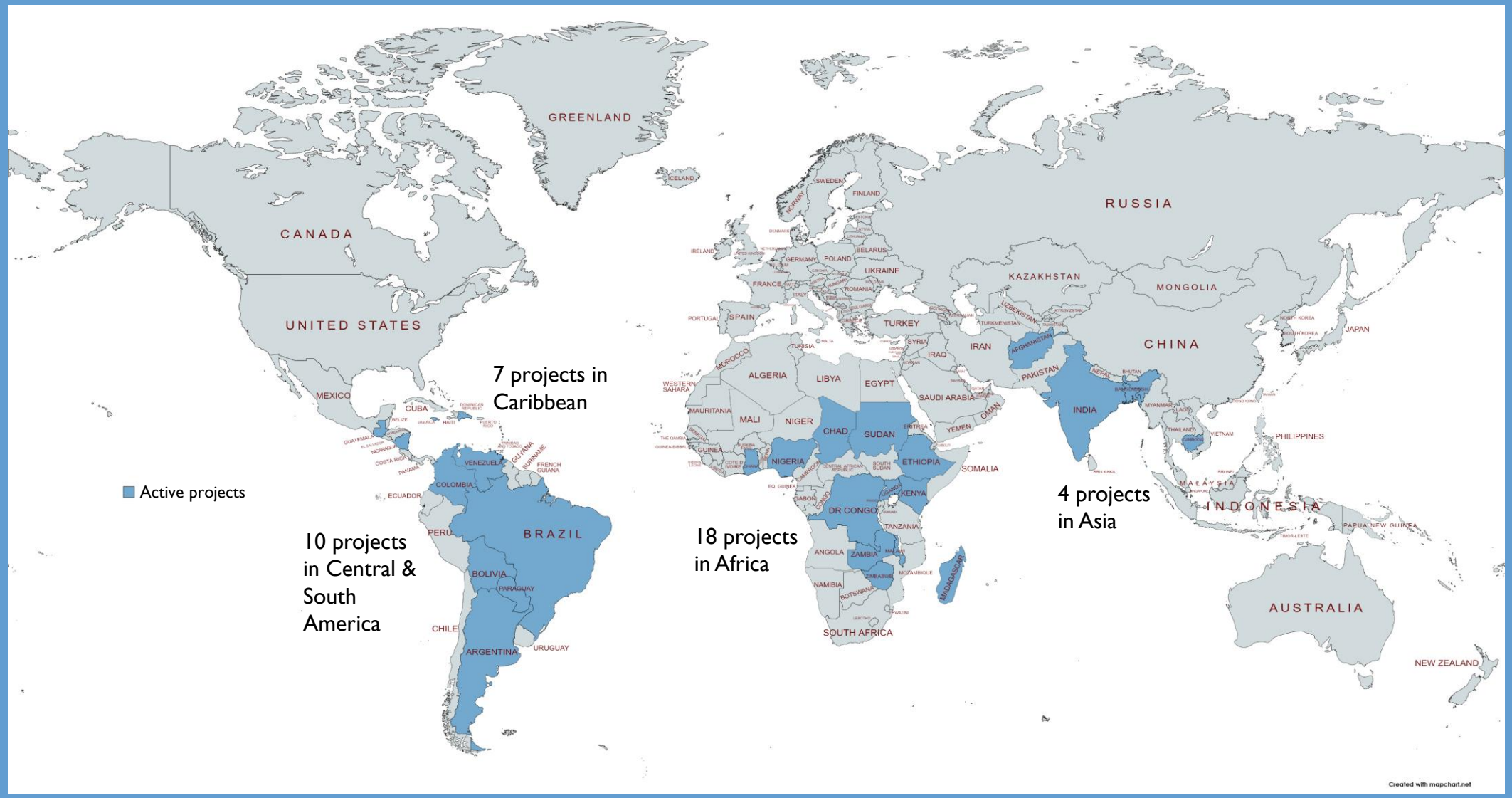
Availability of the LNG IUS

- LNG IUS is only available through the ICA Foundation.
- Registered in Kenya, Ghana, and Nigeria.

THE ICA FOUNDATION HAS DELIVERED 212, 022 LNG IUS TO 39 COUNTRIES



THE ICA FOUNDATION HAS 39 ACTIVE PROJECTS IN 32 COUNTRIES



Available Resources

- Client and provider resources, including a training manual, are available on the ICA Foundation website: https://ica-foundation.org/project-resources/information-materials/

THANK YOU


ICA FOUNDATION
International Contraceptive Access
LNG IUS
Training Manual for Family Planning
LNG IUS
NOT FOR USE IN HUMANS

Procurement Considerations

USAID
GHSC-PSM
-
UNFPA

USAID
FROM THE AMERICAN PEOPLE

USAID GLOBAL HEALTH SUPPLY CHAIN PROGRAM
Procurement and Supply Management

Hormonal IUD 101: GHSC-PSM Presentation

February 24, 2023

GHSC-PSM Purpose and Objectives

To ensure an uninterrupted supply of public health commodities that save lives.

GLOBAL COMMODITY PROCUREMENT AND LOGISTICS

COUNTRY SUPPLY CHAIN SYSTEMS STRENGTHENING

GLOBAL COLLABORATION

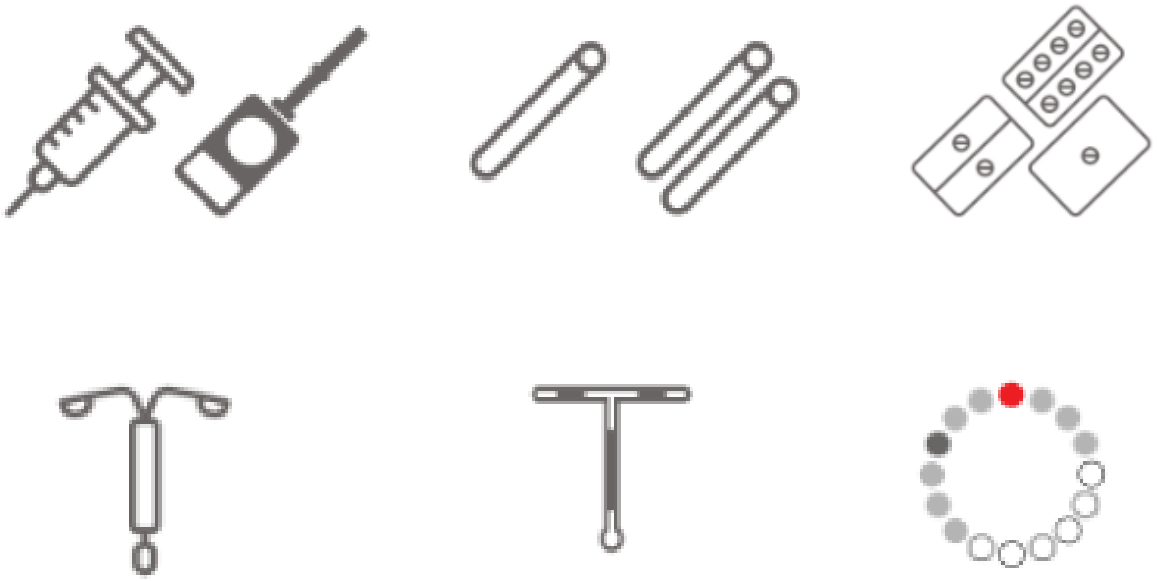
GHSC-PSM By the Numbers
Family Planning/Reproductive Health Task Order

$10.5M
DELIVERED
In Q4, FY2022

$237M
of FP/RH
commodities
DELIVERED

$14M
COST SAVINGS
on FP/RH
commodities

Methods Overview



Hormonal IUD Procurement through GHSC-PSM

- Countries that have indicated strong government interest in adding the hormonal IUD to their method mix, have articulated provider readiness to provide the method and have begun development of plans for public sector introduction, please contact your USAID Mission to express interest in procuring hormonal IUD through GHSC-PSM!

- For additional procurement information, please contact USAID (jvivalo@usaid.gov, amsmith@usaid.gov) and GHSC-PSM (PSM-Hormonal-IUD@ghsc-psm.org).

Key Considerations

- As with other products, the responsibility for ensuring appropriate handing of the hormonal IUD rests with the receiving public health supply chain authorities and program implementer. Recipient supply systems will be held accountable for proper handling of hormonal IUDs. **Systems must monitor the movement of the hormonal IUD throughout the supply chain**—from central or regional warehouses and distribution centers to districts and point-of-care facilities, including distribution of products by social marketing organizations.

- All stakeholders involved in the handling or distribution of the product must take measures to prevent leakage, and report inventory data to responsible authorities.

UNFPA Strategy for Family Planning 2022–2030:

Expanding Choices – Ensuring Rights in a Diverse and Changing World

Human rights-based and gender-transformative approaches to family planning

Promote gender equality and women empowerment, and uphold and realize human rights including the right to decide the number, spacing and timing of children, the rights to health and life, the right to non-discrimination and the right to private life.

SUPPORTED BY

Partnerships and coordination

Roles and responsibilities

Committed & aligned resources

Prevent duplication or gaps

Timing procurement and delivery to align with capacity building and demand generation

Systems strengthening approach

Government-led plans
Integrated programming

Technical assistance e.g., UNFPA Supplies
Transformative Action (supply chain management, RHCS, enabling environment, Seed Fund)

Accountability, transparency and efficiency

Monitoring and reporting on implementation of introduction plan to inform on scale up

Quarterly stock status reports to optimize supply planning

Last Mile Assurance to verify product reaches intended users

Procurement Considerations

Product

- Is the product quality assured – WHO PQ or SRA-approved?
- Is the product in WHO model list & guidelines?
- Is the product in national EML & treatment guidelines of programme countries?
- What is the registration/ waiver status in programme countries?

Readiness

- Are countries interested in the product to expand access and contraceptive choices?
- Is an introduction plan in place, including quantification and distribution plan?
- Is there a capacity building plan (ToT, cascade, supportive supervision/ mentoring)?
- Are there plans to integrate product in national HMIS & LMIS?

Source

- How many manufacturers offer the product?
- What is the average lead time?
- Will the production capacity match forecasted growth in demand?
- Are there restrictions on regions or countries that can access the product?

Financing

- What are the price points?
- Is price likely to be a barrier to introduction and sustainable financing?
- Who will/ can pay for it, with LNOB in mind? - New and Lesser Used Commodities Fund
- Are resources available for introductory activities (e.g., advocacy, demand generation/SBCC materials, training of providers, procurement, job aids, incorporation into existing systems and tools etc.) - Seed Fund

Q&A

Moderator:
Andrée Sosler,
FHI 360

Closing Remarks

Mark Barone
-
Bill & Melinda Gates Foundation

For Additional Information:

Visit www.hormonaliud.org for introduction resources

Contact info@hormonaliud.org to connect with the Access Group

This event's slides and recording will be sent to all registrants and posted on hormonaliud.org