



**POUR ELLE**

BRUSSELS | 20-22 MARCH 2018

**18<sup>TH</sup> GENERAL MEMBERSHIP MEETING OF THE  
REPRODUCTIVE HEALTH SUPPLIES COALITION**

# Beginning with the End in Mind: Multiple Meanings for Contraceptive Research & Development

Kate Rademacher, Technical Advisor, FHI 360

# Begin with the end in mind in order to achieve...



Availability



Quality



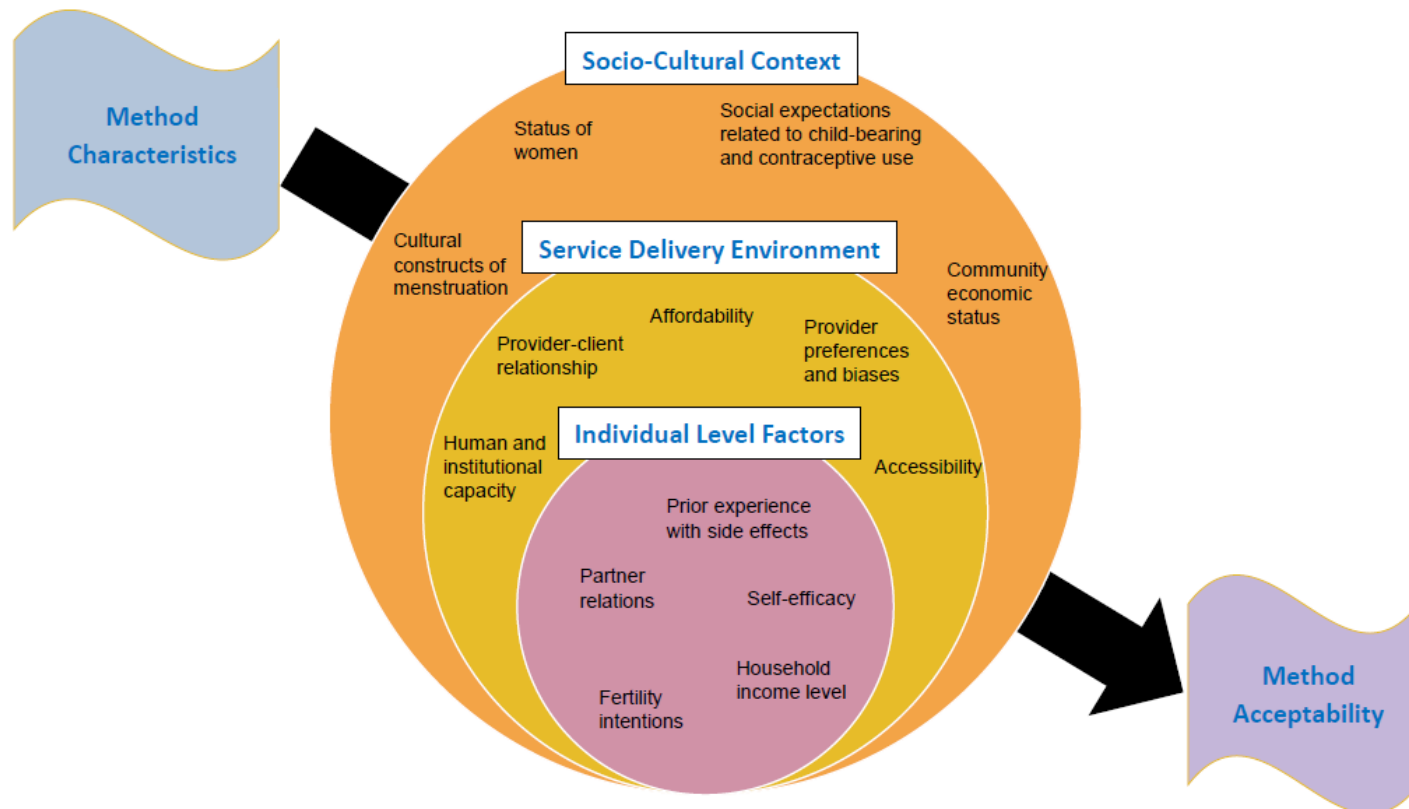
Equity



Choice

# Strategy #1: Conduct acceptability research at all phases of development and introduction

## *A conceptual framework*



Callahan R, et al. 2017

# Strategy 2: Reflect service delivery contexts when designing and developing new products



Condoms by Drone, NPR

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**Target Product Profile for a Longer-acting Injectable Contraceptive**

Characteristic	Desired target	Minimum accept. (if target)
<b>Intended use</b>	Contraception for 6 months	None
<b>Target population</b>	All reproductive age women (including adolescents and HIV-positive women) who would like to space or prevent pregnancy for at least one year	None
<b>Contraindications, warnings, precautions</b>	Pregnancy, no other contraindications can be used immediately after birth and should not interfere with breastfeeding	None
<b>Route of administration</b>	Subcutaneous injection, injectable in arm	None
<b>Effectiveness</b>	Perfect use greater than 99%	None
<b>Usage schedule</b>	Single injection every 6 months (at least 100% of women during a pregnancy period) within 12 months following the period of product effectiveness (includes delay effects)	None
<b>Returns to fertility</b>	At least 80% of women during a pregnancy period should conceive (positive pregnancy test) within 12 months following the period of product effectiveness (includes delay effects)	None
<b>Side effect profile</b>	Injectable formulation after 3 months of use, no symptoms or associated delay effects (e.g., regional atrophy, bone density effects)	None
<b>Stability</b>	<ul style="list-style-type: none"> <li>Product is not required to be stored</li> <li>Product is stable for 3 years at 40°C/75% RH</li> <li>Product is stable for 5 years at 25°C/75% RH</li> <li>Product is stable for 5 years at 15°C/75% RH</li> <li>Product is stable for 5 years at 5°C/75% RH</li> </ul>	<ul style="list-style-type: none"> <li>Product is stable for 3 years at 40°C/75% RH</li> <li>Product is stable for 3 years at 25°C/75% RH</li> <li>Product is stable for 3 years at 15°C/75% RH</li> <li>Product is stable for 3 years at 5°C/75% RH</li> </ul>
<b>Procurement Pkts</b>	Product is supplied in a single-use, pre-filled, disposable syringe (e.g., 100mg/10ml)	Product is supplied in a single-use, pre-filled, disposable syringe (e.g., 100mg/10ml)
<b>Product presentation</b>	Product is supplied in a single-use, pre-filled, disposable syringe (e.g., 100mg/10ml)	Product is supplied in a single-use, pre-filled, disposable syringe (e.g., 100mg/10ml)
<b>Volume</b>	Product is supplied in a single-use, pre-filled, disposable syringe (e.g., 100mg/10ml)	Product is supplied in a single-use, pre-filled, disposable syringe (e.g., 100mg/10ml)
<b>Infrastructure requirement</b>	Minimal of 1.0 ml	Minimal of 2.0 ml
<b>Health benefit</b>	Injectable formulation after 3 months of use, no symptoms or associated delay effects (e.g., regional atrophy, bone density effects)	Injectable formulation after 3 months of use, no symptoms or associated delay effects (e.g., regional atrophy, bone density effects)

Revised on April 29, 2014

# Strategy 3: Include actionable, binding terms in contractual agreements



# Strategy 4: At all stages, work to keep Cost of Goods Sold as low as possible



## Strategy 5: Be flexible & embrace change







# ***Contraceptive Technology Innovation at FHI 360***

**Expanding Access to  
Underutilized Contraceptive Methods**



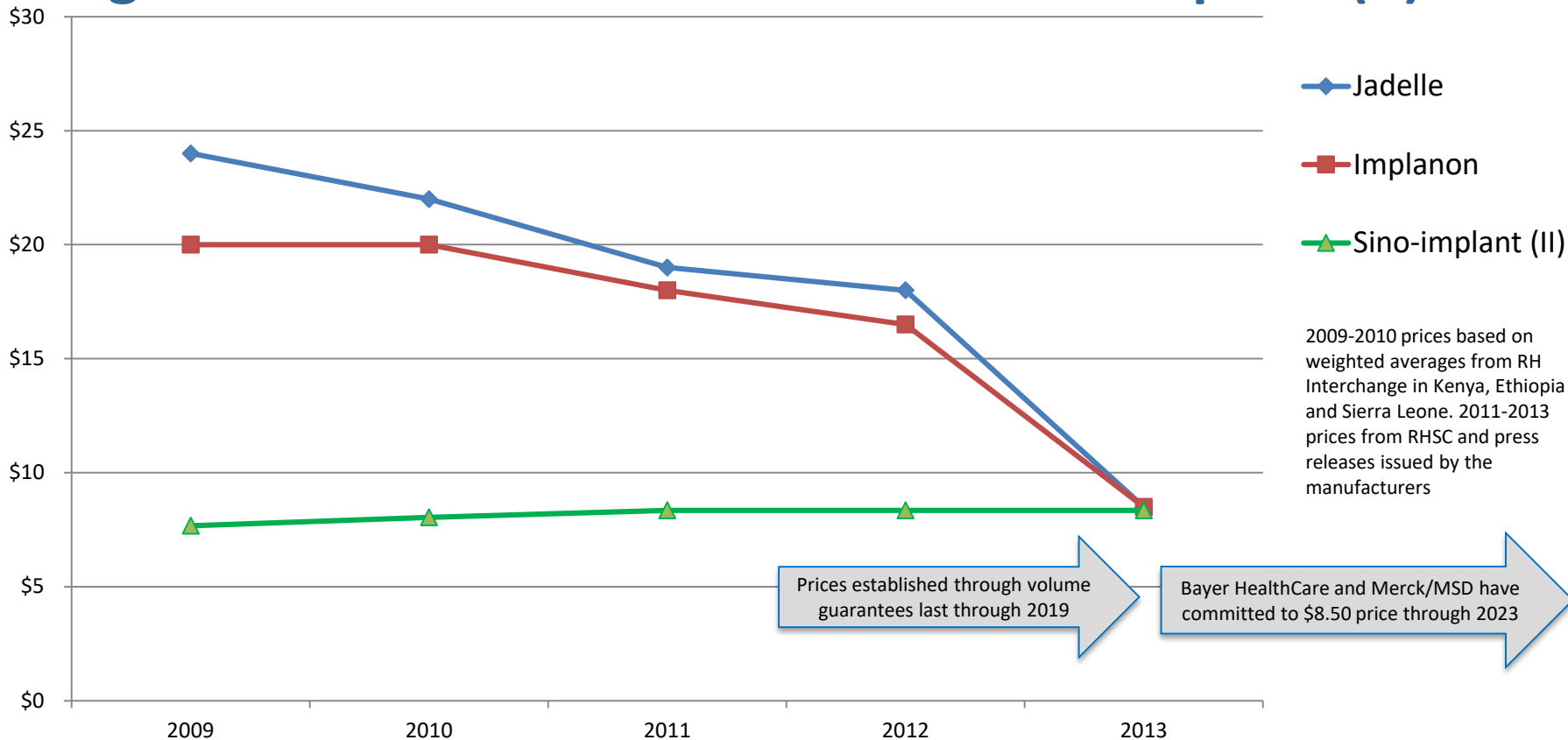
## Levoplant/Sino-implant (II)

Prequalified by the World Health Organization  
in June 2017



- Manufactured by Shanghai Dahua Pharmaceutical
- “Levoplant” is global trade name for product with new levonorgestrel supplier; currently being re-registered
- DKT International is new global marketing partner
- WHO Prequalified for 3 years of use

# Contraceptive Implant Prices 2009-2013: Changes Since Global Introduction of Sino-implant (II)



Prices established through volume guarantees last through 2019

Bayer HealthCare and Merck/MSD have committed to \$8.50 price through 2023

Key Milestones

**2009:** Sino-implant (II) registered in Kenya under trade name Zarin; first registration outside of Asia

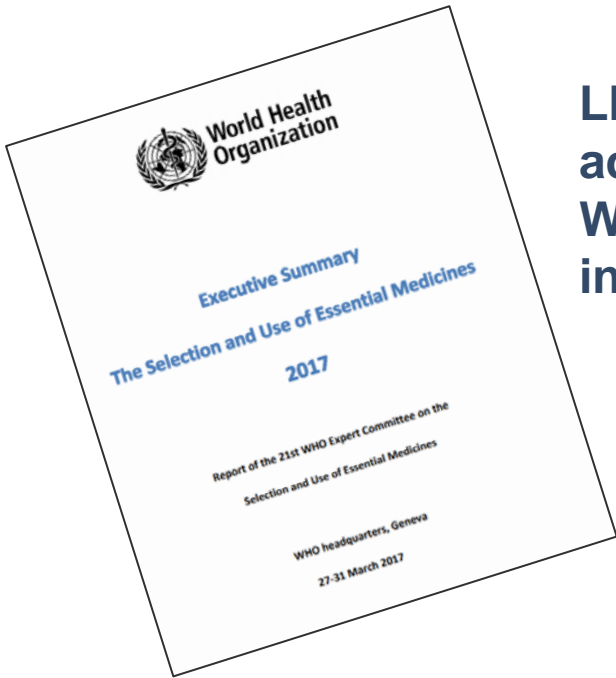
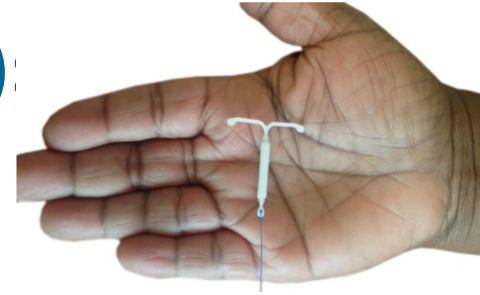
**2011-2012:** Under agreement with partners, Merck/MSD reduces price of Implanon to \$18/unit, with retro-active reduction to \$16.50 when volume thresholds reached in Dec 2012

**2011-2012:** Bayer HealthCare reduces price of Jadelle to \$19/unit and then subsequently to \$18/unit

**2012-2013:** Bayer HealthCare and Merck/MSD lower the prices of Jadelle and Implanon to US\$8.50 per unit as part of volume guarantees

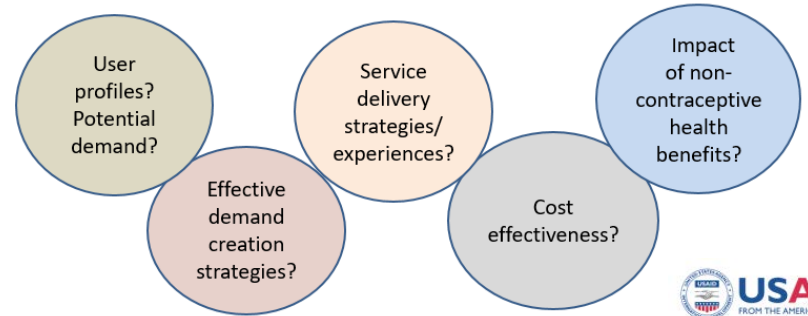
**2009-2014:** Over 1 million Sino-implant (II) units procured in countries under Gates initiative since 2009, resulting in over \$10 million in commodity savings

# Levonorgestrel Intrauterine System (LNG-IUS): Access to Method Remains Limited



LNG-IUS added to WHO EML in 2015

Global learning agenda developed in 2016



- ✓ First approved for use in 1990, the LNG-IUS has a nearly 30-year research-to-practice gap in FP 2020 countries
- ✓ Landscape may be changing as more affordable products become available



# ***Contraceptive Technology Innovation at FHI 360***

## **New Methods Under Development**

# Development of a 6-month injectable

- Currently, no injectable is labeled more than 3 months
- Discontinuation rates are high, in part due to late or missed re-injection visits

## A longer-acting injectable would likely:

- Improve re-injection compliance
- Reduce time & travel costs for clients
- Reduce burden on health system

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**Target Product Profile for a Longer-acting Injectable Contraceptive**

Characteristic	Desired goal	Minimum success criteria
<b>Intended use</b>	Contraception for 6 months	None as desired target
<b>Target population</b>	All reproductive-aged women (including adolescents, lactating and HIV+) who would like to space and/or avoid pregnancy for at least one year	None as desired target
<b>Contraindications, warnings, precautions</b>	Pregnancy on other contraceptives; use of other hormonal contraceptives; use of enzyme-inducing drugs; use of enzyme-inhibiting drugs	Pregnancy; minimal other contraindications; all studies with biocidal
<b>Route of administration</b>	Injectable	Injectable
<b>Injection schedule</b>	Single injection every 6 months (or 180 days)	Injectable
<b>Return to fertility</b>	At least 80% of women desiring a pregnancy should conceive (within 12 months following discontinuation of product effectiveness) within 6 months of discontinuation of product effectiveness	None as desired target
<b>Side effect profile</b>	Injectable with following pattern after 3 months: • No effect on weight • No effect on blood pressure • No effect on cholesterol • No effect on glucose • No effect on hemoglobin A1c • No effect on hemoglobin • No effect on ferritin • No effect on iron • No effect on vitamin D • No effect on calcium • No effect on magnesium • No effect on potassium • No effect on sodium • No effect on zinc • No effect on selenium • No effect on iodine • No effect on copper • No effect on manganese • No effect on chromium • No effect on molybdenum • No effect on cobalt • No effect on nickel • No effect on boron • No effect on silicon • No effect on phosphorus • No effect on sulfur • No effect on oxygen • No effect on carbon • No effect on nitrogen • No effect on hydrogen • No effect on helium • No effect on neon • No effect on argon • No effect on krypton • No effect on xenon • No effect on radon • No effect on francium • No effect on actinium • No effect on thorium • No effect on protactinium • No effect on uranium • No effect on neptunium • No effect on plutonium • No effect on americium • No effect on curium • No effect on berkelium • No effect on californium • No effect on einsteinium • No effect on fermium • No effect on mendelevium • No effect on nobelium • No effect on lawrencium	None as desired target
<b>Stability</b>	Injectable with following pattern after 3 months: • No effect on weight • No effect on blood pressure • No effect on cholesterol • No effect on glucose • No effect on hemoglobin A1c • No effect on hemoglobin • No effect on ferritin • No effect on iron • No effect on vitamin D • No effect on calcium • No effect on magnesium • No effect on potassium • No effect on sodium • No effect on zinc • No effect on selenium • No effect on iodine • No effect on copper • No effect on manganese • No effect on chromium • No effect on molybdenum • No effect on cobalt • No effect on nickel • No effect on boron • No effect on silicon • No effect on phosphorus • No effect on sulfur • No effect on oxygen • No effect on carbon • No effect on nitrogen • No effect on hydrogen • No effect on helium • No effect on neon • No effect on argon • No effect on krypton • No effect on xenon • No effect on radon • No effect on francium • No effect on actinium • No effect on thorium • No effect on protactinium • No effect on uranium • No effect on neptunium • No effect on plutonium • No effect on americium • No effect on curium • No effect on berkelium • No effect on californium • No effect on einsteinium • No effect on fermium • No effect on mendelevium • No effect on nobelium • No effect on lawrencium	None as desired target
<b>Product presentation</b>	Injectable with following pattern after 3 months: • No effect on weight • No effect on blood pressure • No effect on cholesterol • No effect on glucose • No effect on hemoglobin A1c • No effect on hemoglobin • No effect on ferritin • No effect on iron • No effect on vitamin D • No effect on calcium • No effect on magnesium • No effect on potassium • No effect on sodium • No effect on zinc • No effect on selenium • No effect on iodine • No effect on copper • No effect on manganese • No effect on chromium • No effect on molybdenum • No effect on cobalt • No effect on nickel • No effect on boron • No effect on silicon • No effect on phosphorus • No effect on sulfur • No effect on oxygen • No effect on carbon • No effect on nitrogen • No effect on hydrogen • No effect on helium • No effect on neon • No effect on argon • No effect on krypton • No effect on xenon • No effect on radon • No effect on francium • No effect on actinium • No effect on thorium • No effect on protactinium • No effect on uranium • No effect on neptunium • No effect on plutonium • No effect on americium • No effect on curium • No effect on berkelium • No effect on californium • No effect on einsteinium • No effect on fermium • No effect on mendelevium • No effect on nobelium • No effect on lawrencium	None as desired target
<b>Volume</b>	Injectable with following pattern after 3 months: • No effect on weight • No effect on blood pressure • No effect on cholesterol • No effect on glucose • No effect on hemoglobin A1c • No effect on hemoglobin • No effect on ferritin • No effect on iron • No effect on vitamin D • No effect on calcium • No effect on magnesium • No effect on potassium • No effect on sodium • No effect on zinc • No effect on selenium • No effect on iodine • No effect on copper • No effect on manganese • No effect on chromium • No effect on molybdenum • No effect on cobalt • No effect on nickel • No effect on boron • No effect on silicon • No effect on phosphorus • No effect on sulfur • No effect on oxygen • No effect on carbon • No effect on nitrogen • No effect on hydrogen • No effect on helium • No effect on neon • No effect on argon • No effect on krypton • No effect on xenon • No effect on radon • No effect on francium • No effect on actinium • No effect on thorium • No effect on protactinium • No effect on uranium • No effect on neptunium • No effect on plutonium • No effect on americium • No effect on curium • No effect on berkelium • No effect on californium • No effect on einsteinium • No effect on fermium • No effect on mendelevium • No effect on nobelium • No effect on lawrencium	None as desired target
<b>Substructure requirements</b>	Injectable with following pattern after 3 months: • No effect on weight • No effect on blood pressure • No effect on cholesterol • No effect on glucose • No effect on hemoglobin A1c • No effect on hemoglobin • No effect on ferritin • No effect on iron • No effect on vitamin D • No effect on calcium • No effect on magnesium • No effect on potassium • No effect on sodium • No effect on zinc • No effect on selenium • No effect on iodine • No effect on copper • No effect on manganese • No effect on chromium • No effect on molybdenum • No effect on cobalt • No effect on nickel • No effect on boron • No effect on silicon • No effect on phosphorus • No effect on sulfur • No effect on oxygen • No effect on carbon • No effect on nitrogen • No effect on hydrogen • No effect on helium • No effect on neon • No effect on argon • No effect on krypton • No effect on xenon • No effect on radon • No effect on francium • No effect on actinium • No effect on thorium • No effect on protactinium • No effect on uranium • No effect on neptunium • No effect on plutonium • No effect on americium • No effect on curium • No effect on berkelium • No effect on californium • No effect on einsteinium • No effect on fermium • No effect on mendelevium • No effect on nobelium • No effect on lawrencium	None as desired target
<b>Health benefits</b>	Injectable with following pattern after 3 months: • No effect on weight • No effect on blood pressure • No effect on cholesterol • No effect on glucose • No effect on hemoglobin A1c • No effect on hemoglobin • No effect on ferritin • No effect on iron • No effect on vitamin D • No effect on calcium • No effect on magnesium • No effect on potassium • No effect on sodium • No effect on zinc • No effect on selenium • No effect on iodine • No effect on copper • No effect on manganese • No effect on chromium • No effect on molybdenum • No effect on cobalt • No effect on nickel • No effect on boron • No effect on silicon • No effect on phosphorus • No effect on sulfur • No effect on oxygen • No effect on carbon • No effect on nitrogen • No effect on hydrogen • No effect on helium • No effect on neon • No effect on argon • No effect on krypton • No effect on xenon • No effect on radon • No effect on francium • No effect on actinium • No effect on thorium • No effect on protactinium • No effect on uranium • No effect on neptunium • No effect on plutonium • No effect on americium • No effect on curium • No effect on berkelium • No effect on californium • No effect on einsteinium • No effect on fermium • No effect on mendelevium • No effect on nobelium • No effect on lawrencium	None as desired target

Revised on April 26, 2014

FHI 360 and collaborators are currently evaluating multiple formulations

# Development of a Biodegradable Implant

Currently, implants require removal by a skilled provider

A biodegradable implant would address current problems including:

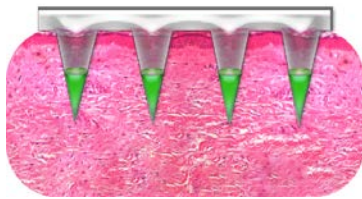
- Lack of trained personnel
- Inability among women to access or afford the procedure
- Burden on health system
- In addition, product with “intermediate” duration of efficacy would fill method mix gap

FHI 360 and collaborators are evaluating multiple designs/formulations

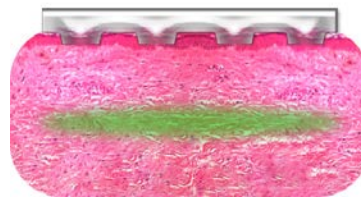


# Adapting microneedle patches for contraception

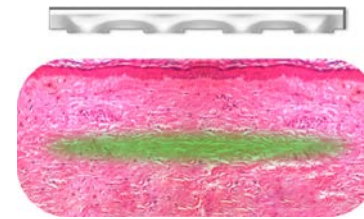
Targeting contraceptive steroid hormones to the dermal versus subcutaneous space



Microneedle patch is applied to skin

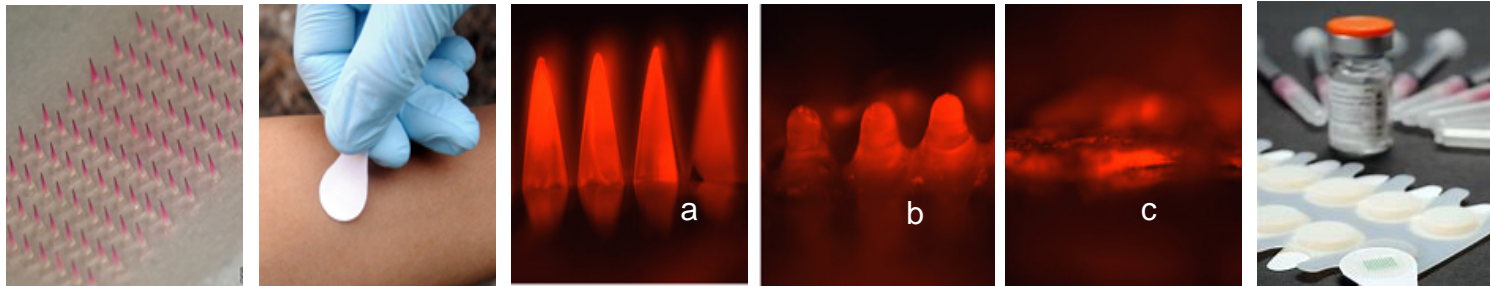


Microneedles dissolve and release the contraceptive



Sharps-free backing is removed and discarded

## Polymer Microneedles



Adapted from Micron Biomedical and Mark Prausnitz



# Microneedles Acceptability Research

**Goal:** Incorporate end user feedback into product design decisions

**Study objectives:**

- Explore initial acceptability of the microneedle patch for contraceptive delivery and potential barriers to use;
- Define desired qualities or characteristics of a microneedle patch for contraceptive use;
- Quantify relative importance of various contraceptive microneedle patch attributes

**Study sites:** New Delhi, India and Ibadan, Nigeria





# Contraceptive Technology Innovation

## Global Knowledge Sharing

# CTI Exchange



CONTRACEPTIVE  
TECHNOLOGY **INNOVATION** EXCHANGE

## CALLIOPE

*kah-LY-ah-pee*

Contraceptive Pipeline  
Database

**Calliope, the Contraceptive Pipeline Database**, includes information on potential contraceptive targets and leads, products in development, and a selection of products only available in limited markets.



## CAPRI

Contraceptive Active  
Pharmaceutical Ingredient  
Database

**CAPRI, the Contraceptive Active Pharmaceutical Ingredient Database**, lists biological and chemical properties for 27 active pharmaceutical ingredients found in contraceptives, along with data on their pharmacology, toxicology, impurities, metabolites, and use in marketed products.

[www.ctiexchange.org](http://www.ctiexchange.org)



**Thank you!**  
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