Contraceptive Technology Update
And is there an Unfinished Agenda?
2011 International Conference on FP
December 1, 2011

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Office of Population and RH
Bureau for Global Health
USAID/Washington
TOPICS:

- Rationale for Family Planning
- Family Planning Use and Need in Africa
- Priorities in Contraceptive Technology
- Existing/Current Contraceptive Technology
- LAPMs
  - Sino-Implant (Zarin)
  - NES/EE Vaginal Ring
  - LNG-IUS
- Depo-Provera SubQ and Uniject
- SILCS Diaphragm
- Women’s Condom
- Priorities for New Contraceptive Methods
Family Planning: Responds to a panoply of problems

- Enables couples to decide number-spacing of births
- Reduces child mortality
- Reduces maternal mortality/morbidity
- Reduces abortion
- Improves women’s opportunities
- Key intervention in HIV settings
- Essential component of health programs
- Mitigates adverse effects of population dynamics on:
  - natural resources, including water and food
  - environment and climate change
  - economic growth
  - state stability
  - Infectious diseases (zoonotic)
Priorities in Contraceptive Technology

Concerning contraceptive technology, the priorities for preventing unintended pregnancies are:

- Expand access to, and availability of, existing contraceptive methods in the public and private sectors, in facilities/clinics and in non-clinical and community based programs.

- Tinker with existing methods to make them easier to use, easier to deliver, less expensive, and/or more acceptable, sometimes referred to as “adaptive technologies.”

- Develop totally new technology that is viewed by programs as filling a vital function that cannot be met by existing or adaptive technologies.
**EXISTING CONTRACEPTIVE TECHNOLOGY**

**MORE EFFECTIVE**
Less than 1 pregnancy per 100 women in one year

- **Implants, IUD, female sterilization:** After procedure, little or nothing to do or remember
- **Vasectomy:** Use another method for first 3 months
- **Injectables:** Get repeat injections on time
- **Lactational Amenorrhea Method (for 6 months):** Breastfeed often, day and night
- **Pills:** Take a pill each day
- **Patch, ring:** Keep in place, change on time
- **Condoms, diaphragm:** Use correctly every time you have sex
- **Fertility awareness methods:** Abstain or use condoms on fertile days. Newest methods (Standard Days Method and TwoDay Method) may be easier to use.
- **Withdrawal, spermicides:** Use correctly every time you have sex

**LESS EFFECTIVE**
About 30 pregnancies per 100 women in one year
Long-Acting & Permanent Methods

- Highly effective
- Long lasting
- High continuation / low discontinuation
- Cost-effective
- Wide eligibility
Zarin® (Sino-implant II)

- **Subdermal Contraceptive Implant**
## Comparison of Hormonal Implants

<table>
<thead>
<tr>
<th></th>
<th>Jadelle</th>
<th>Implanon</th>
<th>Sino-implant (II)/Zarin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Manufacturer</strong></td>
<td>Bayer Healthcare</td>
<td>Merck/MSD</td>
<td>Shanghai Dahua Pharmaceutical Ltd.</td>
</tr>
<tr>
<td><strong>Formulation</strong></td>
<td>150 mg levonorgestrel in 2 rods</td>
<td>68 mg etonogestrel in 1 rod</td>
<td>150 mg levonorgestrel in 2 rods</td>
</tr>
<tr>
<td><strong>Mean Insertion &amp; Removal time</strong></td>
<td>Insertion: 2 min Removal: 5 min</td>
<td>Insertion: 1 min Removal: 2-3 min</td>
<td>Insertion: 2 min Removal: 5 min</td>
</tr>
<tr>
<td><strong>Labeled duration</strong></td>
<td>5 years</td>
<td>3 years</td>
<td>4 years</td>
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<tr>
<td><strong>Trocars</strong></td>
<td>Autoclavable / Disposable</td>
<td>Pre-loaded disposable</td>
<td>Disposable</td>
</tr>
<tr>
<td><strong>Cost of implant (US$)</strong></td>
<td>$21.00</td>
<td>$18.00</td>
<td>$8.00</td>
</tr>
<tr>
<td><strong>Cost per Year (if used for duration)</strong></td>
<td>$4.20</td>
<td>$6.00</td>
<td>$2.00</td>
</tr>
<tr>
<td><strong>WHO Prequal</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Application submitted</td>
</tr>
</tbody>
</table>

1 FOB price in country of origin.
Sino-implant (II) Registration Status
Nov 2011

Registered (n=19)
Burkina Faso†
Cambodia†
Chile
China
Fiji†
Ghana†
Indonesia
Kenya†
Madagascar†
Mali †
Mozambique‡
Malawi ‡
Mongolia†
Nepal
Pakistan†
Sierra Leone‡
Uganda‡
Zambia‡
Zanzibar‡

†Distributed by Marie Stopes International (MSI);
‡ Distributed by Pharm Access Africa Ltd. (PAAL)
Nestorone® / Ethinyl Estradiol 1-Year Ring (CVR)

8.4 mm (3/8”) in cross section

58 mm (2 1/4”) in diameter

*Delivers NES/EE 150/15µg /day, 13 cycles 3 weeks on followed by 1 week off

Developed by the Population Council
Sponsored by USAID, NICHD, WHO
Most trial participants were satisfied, found the CVR easy to use, would pay for it if available, recommend it to friends, and preferred it to other methods they have used (Results: N=861)
Acceptability & Pregnancies: Adherence (T2)

- **P < 0.01**

**How Often Do You Remove the Ring?**
- Not Pregnant:
  - Never: 80%
  - Rarely: 20%
  - Sometimes: 10%
  - Very Often: 10%

**How Many Times in the Past 3 Weeks Did You Take the Ring Out and Leave It Out for More Than 2 Hours?**
- Not Pregnant:
  - Sometimes: 10%
  - Rarely: 10%
  - Never: 80%

- Pregnant:
  - Sometimes: 40%
  - Rarely: 40%
  - Never: 20%
The CVR is an effective, convenient, easily-used new contraceptive method.

**Strengths**

- **Monthly ring-good for one year**
  - Daily action not required
  - Not coitus dependent
  - Eliminates need for repeated visits to doctor & pharmacy
- **Effective**
- **Lack of androgen effect**
  - Weight /lipids favorable
- **High level of user satisfaction**
- **Under a woman’s control**
  - She decides when to stop & start
  - No need for a trained health provider
  - Rapid return to fertility if desired

**Challenges**

- Medical risks & side effects similar to currently available hormonal contraceptives
- Additional safety requirements regarding effect of NCE on cardiac rhythm a new “requirement”- studies still to be done for NDA
- **NDA expected in 2013-2014**
- Manufacturing process improvements underway
- Totally new process needed to meet the requirement that it must be low cost!
The Best of Both Worlds

Oral contraceptives

• Highly effective
• Reduction of menstrual loss
• Reduction of pelvic inflammatory disease

Intrauterine devices

• No daily motivation
• Long-acting
• Estrogen-free
• Rapidly reversible

Levonorgestrel intrauterine system
The levonorgestrel intrauterine system
Change in hemoglobin during 5 years of use
New formulation of Depo-Provera: Depo-subQ Provera 104, for delivery with Uniject

Potential “home run”

Depo-subQ Provera 104:
- New formulation for subQ injection
- 30% lower dose (104 mg vs. 150 mg)
- Rapid onset of action
- Same effectiveness, same length of protection (>3 months)
- Approved by USFDA (2005) and EMA/UK

Uniject:
- Single dose, single package
- Prefilled, sterile, non-reusable
- Short needles for subQ injection (easier use by non-clinical personnel/CHWs)
- Compact; easy to use and store
- Potential for home- and self-injection
- Approval by EMA and LDC registration forthcoming
- PK study completed for injection in arm; Acceptability studies to begin in early 2012; Available for roll-out in late 2012-2013
The LD Formulation of Depo-Provera Is Efficacious at Lower Peak Concentrations

Pharmacokinetic Profiles of the LD Formulation of Depo-Provera and Depo-Provera Contraceptive Injection

**Data on file.**

LD = lower dose.
YOU WANT ME TO PUT WHAT WHERE?!
SILCS Diaphragm: “One size fits most”

Firm insertion edge w/ soft spring in rim for improved comfort

Cervical cup membrane

Silocone rather than latex
Appropriate for OTC use
No pelvic exam or fitting required

Grip dimples and easy insertion

Fingertip dome for easy removal

US CT completed in 2010
USFDA approval in 2012
Woman’s Condom

- Easy to handle/use, insert and remove
- Stable during use
- Comfortable for both partners
- Less expensive than current options
Product Features

- Manufactured by Dahua (China – not same company as for SI-II)

- U.S. clinical trials (2011-2012) will lead to FDA product registration – estimated for 2013

- CE Mark application planned for 2011
New Contraceptive Methods Needed

While tremendous success can be achieved by expanding access to existing methods, some additional methods would likely have immediate application if they were of low cost:

1. Non-hormonal, non-steroidal or non-estrogen or novel progestin-only oral contraceptives
2. Biodegradable progestin-only implants (APS)
3. Non-surgical methods of male and female sterilization
4. Novel multi-purpose/dual protection methods (APS)
5. Post-testicular methods for men
Biodegradable Contraceptive Implant

Picture shows actual size of Anterion Therapeutic's injector and medicinal pellets. The area on the arm indicated by a circle and arrow illustrates the lack of scarring post implantation.
Aim: develop multipurpose prevention options that…

- Prevent unintended pregnancy
- Protect against HIV, other STIs & RTIs
- Provide additional health benefits

Our Ultimate Goal:
An expanded range of
- Effective
- Acceptable
- Accessible

prevention options that address the sexual and reproductive health concerns of women as they change over time.
58 technologies in the contraceptive R&D pipeline

<table>
<thead>
<tr>
<th>Discovery (Target ID, proof-of-principle)</th>
<th>Early Development (Pre-clin, Ph1, Ph2)</th>
<th>Late Development (Ph3)</th>
<th>Developing world registration / Launch</th>
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<tbody>
<tr>
<td>• GnrH II receptor antagonists</td>
<td>• Estetrol + Progestin OC</td>
<td>• Nestorone/EE Vaginal Ring</td>
<td>• Sino-implant (II)</td>
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<td>• LNG butanoate</td>
<td>• Ulipristal Vaginal Ring</td>
<td>• Gestodene and EE Patch</td>
<td>• DMPA + Uniject</td>
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<tr>
<td>• Nestorone/E2 Vaginal Ring</td>
<td>• Nestorone/E2 transdermal gel</td>
<td>• BufferGel</td>
<td>• Ortho Evra</td>
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<td>• Single-rod gestodene implant</td>
<td>• LNG as pericoital gel</td>
<td>• Generic LNG IUS</td>
<td>• Progesterone Only Vaginal Ring</td>
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<tr>
<td>• LNG as pericoital OC</td>
<td>• Meloxicam</td>
<td>• LNG as pericoital OC</td>
<td>• Femilis IUS</td>
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<td>• PC6-inhibitor</td>
<td>• β-hCG</td>
<td>• Cyclofem</td>
<td>• ellaOne®</td>
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<td>• LIF and IL-11</td>
<td>• Erythromycin sterilization</td>
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<td>• SGK1/AKT</td>
<td>• Polidocanol sterilization</td>
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<td>• 4 GCE technologies</td>
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<td>• Carica papaya extract</td>
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<td>• Testicular ultrasound</td>
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<td>• HIFU (High intensity focused ultrasound)</td>
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