

# Responding to Frequently Asked Questions



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# Overview

- If microbicides are such a good idea, why aren't the pharmaceutical companies investing?
- How would it fit within an overall program of HIV prevention?
- How much would it cost to ensure success?
- If a microbicide were available, what public health benefit might we reasonably expect?
- Shouldn't we be concerned about introducing a method that is less efficacious than male condoms?

# So, why is Big Pharma not investing?

- Perception that only poor people need this product
- Concerns about liability and regulatory uncertainty
- Belief that the potential global market is small
- Relative disinterest on the part of most companies in non-prescription drugs

# Ultimately, the killer is “uncertainty”

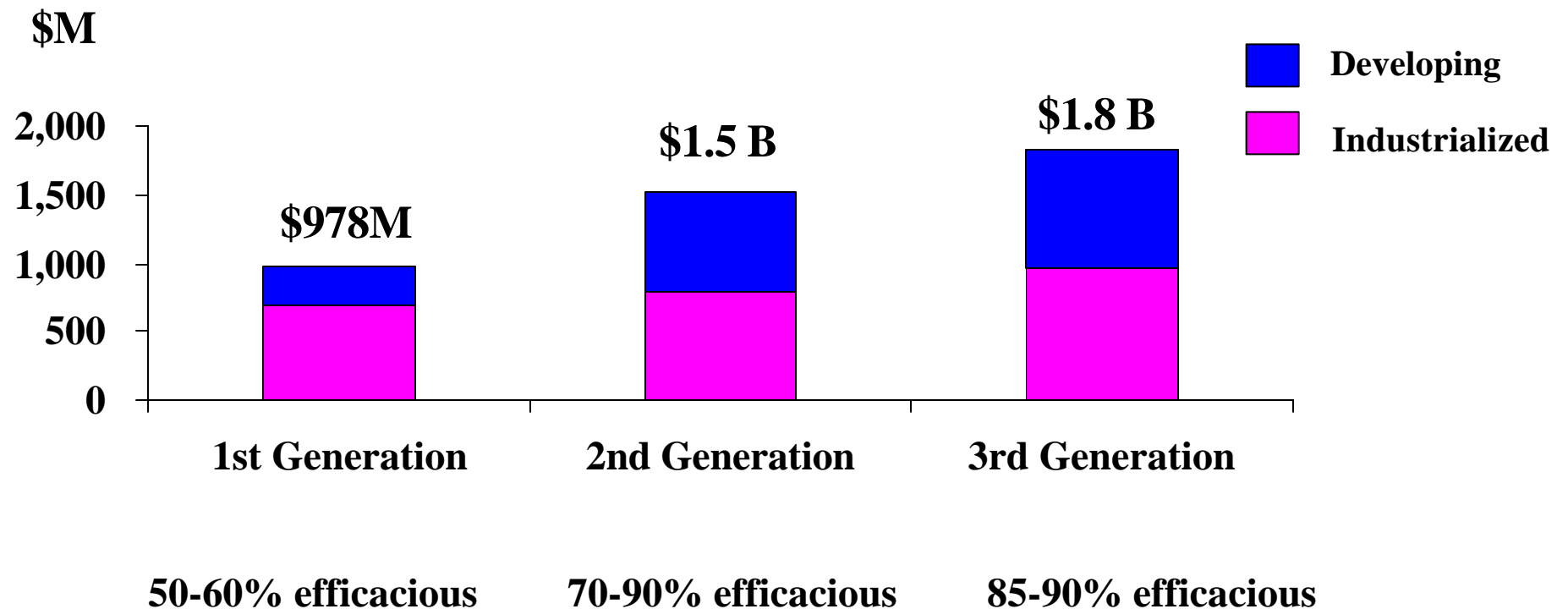
- As an entirely new type of product, it is difficult for pharmaceutical executives to estimate either the costs of development or the potential market
- Need to please stock-holders drives investment decisions towards projects with certain, quantifiable returns

# Rockefeller-funded Pharmaco-Economics Study

- Big Pharma is not investing because in the short term, it is not in their economic self-interest to do so
- The potential returns on investment in a first generation microbicide are negative (i.e. profit potential does not cover costs of development and capital)
- In the short term, government and foundation funding will remain critical

# Longer-term market is sufficient to attract private investment

## Total peak market potential



# The Microbicide Market in Global Context

Female condom	\$6 M
Dental Floss	\$230 M
<b>Microbicide, 3<sup>rd</sup> generation</b>	<b>\$1,440 M</b>
Viagra	\$1,500 M
Oral contraceptive	\$2,240 M
Male condom	\$4,000 M
Shampoo	\$10,992 M

Manufacturer's sales assumed to be 80% of retail

# Take Home Message

- Public subsidy will be required to bring the first generation of microbicide to market
- Advocacy for government and donor funding is therefore essential
- Eventually, the global market for microbicides will be sufficient to attract private capital

# How would microbicides be positioned in an overall program of STI/HIV prevention?

- Microbicides will likely always remain a “second best” option to the male condom
- Prevention messages would shift to a hierarchy of options:
  - *Use a condom and a microbicide every time you have sex; if you absolutely can't use a condom, use a microbicide alone*
- They should not be positioned as a “magic bullet” that eliminates the need to promote condoms or address underlying power imbalances

# GLOBAL HEALTH CONTEXT

## Important Part of Overall Effort to Combat the Epidemic



- Vaccines

- Male and female condoms

- Anti-retroviral therapies

- Anti-retroviral therapies (mother-to-child)

- Opportunistic infection therapies

- Basic care

- **Microbicides**

**Microbicides offer a woman-controlled method to reduce transmission**

# How much will it cost?

<b>Total costs per-product</b> (post discovery)	<b>\$57 million</b>
Pre-clinical development	\$4.5 million
Average cost of phase I trial	\$2.5 million
Phase II	\$3.0 million
<b>Phase III</b>	<b>\$46.4 million</b>
Registration	\$1.0 million

# Observations about costs

- Costs go up exponentially when products enter phase III trials
- When estimating resource needs for the field, one must anticipate the costs of “product failures” as well as the costs of “capital”
- BCG model estimates that it would take \$775 million over 5 years to achieve high likelihood of getting one or more products by 2010.
- This should be considered a “minimum”

# What would this investment buy in terms of saved lives and money?

- A 60 % efficacious microbicide introduced into 73 low income countries would avert **2.5 million** HIV infections over 3 years in women, men and infants

--Watts & colleagues, LSHTM

Women newly infected with HIV (2001)	1.8 million
Adult AIDS Deaths (2001)	2.4 million

# Methodology (Watts et al, 2002)

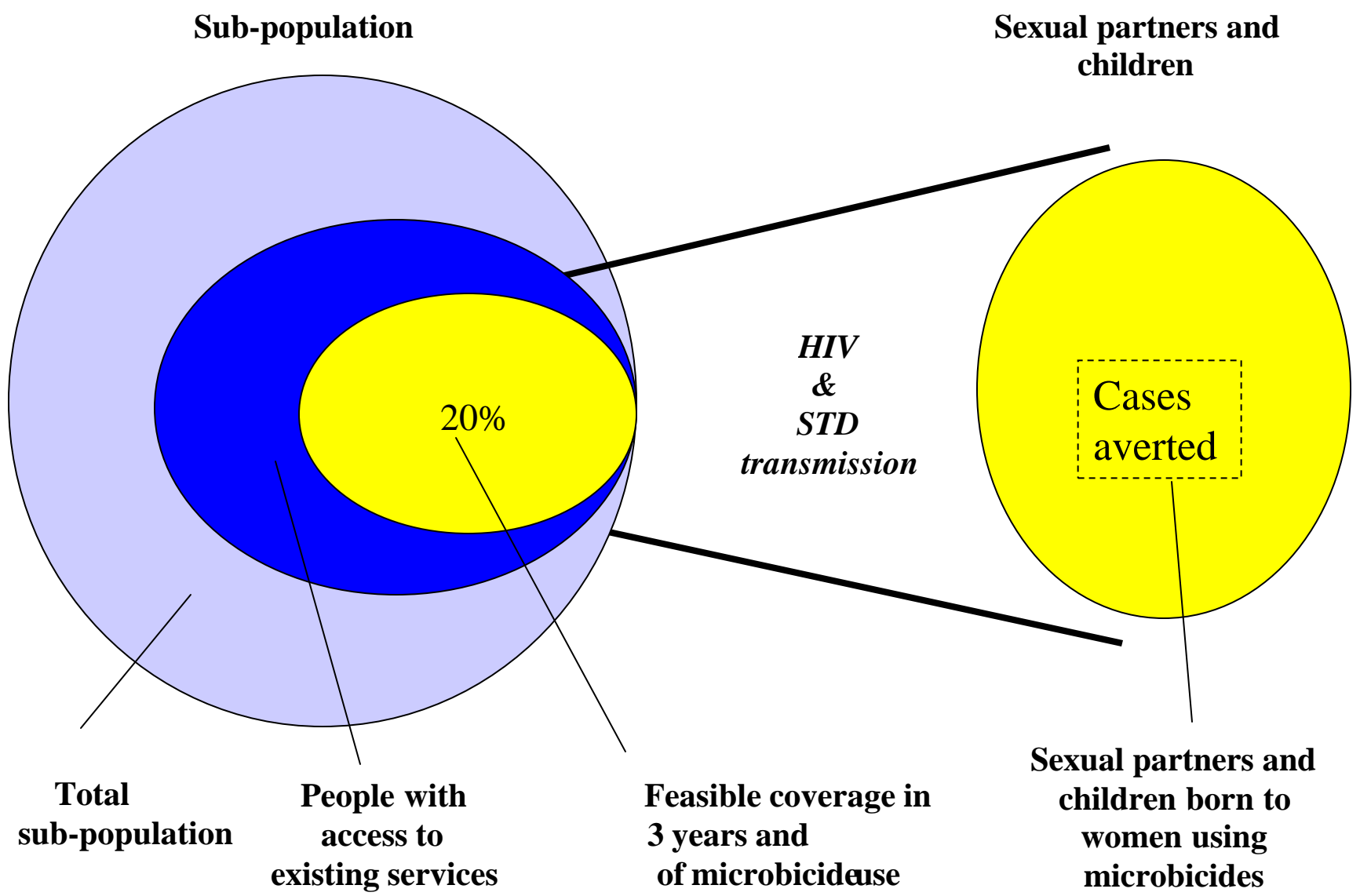
- Estimate is based on sophisticated computer models that estimate the impact of microbicide use on the chain of HIV transmission in different sexual networks
- Models predict HIV transmission among:
  - Sexually active youth
  - Sex workers and clients
  - Women in regular partnerships
  - IVDUs and sex partners

# How do the models work?

- User inputs initial data/assumptions
  - underlying prevalence of STDs/HIV
  - condom coverage & consistency of use; “migration”
  - efficacy of microbicide against HIV & STD
- Model calculates patterns of spread of HIV & STDs over time, with no intervention, condom use only, & condoms and microbicides
- Calculates HIV infections averted over time with and without microbicides for each sub-population

# This estimate conservatively assumes...

- Microbicides are effective only against HIV, not other STDs
- Microbicides are taken up by only 20% of individuals already in contact with services
  - women 15-44 using modern contraception
  - sexually active youth in school
  - sex workers in contact with HIV prevention projects
  - IV drug users in contact with prevention services
- Those who use microbicides do so in 50 percent of acts where they do not use condoms



# **Economic Savings (over 3 years)**

## **Watts et al, 2002**

- **Health care costs averted** **\$2.7 billion**  
(includes only forms of care currently available--no ARVs  
  
(uses country-specific estimates of access to health care)
- **Productivity benefits** **\$1.0 billion**  
(includes time lost for work; training of replacement staff)

# Take Home Messages

- Even a relatively low efficacy microbicide could have a large impact on the epidemic
- The magnitude of impact is strongly influenced by coverage and use

<u>Coverage</u>	<u>Infections averted*</u>
10%	1.4 million
20%	2.5 million
30%	3.6 million

\* over 3 years

# Confronting partial effectiveness

- Concern has been raised about introducing a method that is less efficacious than condoms
- Will individuals default from condoms to microbicides because they are easier to use?
- What should our counseling message be?

## Shift to a “harm reduction approach”

- Microbicides will be promoted as an adjunct and/or back-up to condoms, not as an alternative
- Counseling messages will be presented as a “hierarchy” of options
- Three lines of evidence suggest that introducing microbicides will lead to *more* protection rather than *less*
  - ⇒ experience from family planning
  - ⇒ insights from modeling
  - ⇒ research data

# Experience from Family Planning

- Addition of each new method *increases* overall number of protected acts and *decreases* unintended pregnancies
- Adding a new contraceptive method to those available in an existing program increases prevalence by about 12 percentage points and decreases crude birth rate by 5.3 points

(Ross, J & E. Frankenberg. 1993 *Findings from Two Decades of Family Planning Research*. Population Council)

## Insights from modeling

# The Prevention Equation

- Level of protection conferred (*the number of cases averted*) depends on the product of three factors:
  - ◆ Efficacy of the method
  - ◆ Consistency of use within a partnership
  - ◆ Extent of use in a sub-population (coverage)

# The Prevention “Trade-Off”

- A low efficacy method used consistently can achieve the same protection as a high-efficacy method used less consistently
- A 90% efficacious method (like condoms) used in 20% of sex acts, provides less protection than a:
  - 70% efficacy used > 30% of the time
  - 50% efficacy used > 40% of the time
  - 30% efficacy used > 60% of the time

# What about condom “migration”?

(defaulting from condoms to microbicides)

- South Africa

- Women were given a **choice of three methods** (male condom, female condom and N-9 suppository) and four skill building sessions
- use of some form of protection **increased from 16% to 72%** with no evidence of individuals abandoning the male condom
- without the female condom and suppository option, **14% fewer women** would have been using any form of protection

# Mathematical modeling suggests....

- Under most circumstances, substantial migration can be tolerated without increasing risk of infection
  - either at the level of individuals
  - or among sub-populations
- Migration is potentially a problem only where condom use is high ( $> 70\%$ ) and achieved microbicide consistency is low ( $< 50\%$  of non-condom protected acts)

(Foss et al, 2002)

# Reductions in condom consistency that could be tolerated without increasing risk

*Microbicide HIV/STI efficacy = 50%;  
Used in 50% of acts not protected by condoms*

Condom Consistency

Condom Consistency

BEFORE

AFTER

30%

5%

50%

32%

70%

59%

90%

86%

- If consistency of microbicide use can be increased to 100% of sex acts not protected by condoms, then:
  - Low consistency condom users (30%) could migrate entirely
  - Middle consistency condom users (50%) could migrate entirely
  - Condom use among high consistency users (70%) could drop to 37% of acts
  - Condom use among very high users (90%) could drop to 79% of acts

Assumes microbicide is 50% efficacious against HIV and other STDs

# At a population level....

- For every three high consistency condom users (at 90% consistency) who reduce their condom use to 80%, you need only recruit one non-user to 50% microbicide use in order to have a positive impact on infection rates at a population level.
- If initial condom consistency is 75%, one new recruit to 50% microbicide use compensates for every 20 condom migrators

Assumes microbicide is 50% efficacious against HIV and other STD