

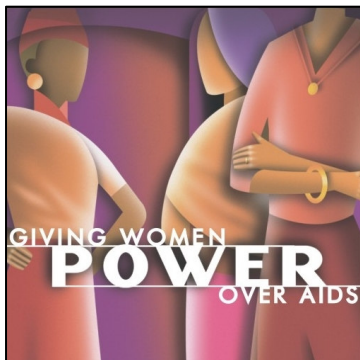
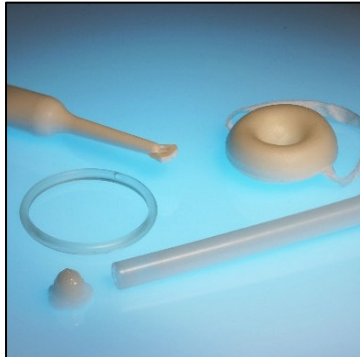
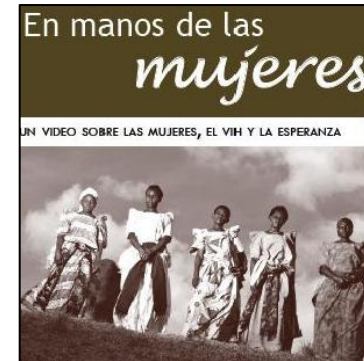
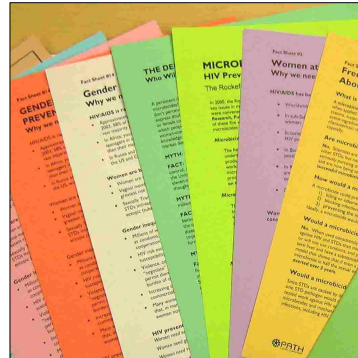
# Standards of Prevention in HIV Prevention Trials

March 26-28, 2009

Lori Heise, Director



Global Campaign  
FOR Microbicides



# GCM Role in Trial Ethics

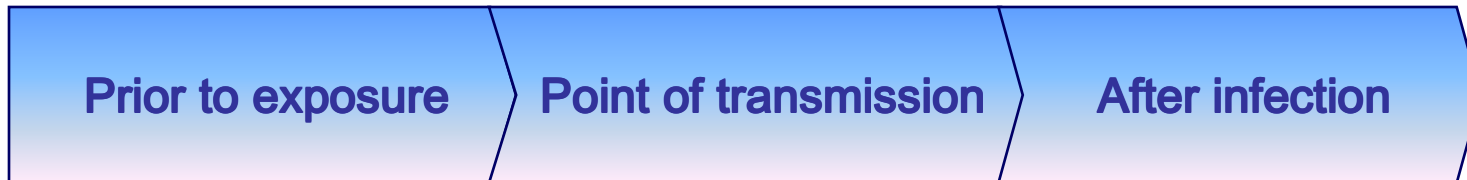
- **Forge consensus** around ethical debates that could delay progress
- **Help negotiate** the fine line between urgency of the HIV epidemic and need for rigorous ethical standards
- **Build capacity** in the activist/civil society sector for ethical deliberation

**Why are we here?**

# Overview of talk

- Review of HIV prevention strategies being tested
- Current trials and the special challenges of prevention research
- What does ethics guidance say on standards of prevention?
- Goals of this consultation

# Prevention Strategies



- Education & Behavior change

- Male circumcision

- Preventive Vaccines

- Pre-exposure prophylaxis (PREP)

- HSV2 suppression

Point of transmission

- Male and female condoms

- PMTCT (mother-to-child)

- Post exposure prophylaxis (PEP)

- Microbicides

- Diaphragm, cervical barriers & new FCs

After infection

- Prevention for Positives

- Therapeutic Vaccines

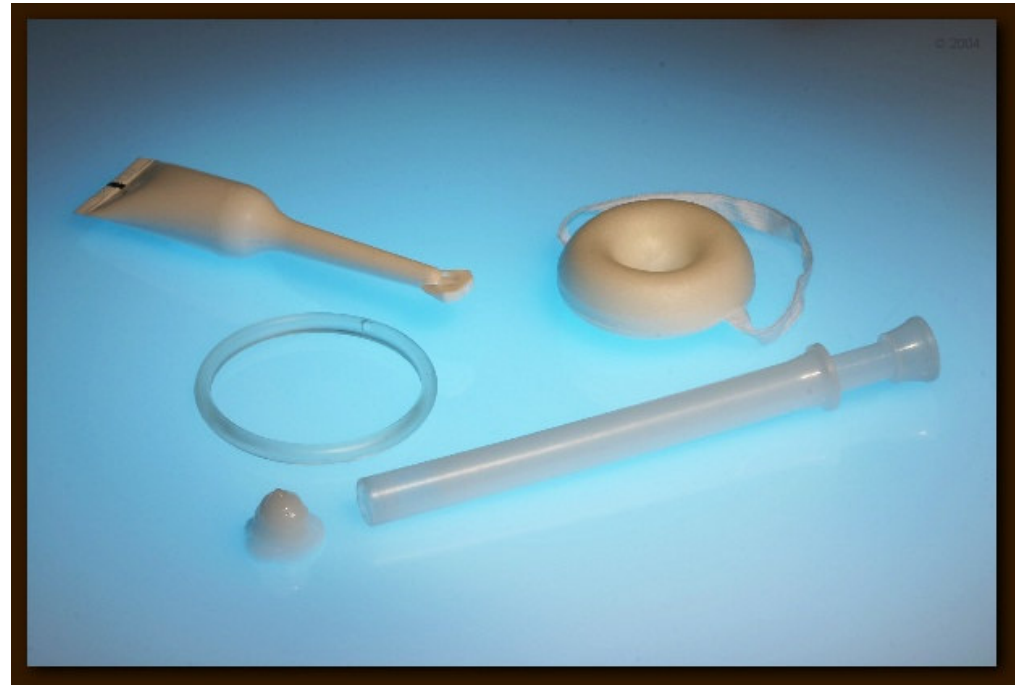
- Treatment of infected partner

# New ARV-based Strategies

## PrEP



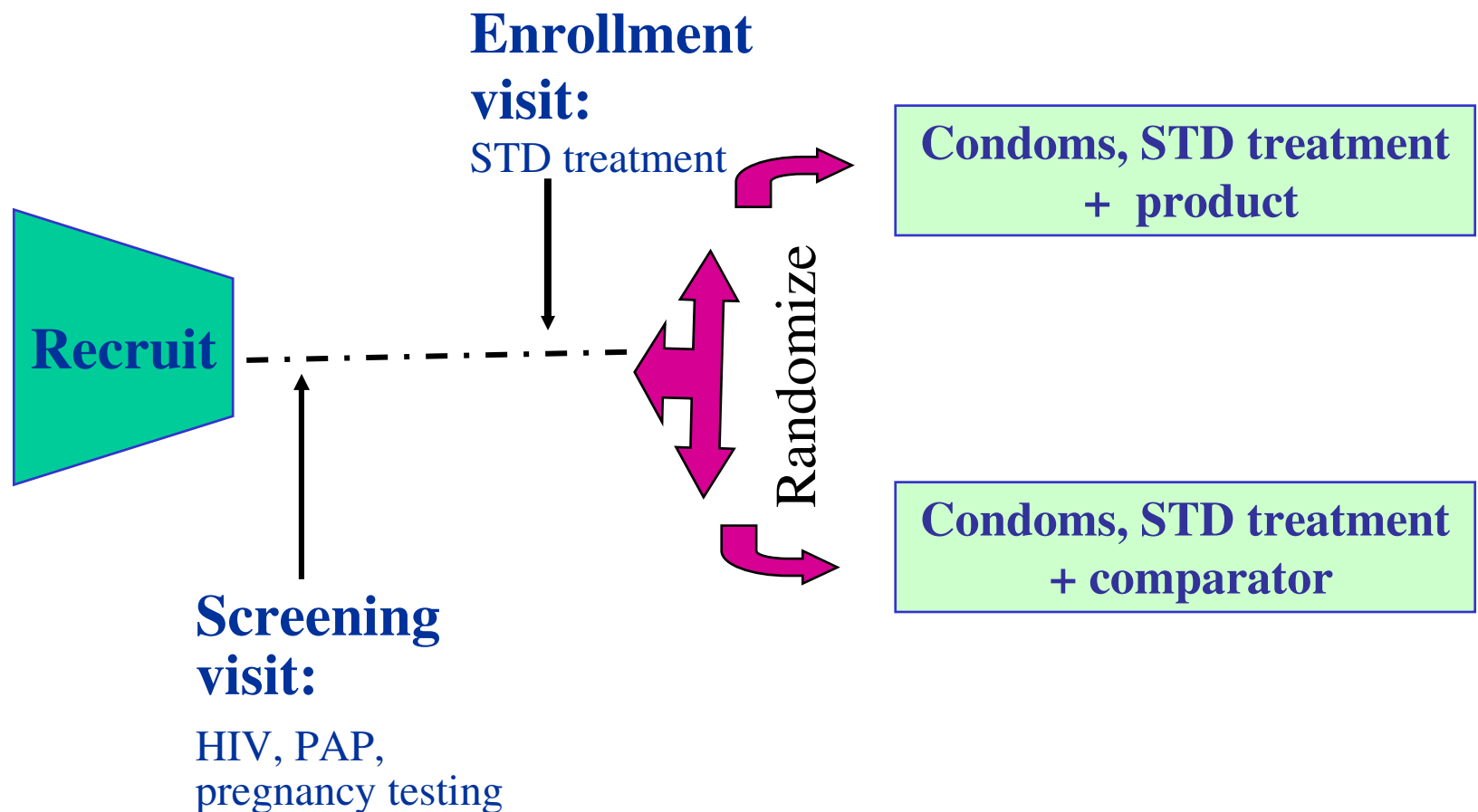
## Microbicides



# Vaginal versus Oral Agents

- **Vaginal/Rectal**
  - Higher levels in genital tissue
  - May not work against all routes of exposure, like IDU
  - Potential for long-acting formulations (e.g rings)
  - Less systemic exposure
    - potentially less need for medical monitoring
  - Potential use in pregnancy/Breast feeding
- **Oral Delivery (Pills)**
  - Greater efficacy ?
  - Pills may be preferred by some people
  - Greater toxicity ?
  - More resistance?
  - Overlap with treatment may increase chance of drug appropriation or sharing

# Basic Design of HIV Prevention Effectiveness Trials (Phase 2B or 3)



# Prevention trial realities

- Most HIV efficacy trials are multi-site and enroll between 2,000 and 10,000 participants
- Trials must enroll populations with at least 3-4 percent incidence to be viable
- Often this means enrolling vulnerable populations – sex workers, IDUs, MSM, or women in high risk partnerships
- Several trials have had to close down or add sites because incidence rates turned out to be too low

# Prevention Trial Realities

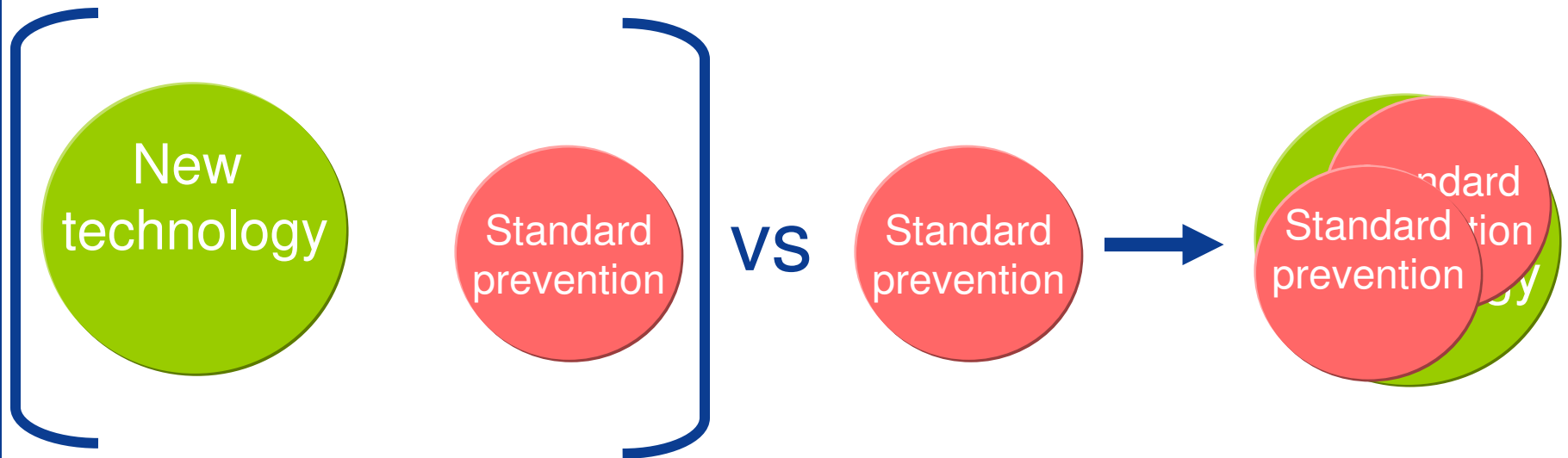
- All new methods are likely to reduce but not eliminate risk of HIV acquisition.
- Current trials are powered to detect a reduction in incidence between the groups of 40 to 60 percent.
- Many trials are designed as phase 2B screening trials and licensure or implementation may require additional trials.
- Unlike treatment trials, prevention trials enroll healthy people; plus there are no clear surrogate endpoints.

# Evaluating New Prevention Technologies

Intervention

Control

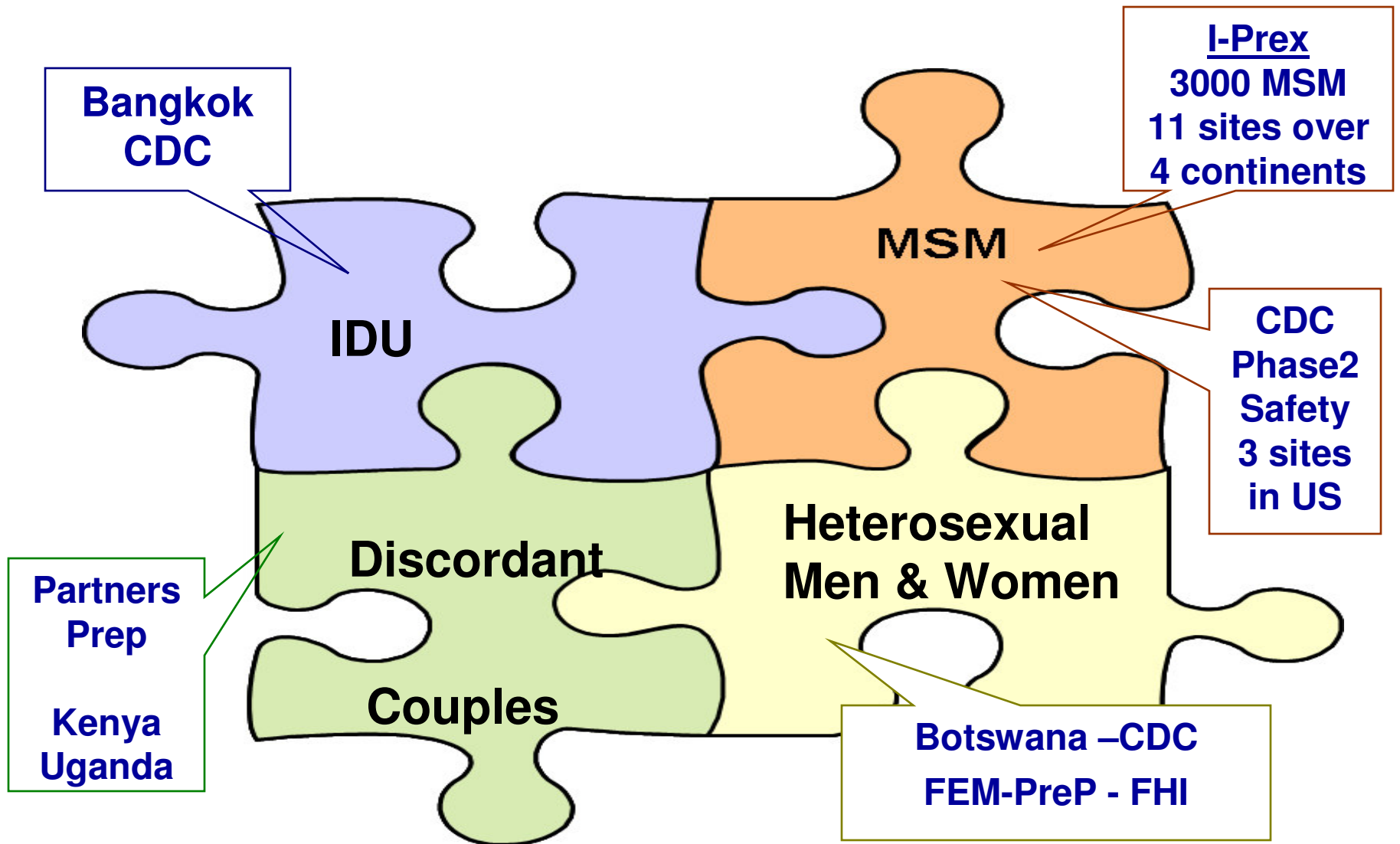
Attributable fraction



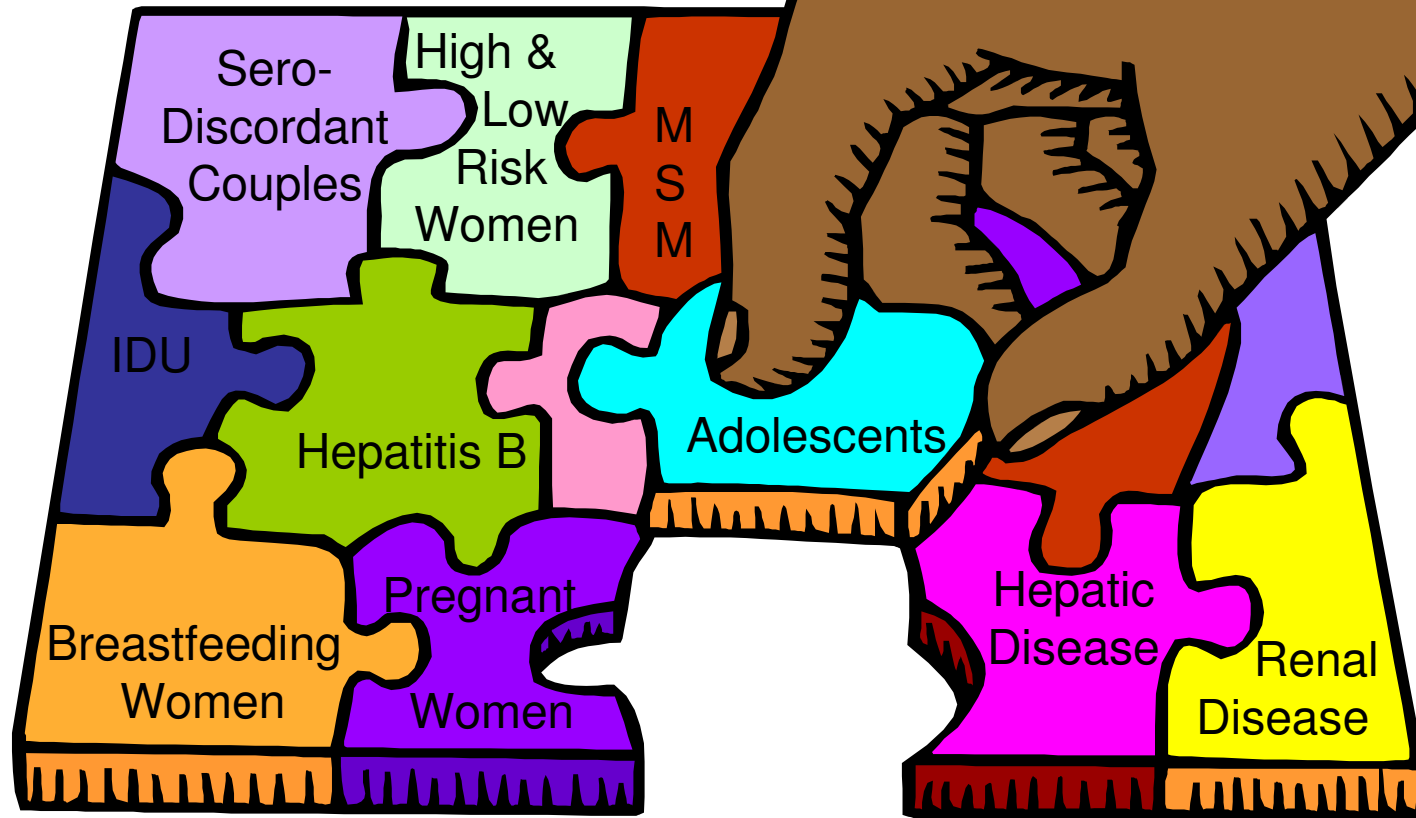
*Source: N. Padian (pers. comm.)*

# On-Going Studies

# The Ongoing PrEP Studies



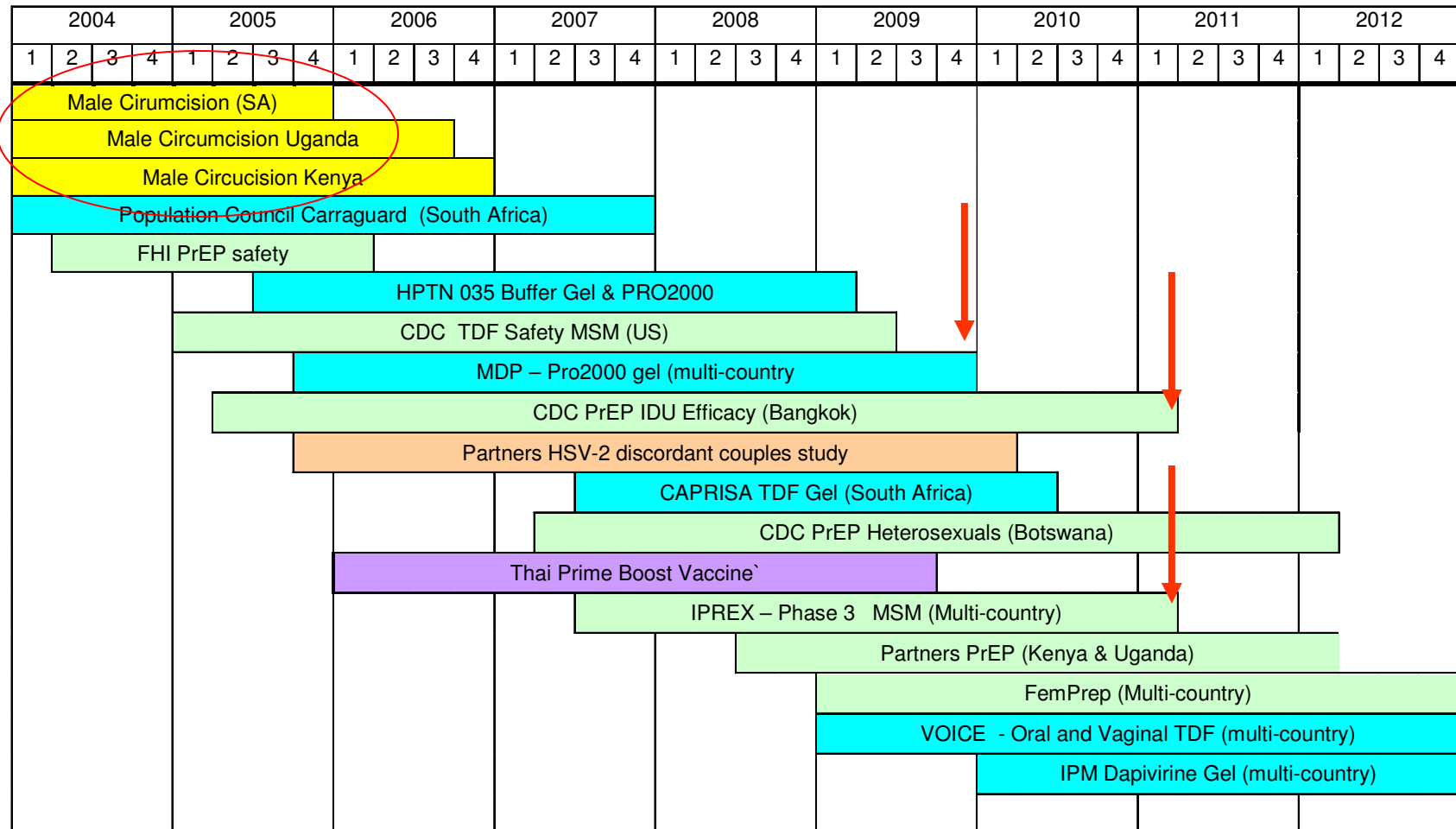
# More studies will be needed...



## To complete the PrEP puzzle

Hillier, CROI 2009

# Recent and planned prevention trials



# **Standards of Prevention**

**What Does Current Ethics  
Guidance Say?**

# Declaration of Helsinki (2008)

## Paragraph 32

- The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the *best current proven intervention*
- Use of placebo or no treatment, is acceptable in studies...where for **compelling and scientifically sound methodological reasons** the use of placebo is necessary to determine the efficacy or **safety of an intervention** and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm.

## CIOMS (2002) Guideline 11:

- Research subjects in the control group of a trial ...should receive *an established effective intervention*.
- In some circumstances it may be ethically acceptable to use an alternative comparator, such as placebo or "no treatment".

## US National Bioethics Advisory Commission: Recommendation 2.2

- Researchers and sponsors should design clinical trials that provide members of any control group with **an established effective treatment, whether or not such treatment is available in the host country.**
- Established means “has achieved widespread acceptance by the medical community (2001; 28)”

## Nuffield Council (2002) Chapter 7:

- *... where it is not appropriate to offer a universal standard of care, the minimum standard of care that should be offered is the **best available intervention as part of the national public health system for that disease.***

# UNAIDS/WHO (2007)

## Guidance Point 13:

- Researchers, research staff, and trial sponsors should *ensure....that appropriate counseling and access to all state of the art HIV risk reduction methods are provided to participants*
- New HIV risk-reduction methods should be added, based on consultation among all research stakeholders including the community, as they are scientifically validated or as they are approved by relevant authorities.

# Word Play...

- Be offered.... (Nullfield Council)
  - Be assured of... (Council of Europe)
  - Be provided (Helsinki)
  - Receive (CIOMS)
- 
- An established effective intervention
  - Best current available anywhere
  - Practically attainable and sustainable
  - Proven methods
  - Highest attainable
  - State of the art

# Questions we will explore

- What is the range of current practice in terms of standards of prevention in HIV trials?
- What ethical frameworks can we use to guide our thinking?
- What impact would adding methods have on our ability to evaluate new methods?
- Are we approaching a “feasibility threshold” where it may become increasingly difficult, if not impossible, to evaluate new methods?
- If so, would the urgent public health need for new tools ever justify modifying the prevention package?

# Goals for this Consultation

- Refine our understanding of the scientific, ethical and community issues that are relevant to deciding which prevention services should be offered in future HIV prevention trials
- To the extent possible, identify criteria or processes to aid future decision making
- Identify areas of group agreement and disagreement
- Suggest important next steps for moving this issue forward.

# Thank You

[www.global-campaign.org](http://www.global-campaign.org)



Special thanks to Sharon Hillier,  
Mitchell Warren, Liz McGrory  
and Sean Philpott