

MTN : A Year in Review and the Challenges Ahead

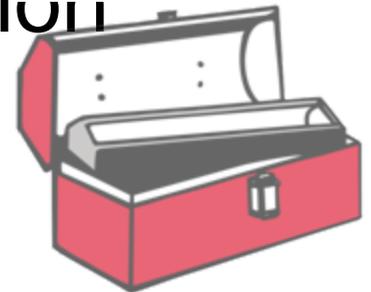
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MTN CORE

Overview

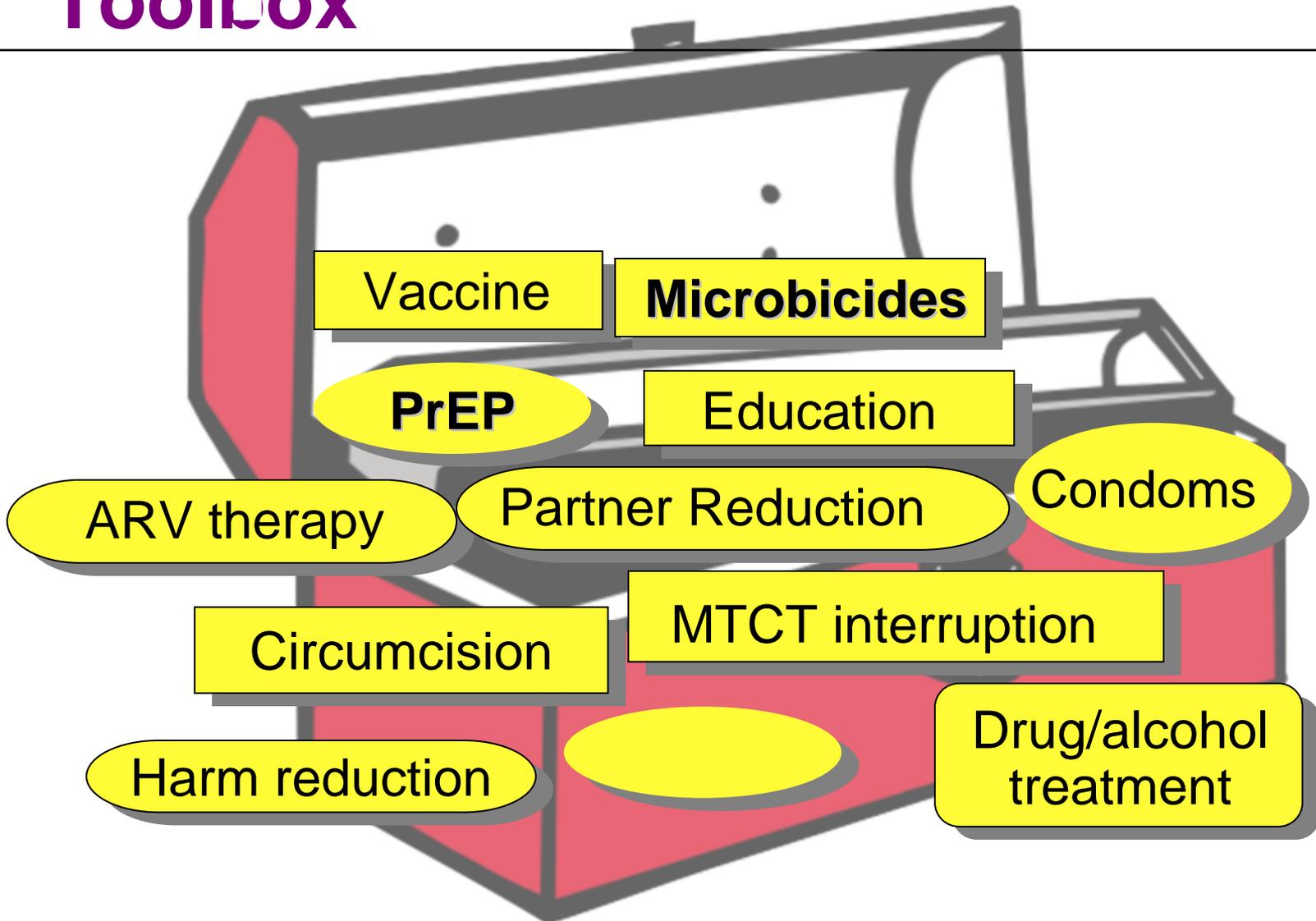
- Review the accomplishments from the MTN family since our previous regional meeting (September 2008)
- Focus on the critical importance of initiation of new sites and rapid accrual for VOICE
- Review our challenges and opportunities moving forward

Role of the MTN: the View from DAIDS

- Prove the concept
 - Show that a topically applied product can substantially reduce HIV transmission
- Maximize the effectiveness
 - Adherence
 - Route of administration
 - Safety
- Integrate into combination prevention strategies and programs



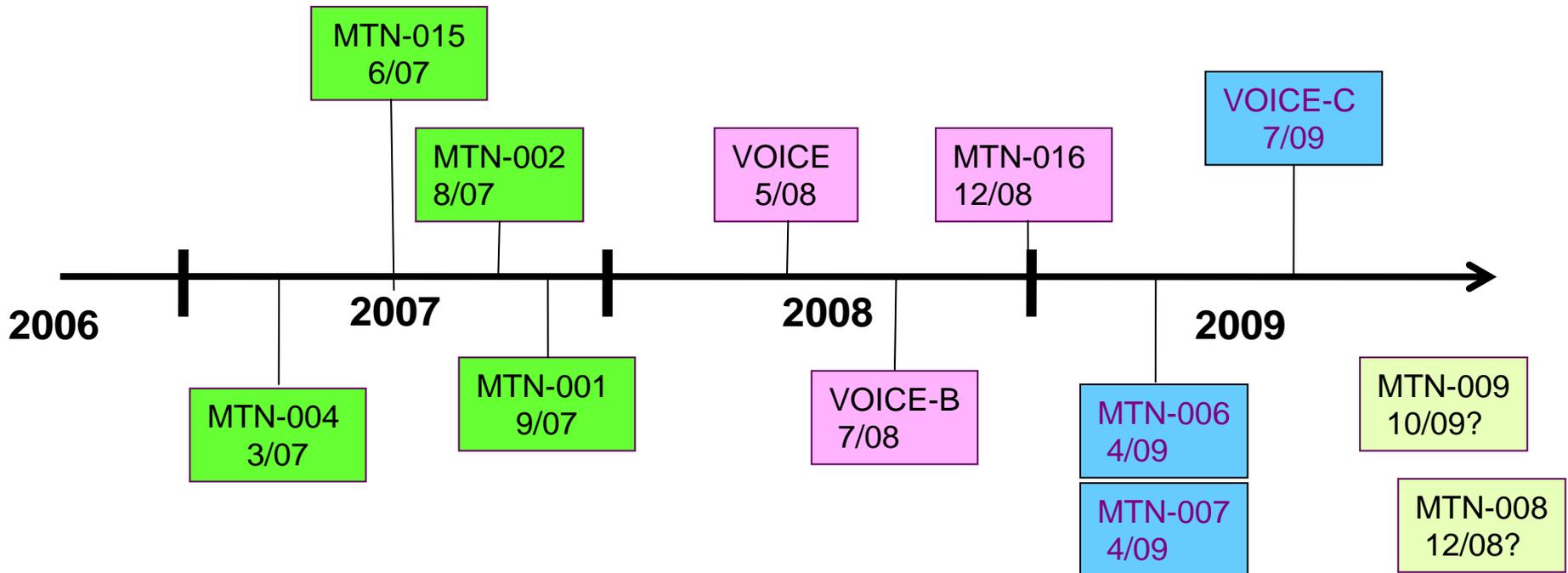
A Comprehensive HIV Prevention “Toolbox”



What Have We Been Doing?

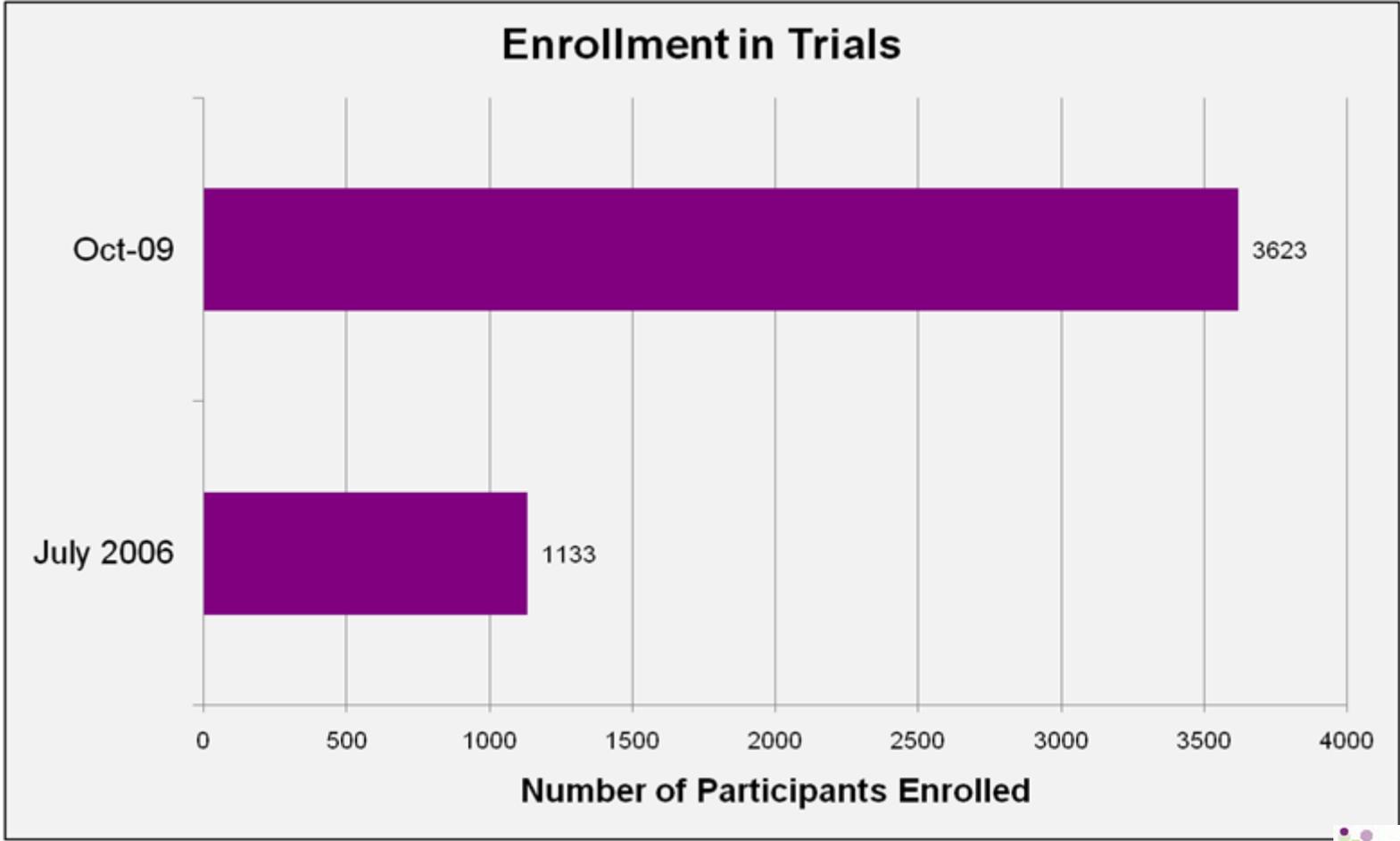
- **Complete our legacy studies from the HPTN:**
HPTN-035 and HPTN-059
- **Develop new protocols which are open:**
 - MTN-001: oral vs topical tenofovir pK
 - MTN-002: tenofovir in pregnancy study
 - MTN-003: VOICE
 - VOICE B: Bone density substudy
 - MTN-004: VivaGel phase 1 study
 - MTN-006: rectal tenofovir gel study
 - MTN-015: seroconverter protocol
 - MTN-016: EMBRACE pregnancy registry

Approved protocols – continuing to build ...





Enrollment in MTN Studies 2006-2009



HPTN 035

- Designed to estimate the safety and effectiveness of BufferGel and 0.5% PRO2000/5 gel
- Enrolled at 7 sites (1 US, 6 Africa) between Feb 2005 and August 2007
- All women followed a minimum of 1 year; some women enrolled early in the study followed for a maximum of 30 months
- Study completed in September 2008; Results presented at CROI Feb '09

The HPTN 035 Study

- Has provided the foundation for success with the VOICE trial
- Has built the NIH's confidence in our ability to execute a high quality trial on time and within budget
- Is recognized as an example of a high quality study within the HIV prevention field

What Are Our Strengths?

- Opportunity to leverage 035 successes: retention, study quality
- Development of a scientific agenda in logical, step-wise manner (topical, oral, rectal, pregnancy, lab/science)
- Enhanced community engagement and capacity building
- Incorporation of social science into our protocols from the concept level
- Capacity to add new sites funded by NIH for VOICE

Getting to the Best Science

- Protocol concepts are provided to a broad range of people for input and suggestion
 - Representatives from each site
 - Representatives from our funder
 - Representatives from the network lab, CORE and SCHARP
 - Representatives from our 3 working groups: Community, Biomedical Science and Behavioral Research

CWG Study-specific Participation

□ MTN-001

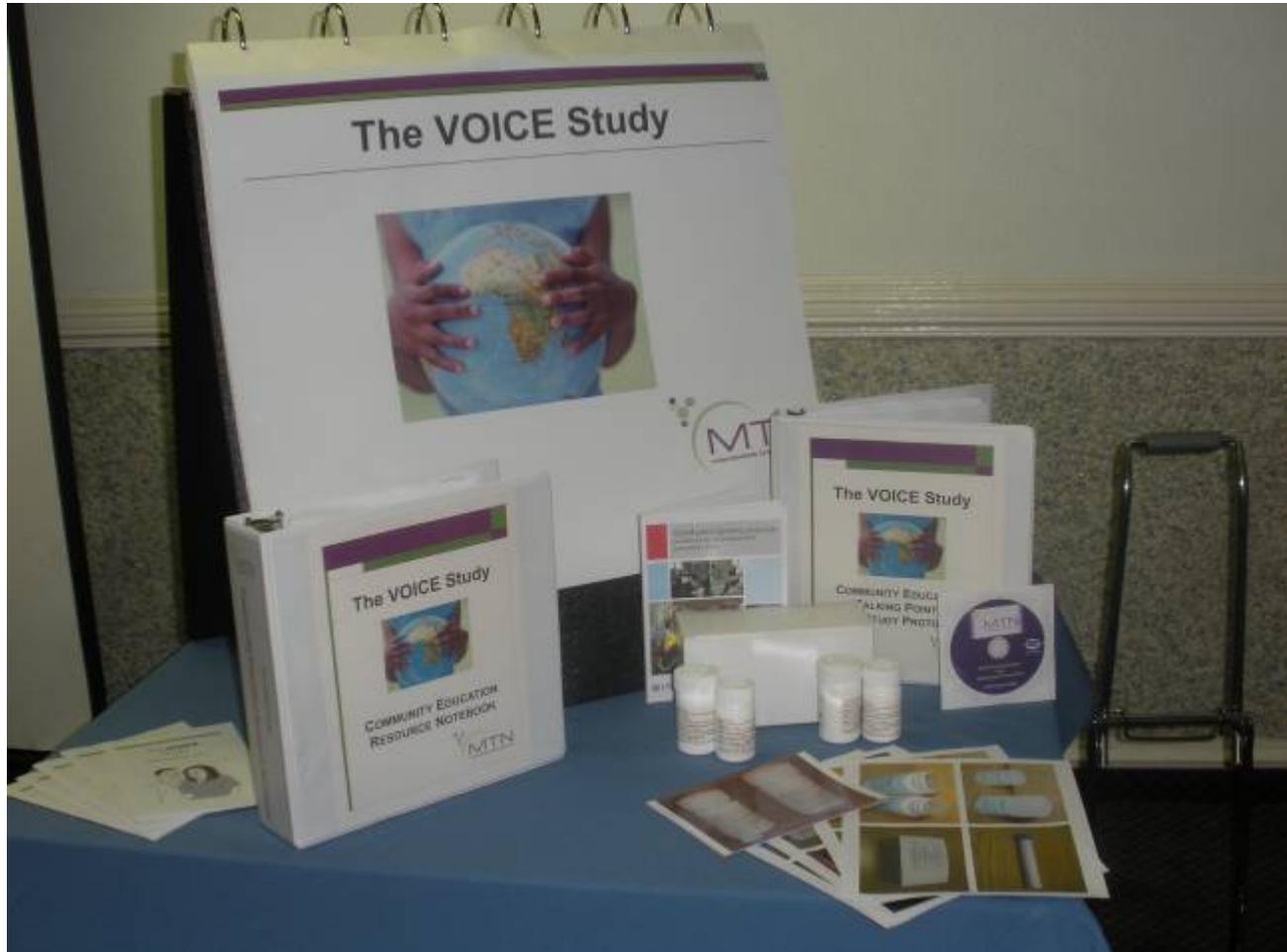
- Monthly presentations by sites regarding community education and recruitment strategies
- Plans for submission of community-focused abstracts to M2010

Study-specific Participation

□ MTN-003

- Final stages of manuscript development regarding July 2008 consultation on understanding and measuring partial product efficacy
- July 2009 consultation on understanding and measuring partial product efficacy (July 2009)
- Distribution of the VOICE Community Education Tool Kit to the Zimbabwe and Uganda CTUs (July and Sept 2009)

VOICE Community Education Tool Kit



CWG Study-specific Participation

- MTN-007
 - 1st CWG call for participating sites will be convened on 26 October

- MTN-008 and 009
 - Protocols reviewed and feedback provided

- MTN-016
 - CWG call to discuss potential community reactions to photographing babies

CWG Cross Network Participation

- Co-facilitation of a round-table discussion at the October 2009 US Conference on AIDS (USCA) entitled *Recommendations for Community Involvement in NIAID HIV/AIDS Clinical Trials Research*

CWG Cross Network Activities

- Participation in HANC Community Partners sub-working groups:
 - Community Evaluation Working Group
 - Community Site-Level Funding Working Group
 - Community Training Working Group
 - Scientific Priorities Working Group
 - Community Partners Executive Committee

CWG Contributions Beyond the MTN

- Participation in agenda development for the Global Campaign for Microbicides' December 2009 Community of Practice meeting in Mombasa, Kenya

Biomedical Science Working Group

Charlene Dezzutti

Craig Hendrix

Betsy Herold

Sharon Hillier

Florian Hladik

Jeanne Marrazzo

John Mellors

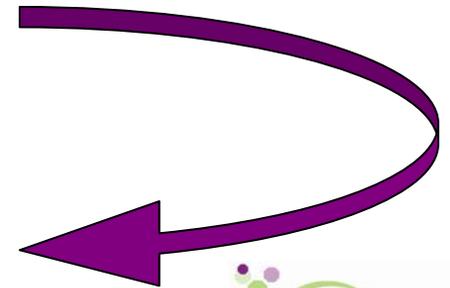
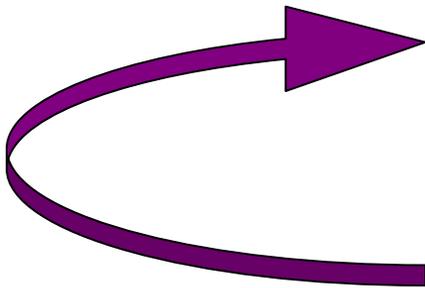
Urvi Parikh

Lei Wang



BSWG Goals and Objectives

- Provide scientific advice on protocol design and implementation
- Translate results obtained in the lab to protocol design
 - Translate clinical trial results **back to the lab**
 - Recommend & implement sub-studies



BSWG: Adding Sample Collection to MTN Trials

- MTN 001 (TFV PK)
 - Collect CVL for vaginal flora proteomics and markers of inflammation
- MTN 003
 - Vaginal and endocervical swabs for biomarkers
- MTN 004 (Vivagel)
 - Swabs for flora, cytokines & endogenous antimicrobial activity

HPTN035 BioRepository

Arm	Number of women			
	with 1 swab	with 2 swabs	with 3 swabs	with 4 swabs
BufferGel	187	289	30	4
PRO 2000/5	150	295	41	2
Placebo	182	288	41	4
No Gel	190	291	35	2
All	709	1163	147	12

Swabs Obtained From HIV Seroconverters

Arm	Number of women	
	with 1 swab	with 2 swabs
PRO 2000/5	7	1
BufferGel	2	3
Placebo Gel	1	2
No Gel	7	3
All	17	9



Behavioral Research Working Group

- Scale up and implement pictorial ACASI in VOICE trial (5 countries/9 languages)
- Develop and implement innovative ethnographic/qualitative research ancillary protocol to support/expand adherence research in VOICE-C
- Plan to expand BRWG membership to scientists from non-US MTN sites



Behavioral Research Working Group

- Develop and implement Expand behavioral research into new MTN populations: Young women (MTN-004)
- Conduct acceptability and adherence of microbicides among pregnant and lactating women (MTN-008)
- Acceptability of rectal microbicides
- Conduct mixed-methods (quantitative/qualitative) behavioral research on adherence and product sharing (MTN-001)

Looking into 2010

- Complete 001, 002, 004
- 001, 002 and 004 analyses and publications
- Open VOICE C, 005, 008, 009, 010



Our Accomplishments

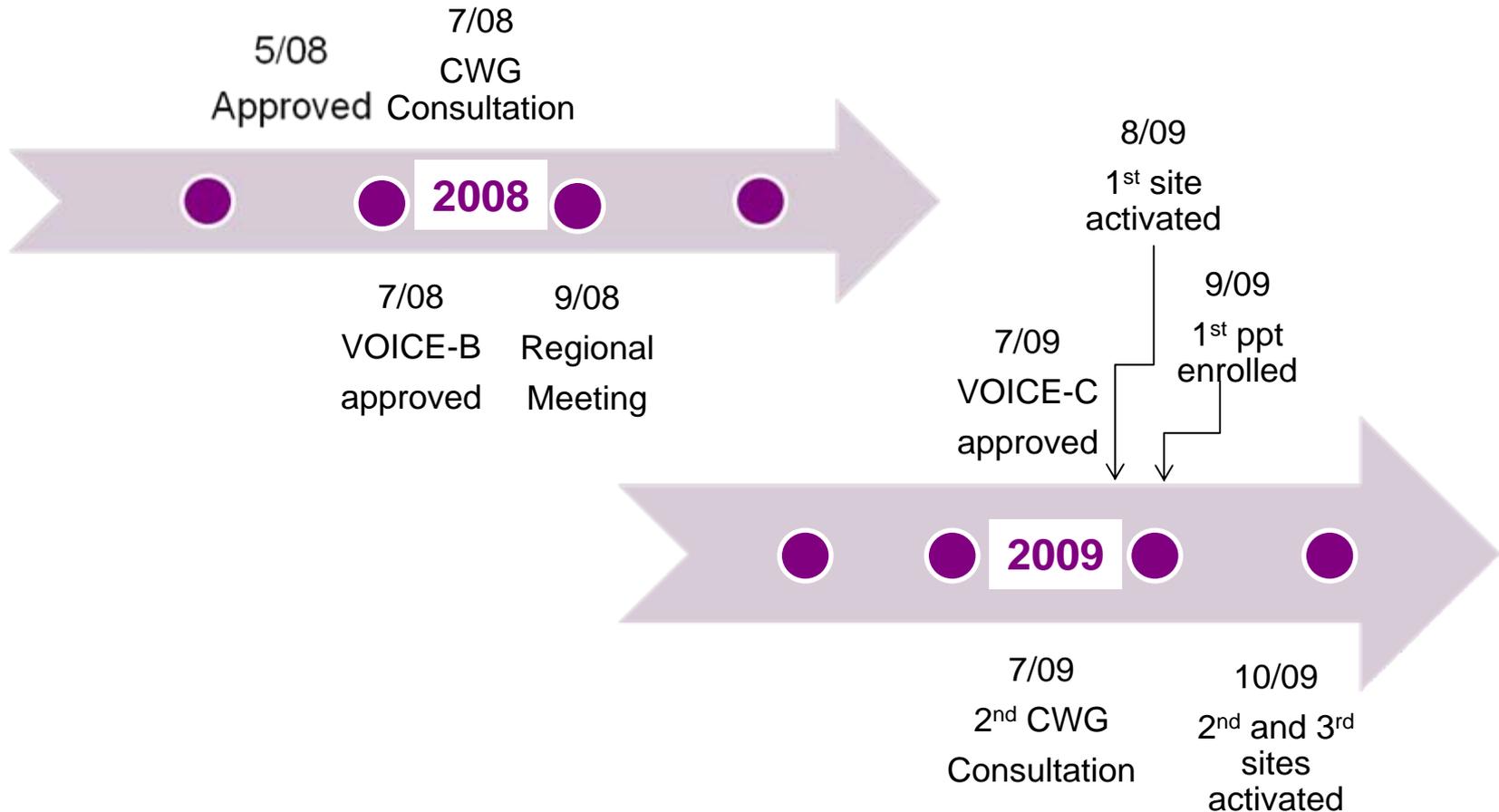
- Enrolled 2500 new study participants and followed a total of 3600
- Developed and received NIH approval for 12 new protocols
- Integrated community, social science and biomedical science each step of the way



VOICE: the MTN Flagship Study

- Phase IIb trial with five study groups testing two different HIV prevention approaches in women:
 - A once-a-day antiretroviral tablet (PrEP)
TDF or TDF/FTC
 - A once-a-day application of a vaginal gel
- 5000 women to be enrolled at 10 centers in Africa
- Last year's target start date: **Feb/ March 2009**

VOICE Milestones





VOICE Study Timeline

- Concept approved by DAIDS: July 2007
- Community, stakeholder and investigator input into the development of the protocol: September 2007
- Protocol version 1.0 approved: May 2008
- First site activated: July 2009
- First participant enrolled: September 2009
- Expected completion: Q4 2012

Ongoing Oral and Topical PrEP Trials

Oral PrEP Studies:

- Bangkok Tenofovir Study (CDC)
- Botswana TDF2 (TDF/FTC) Trial (CDC)
- iPrEX (UCSF/NIAID/BMGF)
- Partners PrEP (UW/BMGF)
- FemPrEP (FHI/USAID/BMGF)

Topical PrEP:

- **CAPRISA-004 (USAID, FHI, CONRAD)**

Oral and Topical PrEP:

- **VOICE (NIAID)**

For VOICE, The Time is Now

- HPTN 035 taught us that the results of other studies can impact our study, even if it is a different product
- There are 6 other studies of oral or topical tenofovir/Truvada underway
- There is a window of opportunity to do the VOICE trial - but we have to move forward rapidly with implementation now
- The results of other tenofovir gel, oral tenofovir and Truvada studies could impact what happens during the VOICE trial

VOICE is in our hands



What We Must Do

- To build on our strengths
- For MTN CORE and the NIH to better understand the challenges at the sites and what we can do to support and assist
- To think strategically about how we can open the remaining VOICE sites as quickly as possible, and execute the study flawlessly as we meet our accrual and retention goals

VOICE must also be in our hearts



In Other Words.....

- There are many reasons we could fail
- We have to join together to make the impossible...**POSSIBLE**
- Communication will always be a challenge



Phone lines in
Old Mombasa

Fulfilling Our Promise

- Use this meeting as an opportunity to learn how to tackle the challenges ahead: your colleagues at another site may have already learned how to address the problem
- Value efficiency
- Publish and present our findings
- Treat every day of delay as a lost opportunity
- We CAN do it!

