

MTN

A Year in Review and the Road Ahead

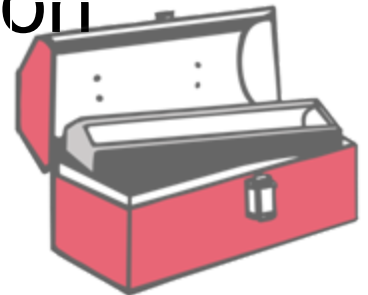
Sharon Hillier, PhD
Ian McGowan, MD, PHD
University of Pittsburgh
MTN CORE

Overview

- Review the accomplishments from the MTN family since our previous regional meeting (October 2009) (Sharon)
- Where we are today and our view of the road ahead (Ian)
- Reflections on why the MTN is such a special organization (Sharon)

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





Proving the Concept

- The CAPRISA 004 study has provided the first proof of concept that a tenofovir used at the time of sex reduces acquisition of HIV in women.
- It is our job to show whether daily tenofovir gel and/or tablets also reduces HIV acquisition in women



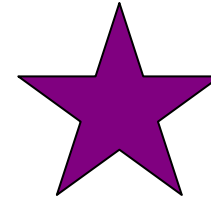
What We Said We Would Do Last Year

- Complete 001 (intensive PK study of oral and topical tenofovir)
- Complete 002 (first study of tenofovir gel in pregnant women)
- Complete 004 (study of VivaGel)
- Open VOICE C, 005, 008, 009, 010

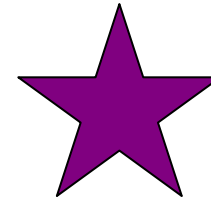


What We Said We Would Do Last Year

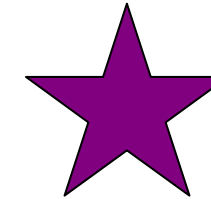
□ Complete MTN-001



□ Complete MTN-002





□ Complete MTN-004

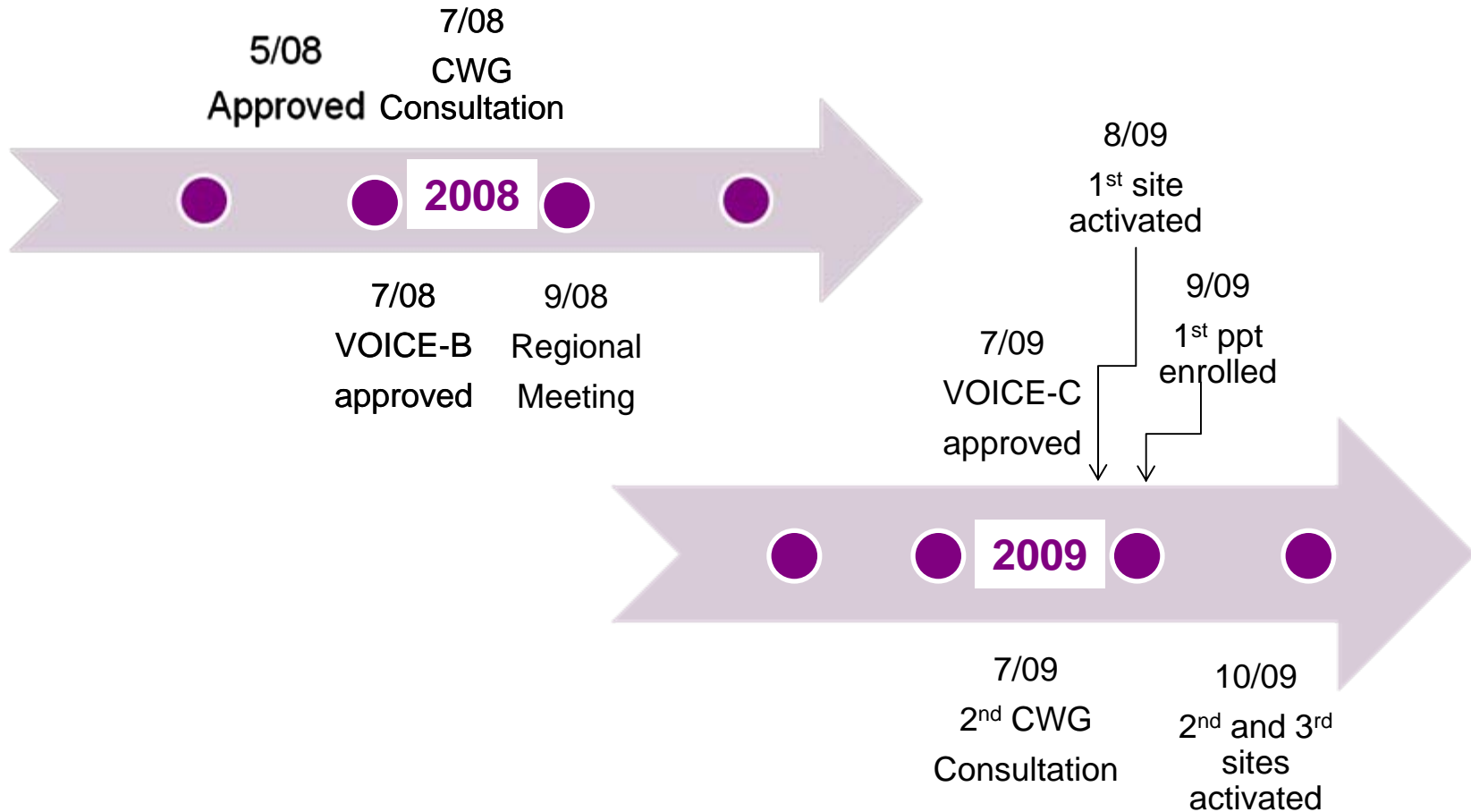




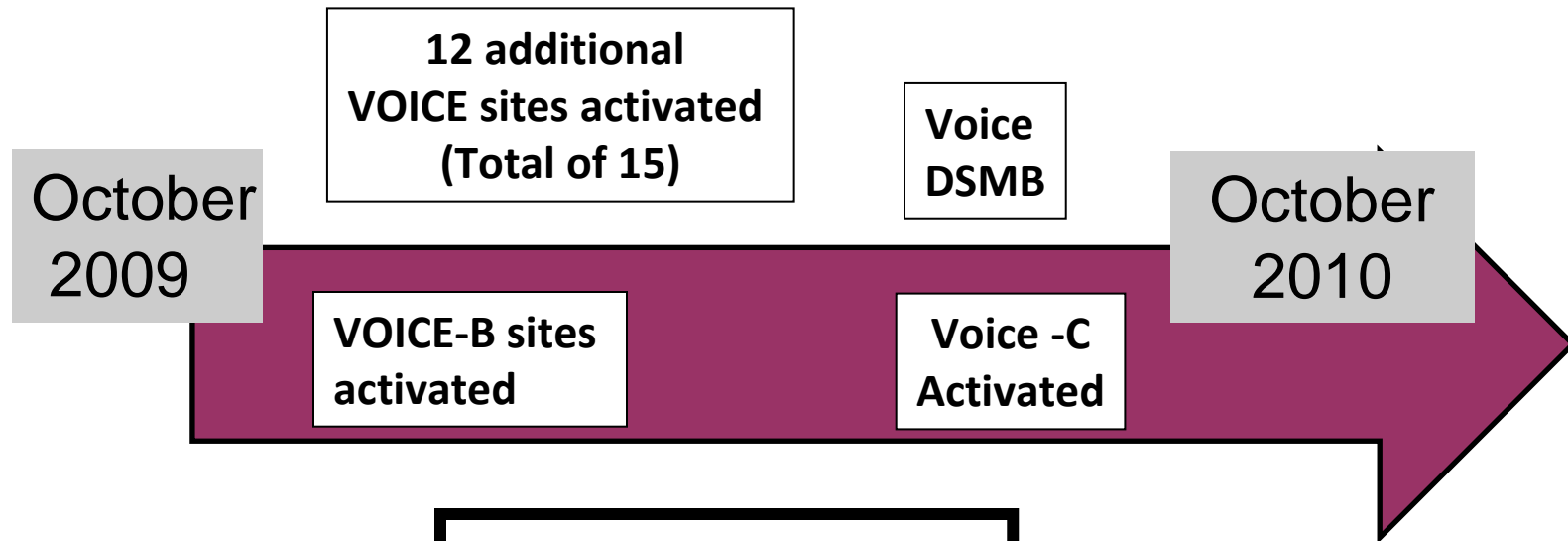
What We Said We Would Do Last Year

- Open VOICE C 
- Open 005: version 1.0 by 2010
- Open 008: extended review because pregnancy protocol
- Open 009 
- Open 010: Product development discontinued

VOICE Milestones



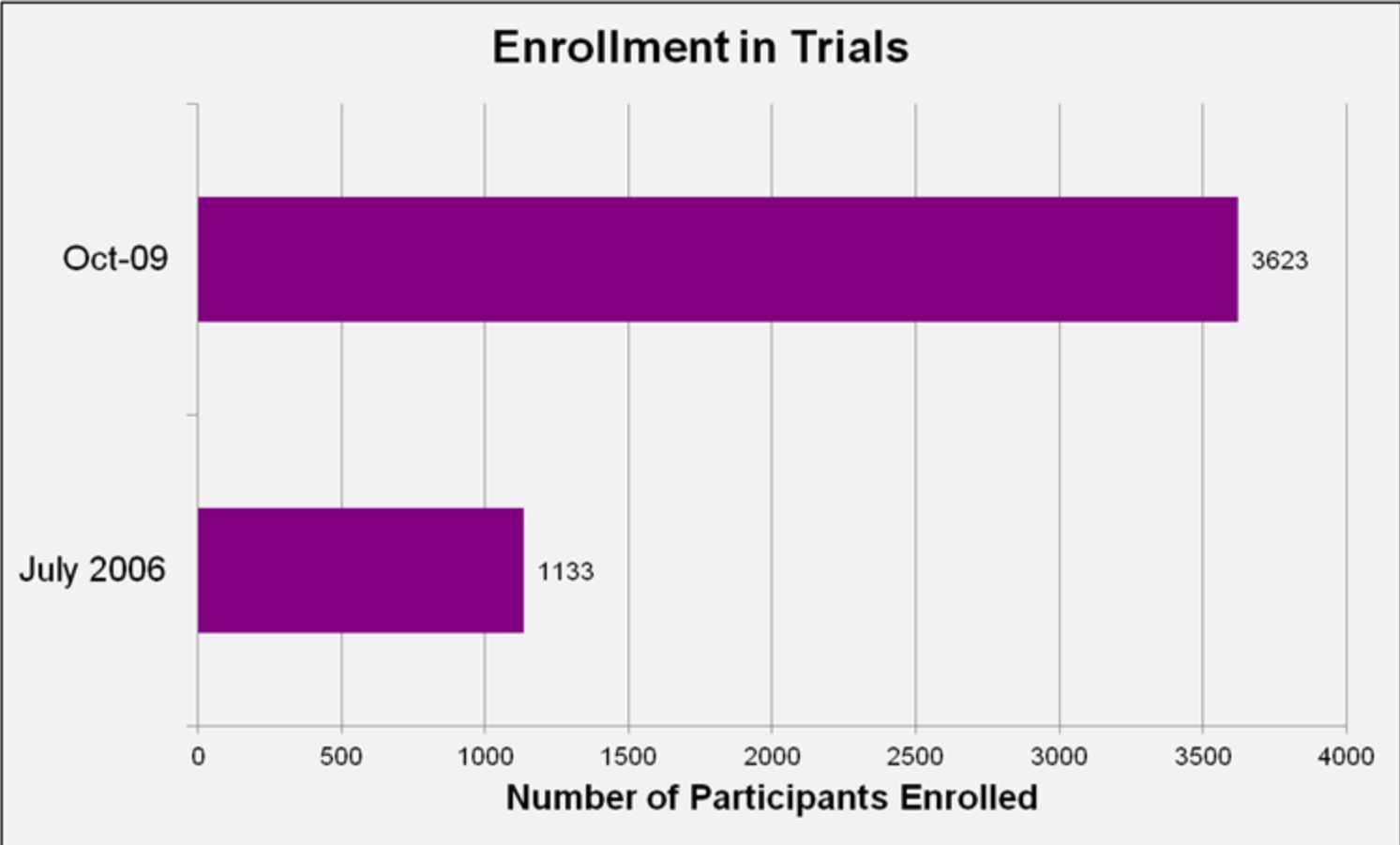
VOICE Milestones 2010



ENROLLMENT	
24-Sep-2010	
VOICE:	1647
VOICE-B:	242
VOICE-C:	17



Enrollment in MTN Studies 2006-2010



October
2010

5323





The MTN Portfolio

The MTN Portfolio

- Vaginal safety
 - MTN-005
 - MTN-013
- Intensive PK/PD
 - MTN-011
 - MTN-014
- Rectal safety
 - MTN-007
 - MTN-017
- Penile tolerance
 - MTN-012
- Pregnancy
 - MTN-008
 - MTN-016
- Effectiveness
 - MTN-003 (VOICE)
- VOICE Sub-Studies
 - MTN-003B
 - MTN-003C
 - MTN-09
 - MTN-015
- Expanded access
 - MTN-018

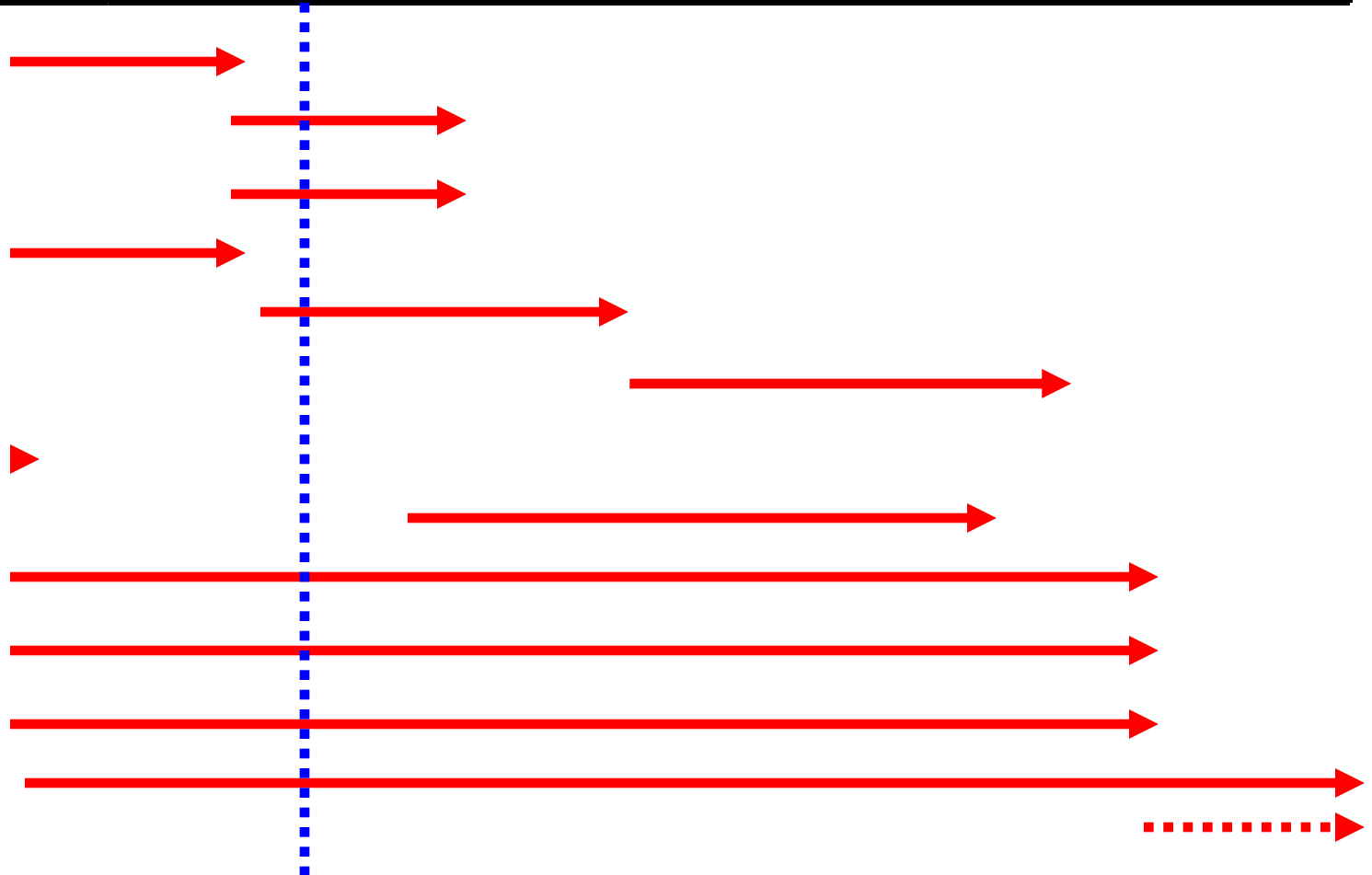
Current MTN Clinical Trial Portfolio

	Phase	Product (s)	10	11	12	13
MTN-003	2B	TVD/TDF/Tenofovir				
MTN-005	1 (VR)	Placebo ring				
MTN-007	1 (R)	Tenofovir/HEC/N-9				
MTN-008	1 (V)	Tenofovir				
MTN-009	Resistance	N/A				
MTN-011	1	Tenofovir				
MTN-012	1 (P)	Dapivirine				
MTN-013	1 (VR)	Dapivirine & Maraviroc				
MTN-014	1 (V & R)	Tenofovir				
MTN-015	Seroconversion	N/A				
MTN-016	Pregnancy	N/A				
MTN-017	2 (R)	Tenofovir				

Tenofovir Gel Timelines

2010				2011				2012			
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4

MTN-001
MTN-011
MTN-014
MTN-006
MTN-007
MTN-017
MTN-002
MTN-008
MTN-003
MTN-003B/C
MTN-009
MTN-015/16
MTN-018



Tenofovir Gel Exposure in Women*

	2011	2012	2013	2014
HPTN-059	50	50	50	50
MTN-001	33	33	33	33
MTN-011	TBD	TBD	TBD	TBD
MTN-014	TBD	TBD	TBD	TBD
MTN-002	< 1	< 1	< 1	< 1
MTN-008	< 2	< 2	< 2	< 2
MTN-003	1000	1800	1800	1800
MTN-018/019			2000	3000
Total	1084	1884	3884	4884

(*Estimated women years exposure to tenofovir gel)

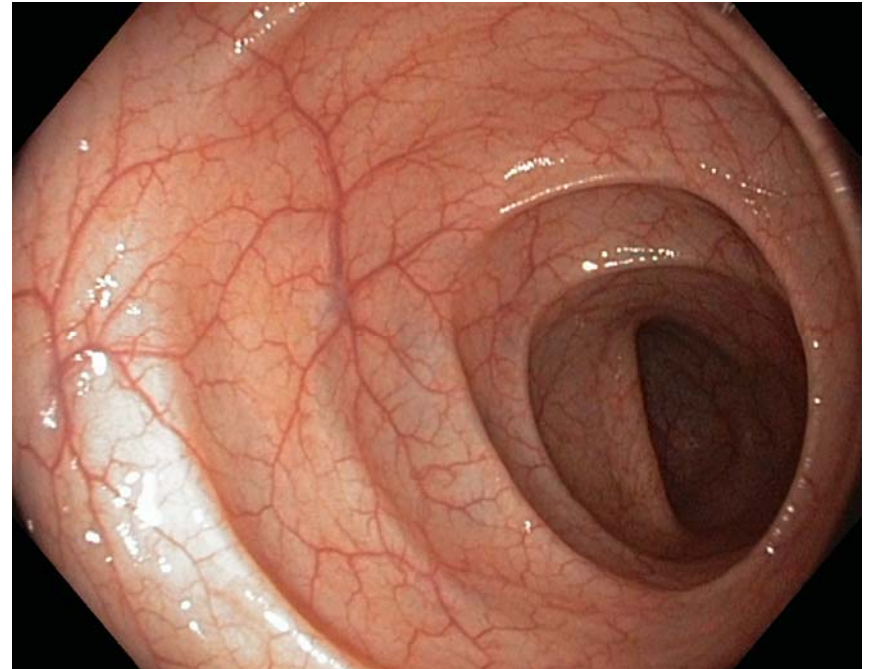


New Concepts in Development

MTN-XXX

□ Rationale

- We have no dose ranging data for RM
- We have animal toxicology up to 10% tenofovir*
- Larger mucosal surface to protect
- GALT activation phenotype and implications for tenofovir
- Safety – GI intolerance





MTN-XXX

- Phase 1 rectal safety and acceptability
- Tenofovir 1%, 3%, 10%
- Single and multiple dosing strategy
- Endpoints
 - Safety, acceptability, PK/PD
- Three arms versus cross-over
- N = about 36, three sites



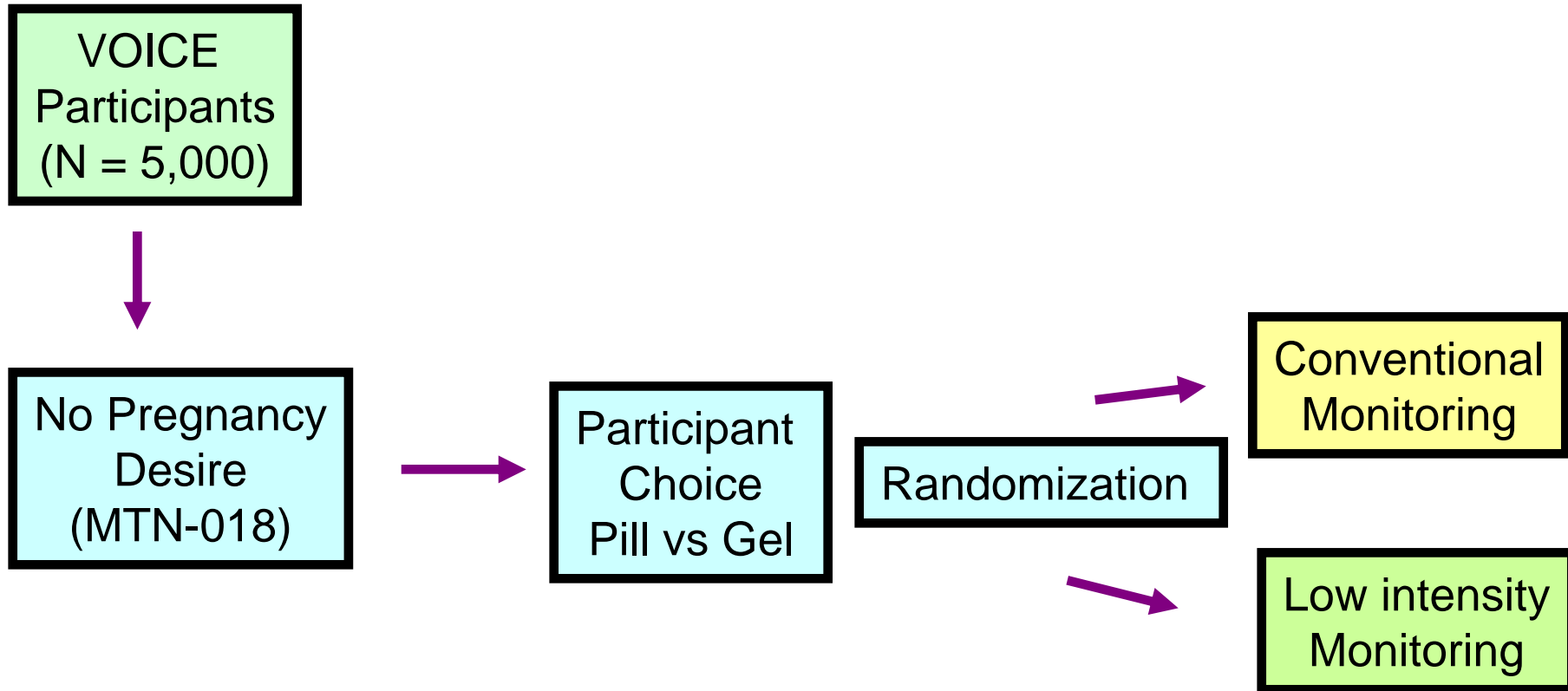
MTN-017

- Phase 2 rectal safety study
- Tenofovir gel and Truvada
- Safety, acceptability, PK/PD
- Compartmental PK/PD in subset
 - US + Thailand
- Sites in US, Peru, and Thailand

MTN-017

Group	N	Period 1 6 weeks	Washout 2 weeks	Period 2 6 weeks	Washout 2 weeks	Period 3 6 weeks	Washout 1 week
A	30	Oral		Rectal		Oral + rectal	
B	30	Rectal		Oral		Oral + rectal	
C	30	Oral + rectal		Oral		Rectal	

MTN-018 Design Concept



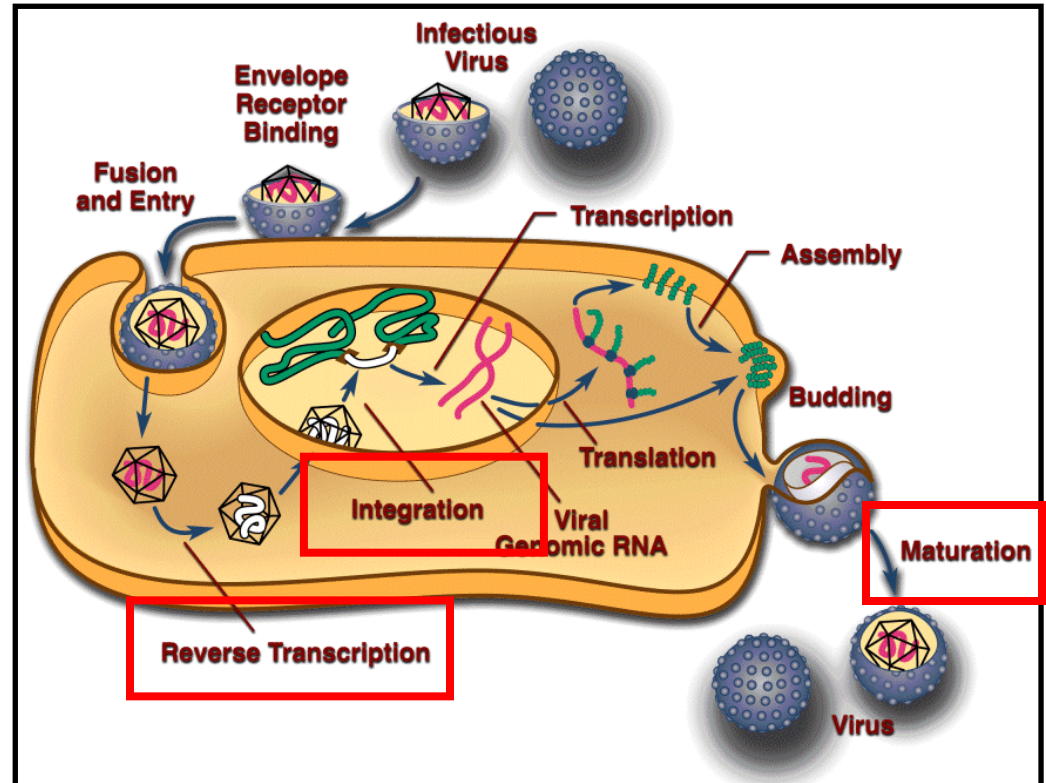


After 2012?

Drug Targets

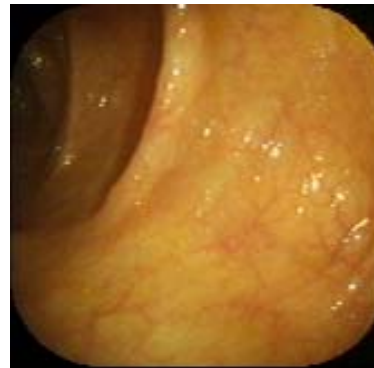


Host



Virus

Routes of Administration



- Product profile
- Feasibility of formulation
- PK/PD profile
- Consumer preference / route of infection



Potential Products

- Integrase inhibitors
 - Merck raltegravir derivatives
- Fusion inhibitors
 - Maraviroc
 - RANTES analogues
- Reverse transcriptase inhibitors
 - TMC-278
 - Gilead compounds
- Protease inhibitors
 - Indinavir (Merck)
- Rectal specific formulations
 - CHARM Program
- Other mechanisms
 - Glycerol monolaurate



Back to Sharon.....

What Are Our Strengths?

- Development of a scientific agenda in logical, step-wise manner (topical, oral, rectal, pregnancy)
- Enhanced community engagement and capacity building
- Incorporation of social science into our protocols from the concept level
- Operational excellence: retention, study quality
- Integration of outstanding lab scientists, statisticians and pharmacists
- Flexibility in response to emerging trends



There are Many Reasons We Could Fail

- The studies are complicated, the work is hard
- We have to join together to make the impossible...**POSSIBLE**
- We have to recognize that growth comes through challenge, and challenge leads to stress
- But as family, we love each other, even though we sometimes at unhappy with each other....







A MICROBICIDE STUDY IN HIV PREVENTION



The Well Woman and Partner Study
Mamwa Clinic







Why Do We Love the MTN Family?

“I wanted to let you know that we had a phone call this morning with the clinician liasons for the safety message board for VOICE.

I have never interacted with such a thoughtful, courteous group of physicians. It's hard to imagine a group of US physicians would be willing to take an hour out of their day to discuss a hypothetical scenario...and be so pleasant and engaged the entire time. I feel so lucky to be working with these doctors!”

A Safety Physician, MTN CORE



Why Do We Love the MTN Family?

“What we enjoy the most are the people with whom we are working: the team itself is driven by motivated, hard-working, caring people, and the site staff are engaged, compassionate to the participants, and demonstrate their commitment daily by asking great questions, sharing with the larger group, and putting in the hours to get an incredible amount of work done. ”

MTN Core FHI



Why Do We Love the MTN Family?

“It is inspiring and humbling to work with this international group of people - truly the best of the best shape this MTN team”.

MTN Core FHI



Why Do We Love the MTN Family?

“If South Africa is the Rainbow Nation then MTN is the Rainbow Network – we bring together a passionate, diverse, focused, and creative group of people committed to ending the HIV epidemic”

MTN Leadership



Why Do We Love the MTN Family?

“On multiple levels, community involvement is one of the essentials for successful conduct of MTN’s research. Based on the Network’s investment in community capacity-building as it relates to HIV prevention clinical research, I am convinced that many within the Network do sincerely respect and appreciate community involvement.

As with anything, we most certainly have room for improvement, but ---- we’ve come a long way baby!”



Why Do We Love the MTN Family?

“Every day we work on studies that will lead to the development of new HIV prevention tools for men and women.

It is a powerful dream- and what a beautiful thing it is to share this dream- and to work together to make this dream a reality.”



Fulfilling Our Promise

- Use this meeting as an opportunity to remember how far we have come
- Treasure the chance to see family members who have you have not seen in some time, or maybe have only heard on the phone before this week
- Think about the road ahead of us in HIV prevention- there is much to do to complete the work which will support licensure of tenofovir
- Treat every day of delay as a lost opportunity
- Remember to love your family, even when they are making you crazy