

# MTN-017: Baseline Data from Four Continents

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# MTN-017

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- A Phase 2 Randomized Sequence Open Label Expanded Safety and Acceptability Study of Oral Emtricitabine/Tenofovir Disoproxil Fumarate Tablet and Rectally-Applied Tenofovir Reduced-Glycerin 1% Gel

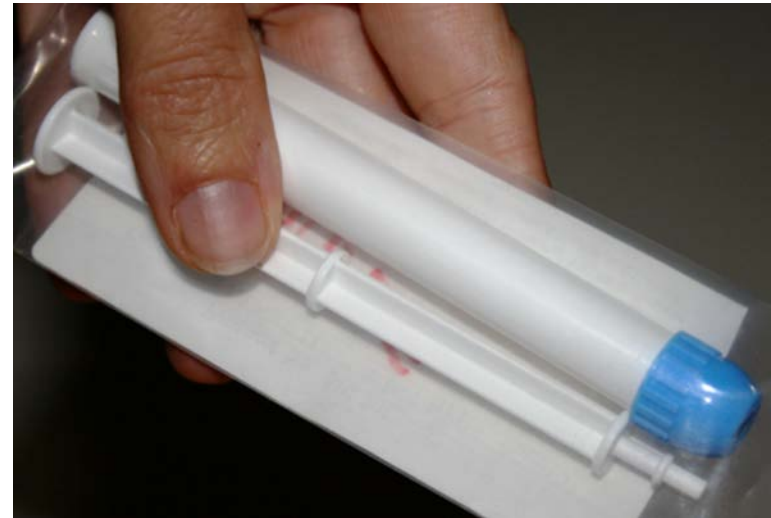
# Study Products

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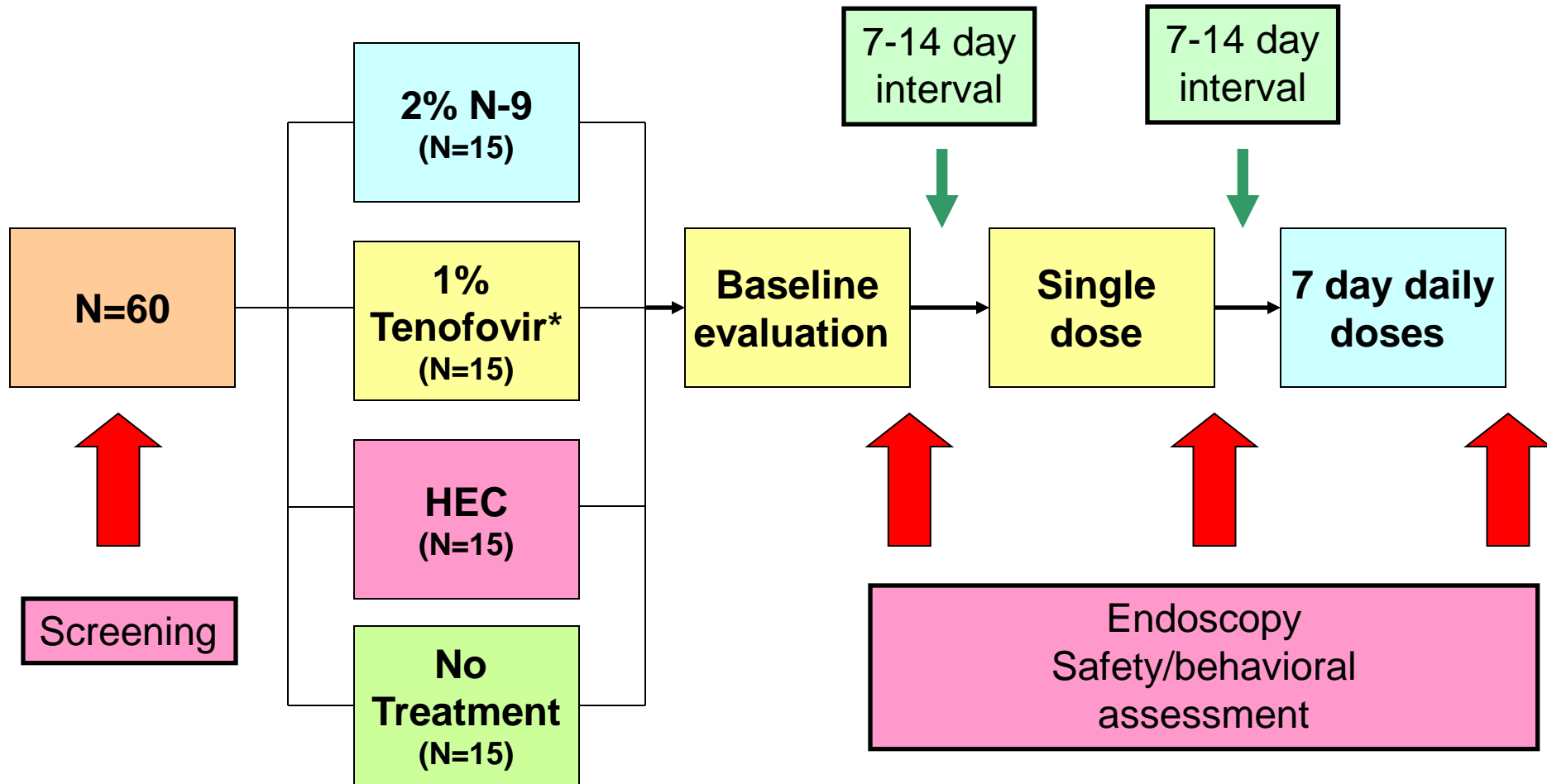
□ FTC/TDF



□ 1% TFV RG Gel



# MTN-007 Study Design



\*1% tenofovir reduced glycerin formulation

# Gastrointestinal Adverse Events

GI Adverse Events in the Tenofovir Arm	MTN-007 (N = 16) RG Formulation		RMP-02/MTN-006 (N = 12) Original Formulation	
	N	%	N	%
Abdominal pain	3	16%	6	50%
Rectal urgency	0	0%	5	42%
Bloating	0	0%	5	42%
Nausea	0	0%	4	33%
Diarrhea	1	6%	7	58%
Flatulence	6	38%	3	25%
Proctalgia	1	6%	0	0%
Other	4	25%	5	42%

# Acceptability

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Product (N)	Intention to Use (%)
RG Tenofovir (15)	87%
HEC Placebo (15)	93%
N-9 (16)	63%



# MTN 017

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## □ Study Population

- Approximately 186 pts
- HIV-uninfected
- MSM or transgender females
- Reported practicing receptive anal intercourse
- Age 18 years or older

## □ Study Duration

- Follow-up: 27 weeks per participant
- Accrual: Projected 6-9 calendar months at each site

# MTN 017 Study Sites

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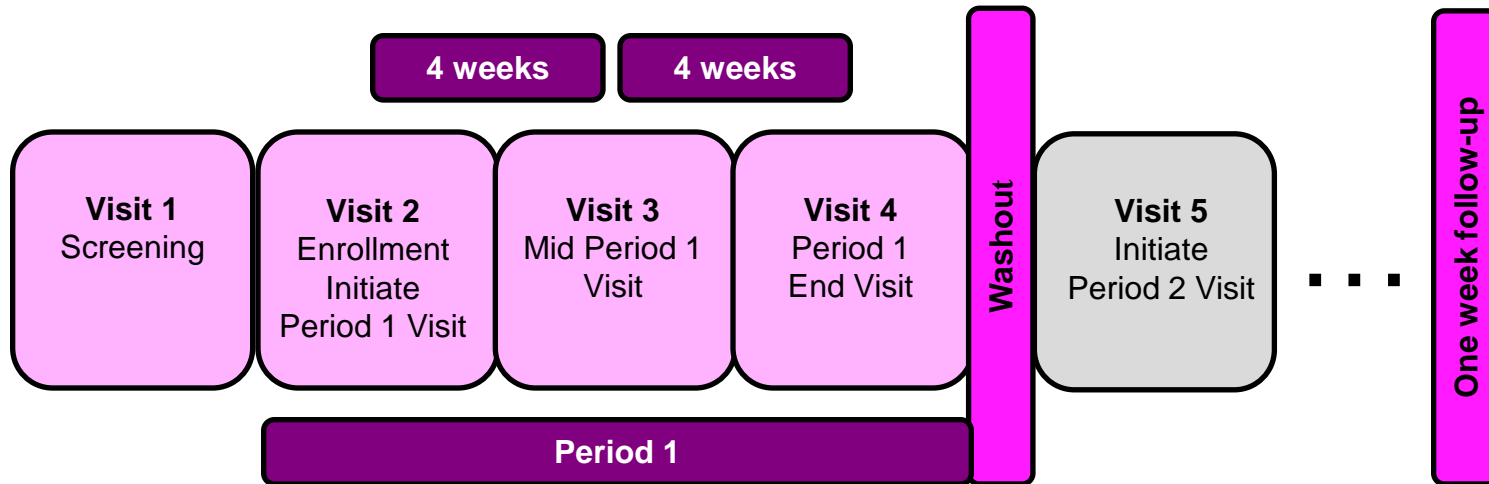


# MTN-017

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- Study regimens include:
  - Rectal tenofovir gel used daily
  - Rectal tenofovir gel used before and after sex (BAT 24)
  - Truvada tablets taken daily
- Each participant will follow all of the study regimens for eight weeks, with a weeklong break between regimens when no product will be used
  - The order in which participants follow study regimens will be based on random assignment
- All participants will receive standard HIV prevention package

# MTN-017 Study Design



# MTN-017 Study Design

Product Sequence	N	Period 1 (8 weeks)	Product Break (1 week)	Period 2 (8 weeks)	Product Break (1 week)	Period 3 (8 weeks)
1	31	Daily FTC/TDF		Daily rectal gel		Rectal gel before and after sex
2	31	Rectal gel before and after sex		Daily FTC/TDF		Daily rectal gel
3	31	Daily rectal gel		Rectal gel before and after sex		Daily FTC/TDF
4	31	Daily rectal gel		Daily FTC/TDF		Rectal gel before and after sex
5	31	Daily FTC/TDF		Rectal gel before and after sex		Daily rectal gel
6	31	Rectal gel before and after sex		Daily Rectal gel		Daily FTC/TDF



# Primary Objectives/endpoints

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## □ Safety

- To compare the safety profiles of daily FTC/TDF tablet, daily TFV RG 1% gel, and RAI-associated TFV RG 1% gel
  - Grade 2 or higher adverse events

## □ Acceptability

- To evaluate and compare acceptability of daily FTC/TDF tablet, daily TFV RG 1% gel, and RAI-associated TFV RG 1% gel
  - Participant self-report of ease of use, liking the product, and likelihood of product use if shown to be effective

# Secondary Objective/Endpoints #1

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- Pharmacokinetics
  - To compare systemic and local pharmacokinetics (PK) among daily FTC/TDF tablet, daily TFV RG 1% gel, and RAI-associated TFV RG 1% gel
    - Tenofovir concentrations
      - blood plasma, rectal tissue\* and rectal fluid
    - Tenofovir-diphosphate concentrations
      - peripheral blood mononuclear cell (PBMC) and rectal tissue\*
    - Emtricitabine concentrations
      - blood plasma, rectal tissue\* and rectal fluid
    - Emtricitabine-triphosphate concentrations
      - PBMC and rectal tissue\*

\* Rectal tissue will be collected on a subset of participants taking part in the Rectal Biopsy/Fluid Subset



# Secondary Objective/Endpoint #2

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## □ Adherence

- To evaluate and compare adherence to daily FTC/TDF tablet, daily TFV RG 1% gel, and RAI-associated TFV RG 1% gel
  - Percentage of prescribed doses taken orally or administered rectally in an 8-week period



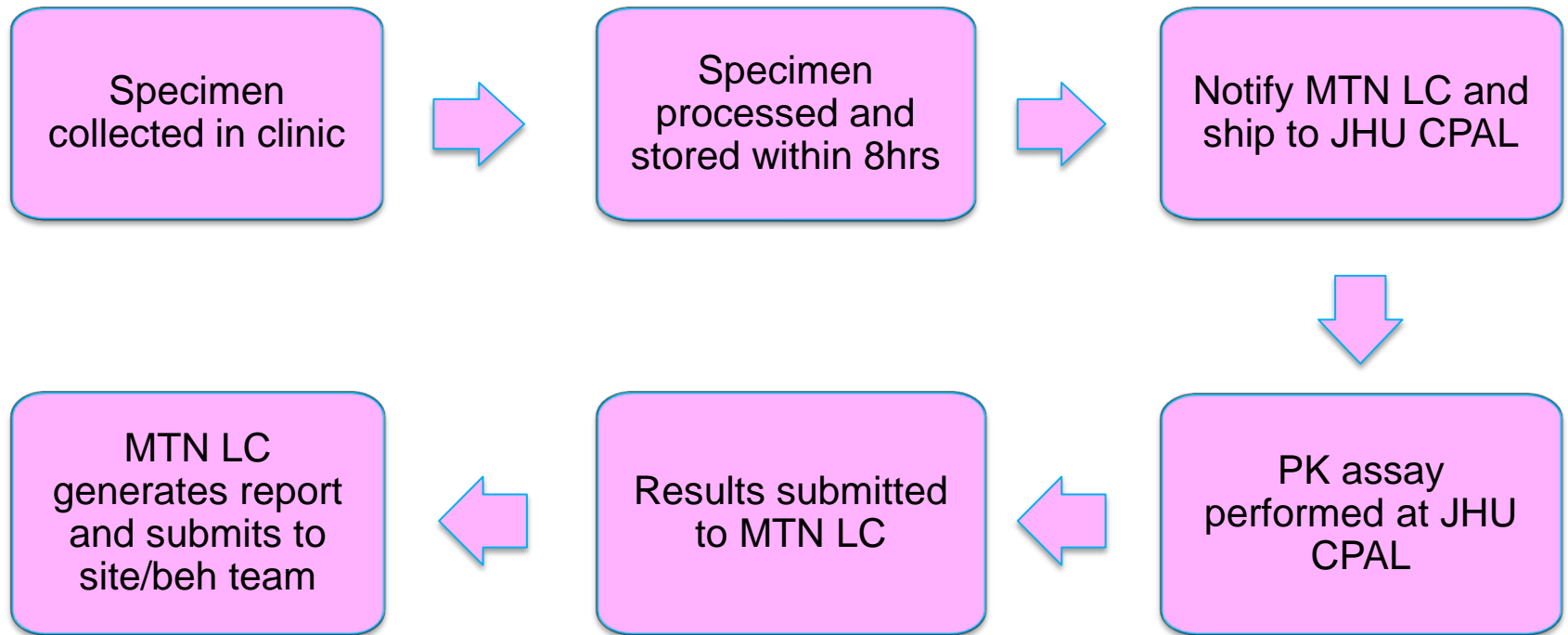
# Exploratory Objectives

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- Characterize pharmacodynamic responses
- Characterize changes in mucosal immunity
- Assess correlation between PK and adherence measures
- Identify factors associated with product adherence and whether they differ by product used
- Examine whether sexual activity or condom use varies by product used
- Determine the level of sharing of study products with non-participants
- Determine the prevalence of behavioral practices associated with anal intercourse that may affect microbicide use

# PK Specimen Flow Chart

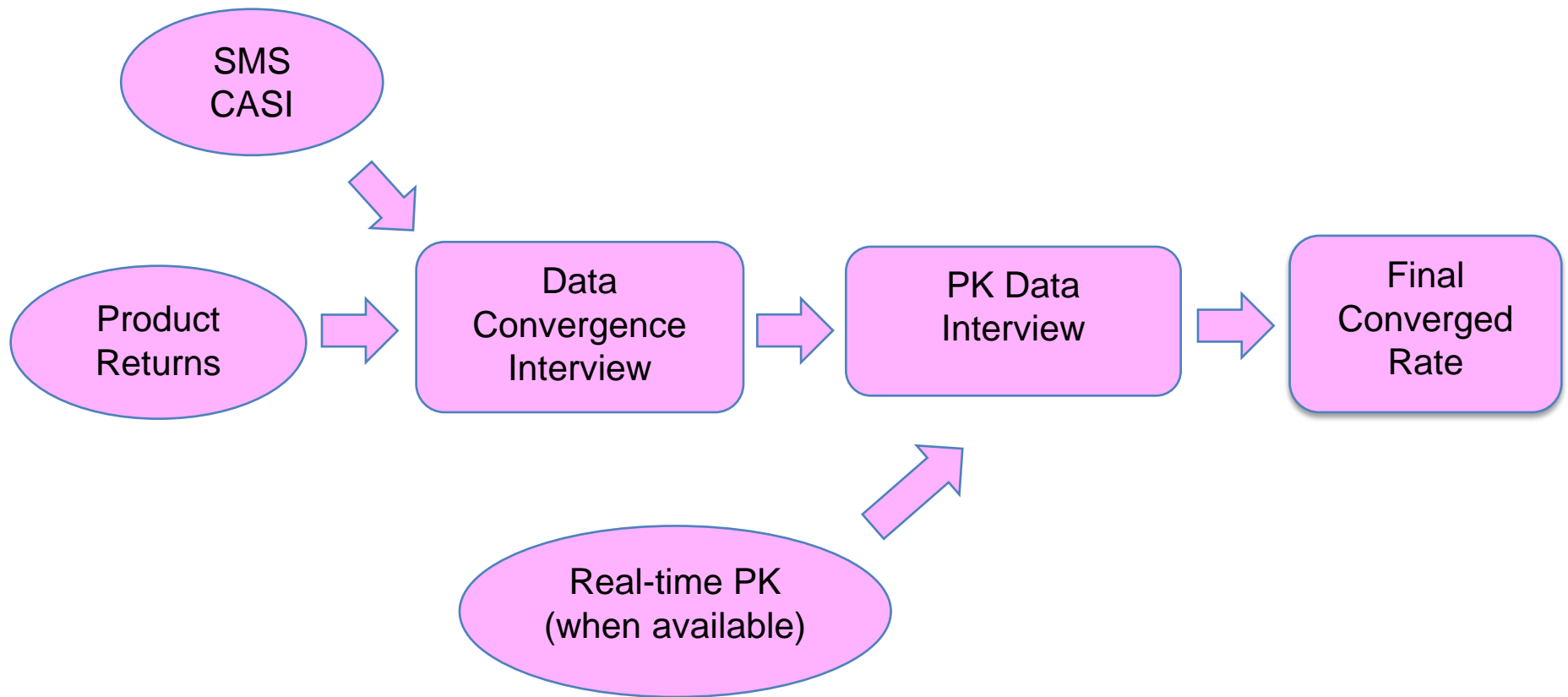
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# MTN 017 Adherence Measurement

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# Timelines

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- Protocol development:
  - Protocol development meeting 09-28-11
  - Community consultations
    - Cape Town Oct 2011
    - Pittsburgh Dec 2011
    - Bangkok and Chiang Mai Jan 2012
    - Boston Mar 2012
    - Lima Mar 2012
  - PSRC 04-03-12
  - Version 1.0 07-13-12

# Site Activation

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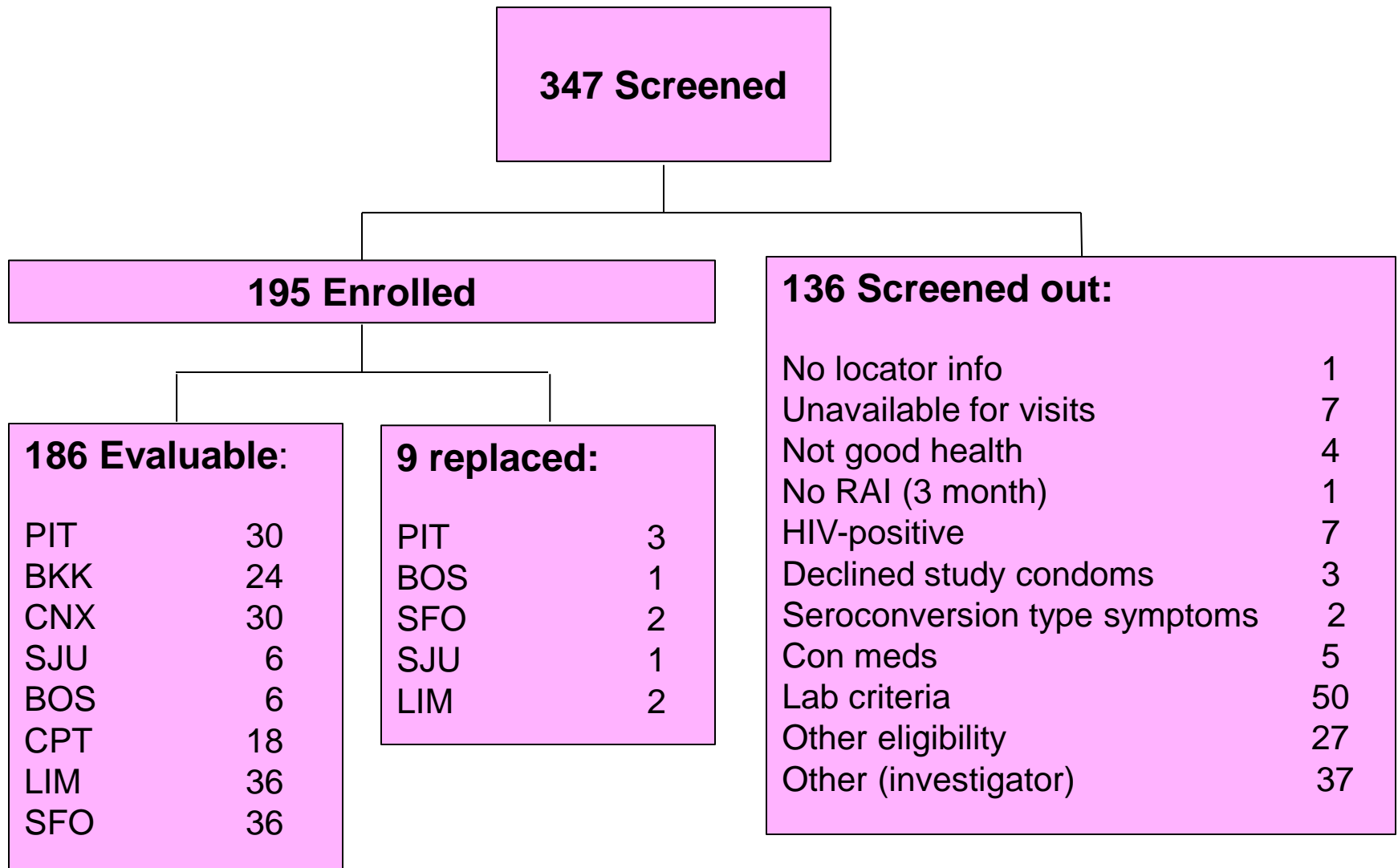
□ Clinical Trial Agreement: 07-11-13

□ Sites:

■ Fenway	09-06-13
■ SFDH	09-24-13
■ Pittsburgh*	09-27-13
■ San Juan	11-15-13
■ Chiang Mai	01-06-14
■ Lima	01-15-14
■ Cape Town	02-28-14
■ Bangkok*	06-27-14

\*Mucosal immunology subset

# Screening and Enrollment



# Replacements

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- Ppts with missing adherence data due to:
  - Participant was not dispensed study product
  - Participant did not report on study product use at least once in the daily gel period, the RAI gel period, or both
  - Loss-to-follow-up
  - Participant non-adherence or refusal of study product
  - site-initiated product holds/discontinuations
- No participants were replace after full accrual

# 017 Activity as of 03-12-15

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Site (n)	Screened	Screen Fail	Enrolled	Completed
Fenway (6)	11	4	7*	7
SFDH (36)	100	62	38*	29
Pittsburgh (30)	45	12	33*	28
San Juan (6)	13	4	7*	7
Chiang Mai (30)	56	27	30	23
Lima (36)	55	18	38*	30
Cape Town (18)	47	29	18	9
Bangkok (24)	33	8	24	12
<b>TOTAL</b>	<b>360</b>	<b>164</b>	<b>195</b>	<b>145</b>

\* Including replacement ppt/s

# Demographics

	LIM	SJU	CPT	BKK	CNX	BOS	PIT	SFO	All
Ppts enrolled	38	7	18	24	30	7	33	38	195
Age (mean)	32.9	30.9	22.8	31.5	27.9	34.6	30.2	35.9	31.1
Age (years)									
<20	2	0	5	0	2	1	0	0	10 (5%)
20-24	7	1	8	3	12	0	10	2	43 (22%)
25-29	6	2	3	4	5	3	9	12	44 (23%)
30-34	7	2	1	12	4	0	6	8	40 (21%)
35-39	7	1	1	2	2	0	2	5	20 (10%)
≥40	9	1	0	3	5	3	6	11	38 (20%)
Hispanic	38	7	0	0	0	2	2	6	55 (28%)

# Race

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	LIM	SJU	CPT	BKK	CNX	BOS	PIT	SFO	All
<b>Ppts enrolled</b>	38	7	18	24	30	7	33	38	<b>195</b>
<b>American Indian</b>	13	0	0	0	0	0	0	0	<b>13 (7%)</b>
<b>Asian</b>	0	0	0	0	0	0	1	3	<b>4 (2%)</b>
<b>African American</b>	0	2	0	0	0	0	3	0	<b>5 (3%)</b>
<b>Thai</b>	0	0	0	24	30	0	0	0	<b>54 (28%)</b>
<b>White</b>	1	2	0	0	0	6	28	27	<b>64 (33%)</b>
<b>Xhosa</b>	0	0	14	0	0	0	0	0	<b>14 (7%)</b>
<b>Mixed</b>	24	2	1	0		0	1	1	<b>29 (15%)</b>
<b>Other African/Other</b>	0	1	3	0	0	1	0	7	<b>12 (6%)</b>



# Education

	LIM	SJU	CPT	BKK	CNX	BOS	PIT	SFO	All
<b>Ppts enrolled</b>	38	7	18	24	30	7	33	38	<b>195</b>
<b>No schooling</b>	0	0	0	0	0	0	0	0	<b>0</b>
<b>Primary incomplete</b>	0	0	0	0	1	0	1	3	<b>1 (1%)</b>
<b>Primary complete</b>	0	0	0	0	0	1	0	0	<b>1 (1%)</b>
<b>Secondary incomplete</b>	1	0	6	0	0	1	1	0	<b>9 (5%)</b>
<b>Secondary complete</b>	10	1	7	3	4	1	0	1	<b>27 (14%)</b>
<b>College</b>	27	6	5	21	25	4	32	36	<b>156 (80%)</b>

# Gender

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	LIM	SJU	CPT	BKK	CNX	BOS	PIT	SFO	All
Ppts enrolled	38	7	18	24	30	7	33	38	195
Male	33	7	14	22	20	7	32	34	169 (87%)
Female	4	0	0	1	0	0	3	0	5 (3%)
Transgender female (including check multiple)	1	0	3	1	10	0	0	4	19 (10%) 14 (7%) TF
Other	0	0	1	0	0	0	0	1	1 (1%)
Declined	0	0	0	0	0	0	1	0	1 (1%)

# Sexually Transmitted Infections (V1)

	LIM	SJU	CPT	BKK	CNX	BOS	PIT	SFO	All
<b>Ppts enrolled</b>	38	7	18	24	30	7	33	38	195
<b>STI</b>									
<b>Syphilis</b>	4	0	0	1	0	0	0	0	5 (3%)
<b>Gonorrhea U</b>	0	0	0	0	0	0	0	0	0 (0%)
<b>Gonorrhea R</b>	0	0	0	0	0	0	0	0	0 (0%)
<b>Chlamydia U</b>	0	0	0	0	0	0	0	1	1 (1%)
<b>Chlamydia R</b>	0	0	0	0	0	0	0	0	0 (0%)
<b>HSV 1 IgG</b>	32	3	12	18	22	6	29	26	136 (70%)
<b>HSV 2 IgG</b>	18	4	6	6	7	1	4	12	58 (30%)

# Anorectal Findings

	LIM	SJU	CPT	BKK	CNX	BOS	PIT	SFO	All
<b>Ppts enrolled</b>	38	7	18	24	30	7	33	38	<b>195</b>
<b>Perianal abnormality (ppt)</b>	1	0	1	8	5	1	0	13	<b>29 (15%)</b>
<b>Fissure</b>	0	0	0	0	0	0	0	4	<b>4 (2%)</b>
<b>Pigmentation</b>	0	0	0	2	0	1	0	4	<b>7 (4%)</b>
<b>Hemorrhoids</b>	1	0	0	0	0	0	0	4	<b>5 (3%)</b>
<b>Skin tags</b>	0	0	1	4	4	0	0	4	<b>13 (7%)</b>
<b>Fistula</b>	0	0	0	0	1	0	0	0	<b>1 (1%)</b>
<b>Erythema</b>	0	0	0	0	1	0	0	0	<b>1 (1%)</b>
<b>Other</b>	0	0	0	3	0	0	0	3	<b>6 (3%)</b>

No perianal warts, ulceration, leukoplakia, petechiae, purpura, ecchymosis, discharge, bleeding reported or abnormality on digital rectal exam

# Anorectal Findings

	LIM	SJU	CPT	BKK	CNX	BOS	PIT	SFO	All
<b>Ppts enrolled</b>	38	7	18	24	30	7	33	38	195
<b>Mucosal Abnormality (ppt)</b>	0	1	2	19	2	0	0	8	<b>32 (16%)</b>
<b>Erythema</b>	0	0	0	0	1	0	0	2	<b>3 (2%)</b>
<b>AbN vessels</b>	0	0	0	0	0	0	0	1	<b>1 (1%)</b>
<b>Friability</b>	0	0	0	0	0	0	0	2	<b>2 (1%)</b>
<b>Bleeding</b>	0	0	2	1	1	0	0	1	<b>5 (3%)</b>
<b>Hemorrhoids</b>	0	1	0	17	0	0	0	2	<b>20 (10%)</b>
<b>Other</b>	0	0	0	4	0	0	0	3	<b>7 (4%)</b>

No mucosal ulceration, discharge, polyps, reported

# Anticipated Timeline

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- 3<sup>rd</sup> SMC review on April 1<sup>st</sup> 2015

Topic	Date of Completion
Accrual	November 2014
Follow up (27 weeks)	June 2015
Data clean up	September 2015
Data lock	October 2015
Primary results	February 2016

# The MTN-017 Team

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**MTN Core:** Sharon Hillier, Ian McGowan, Beth Galaska Burzuk, Judy Jones, Maria Foster, Cindy Jacobson, Lindsay Kramzer, Ken Ho, Devika Singh **Network Lab:** Charlene Dezzutti, Craig Hendrix, Pam Kunjara, Florian Hladik **DAIDS:** Roberta Black, Jeanna Piper, Cynthia Grossman **BSWG:** Alex Carballo-Dieiguez, Rebecca Gigiere, Ivan Balan, Titcha Ho **SCHARP:** Barbra Richardson, Karen Patterson, Marla Husnik, Yevgeny Grigoriev, Karen Liu, Danica Wright, Martha Doyle, Katie Weaver, Lori Filipcic, Della Wilson, Katie Snapinn **FHI:** Sherri Johnson, Kaila Gomez, Stephanie Horn, Jonathan Lucas **CWG:** Jim Pickett **Fenway:** Kenneth Mayer, Lori Panther, Jennifer Mitty, Ami Multani, Marcy Gelman, Ian Lemieux, Jesse Ripton, Amber Rucker, Ralph Mele, Sinclair Lao, Janet Dargon, Julia Gaggin, Erika Woodbury, Jessica LaCroix, Anna Hidalgo, Douglass Krakower, Jake Tinsely, Glory Mercilus, Sachin Jain **Pittsburgh:** Carol Mitchell, Carly Mowrey, Christy Pappalardo, Jennifer van Panhuis, Jonathan Baker, Sharon Riddler, Jim Gavel, Ray Cefola, Carol Oriss, Deborah McMahon, Benard Macatangay, Christine O Neill, Stacy Edick, Randall Brand, Janet Harrison, Richard Duerr **SFDH:** Susan Buchbinder, Albert Liu, Alfonso Diaz, Deawodi Ladzekpo, Elizabeth Faber, Hailey Gilmore, Kerry Murphy, Kimberly Marsh, Ryan Gonzalez, Sally Grant, Zoe Lehman, Tim Matheson, Janie Vinson, Jobert Poblete, Jose Carlos Asencios, Toren Jones, Jenese Jackson, Myra Ozaet, Monique Biega, Scott Fields, Diana Ng Wong, Yelena Koplo, Chris Quan, Beth Osterbauer, Marcelle Millian, Ian Schneider, Montica Levy, Emily Schaeffer, Alani Kalfayan **San Juan:** Carmen D. 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- MTN-017 participants



# Thank You!

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