# Setting the stage:
## How did the VOICE results impact future HIV prevention trials?

Optimization of Adherence after VOICE Meeting

September 1-2, 2015

National Institute of Allergy and Infectious Diseases

# VOICE Development (2006-2009)

- Success of treatment roll-out in Africa
  - Adherence higher than anticipated
- Empowerment of women
  - Putting control of HIV prevention in women's hands
- Insufficiency of "ABC"-based prevention efforts
- Good safety profile of tenofovir-based treatment

# VOICE Development (2006-2009)

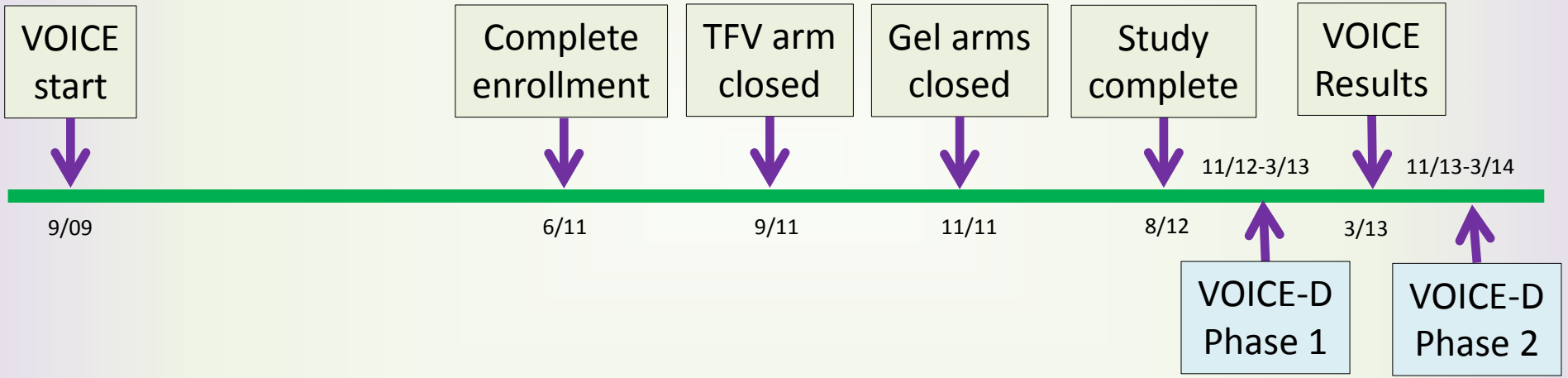
**Trials completed**

- HPTN-035
- MDP-301
- Carragard
- MIRA
- Cellulose Sulfate

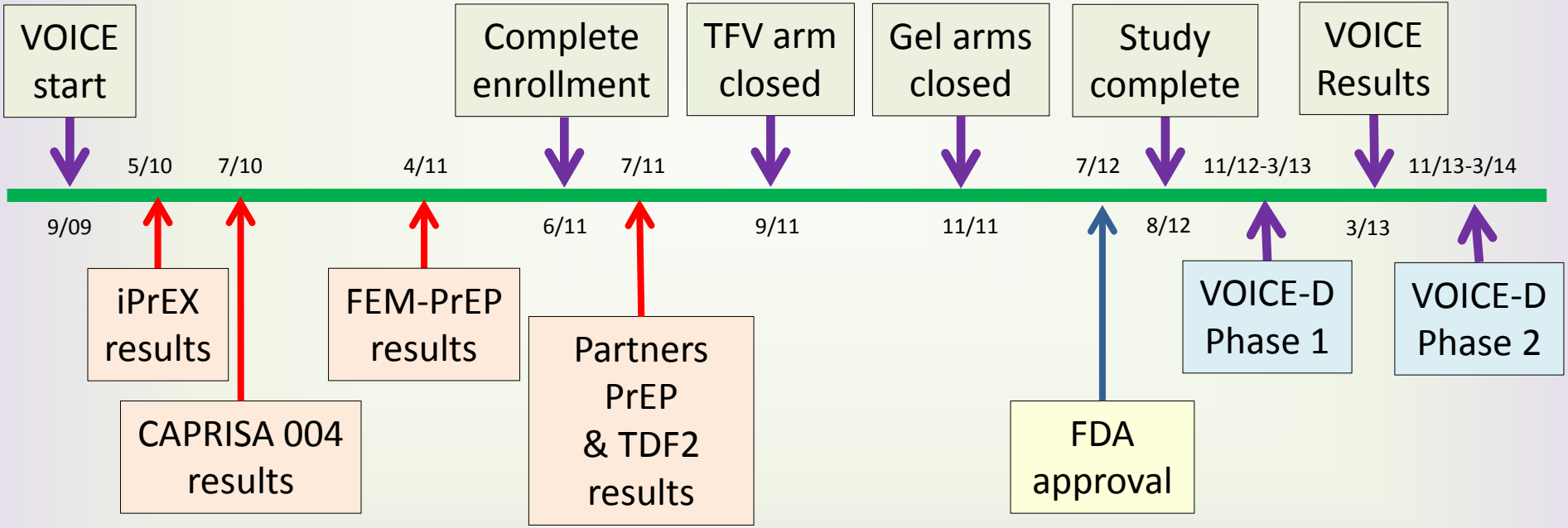
**Trials initiated**

- iPrEX
- Partners PrEP
- TDF2
- CAPRISA 004
- FEM-PrEP

# Key events


VOICE start
Complete enrollment
TFV arm closed
Gel arms closed
Study complete
VOICE Results
11/12-3/13
11/13-3/14
9/09
6/11
9/11
11/11
8/12
3/13
VOICE-D Phase 1
VOICE-D Phase 2

# Key events


VOICE start
Complete enrollment
TFV arm closed
Gel arms closed
Study complete
VOICE Results
5/10
7/10
4/11
7/11
7/12
11/12-3/13
11/13-3/14
9/09
6/11
9/11
11/11
8/12
3/13
iPrEX results
CAPRISA 004 results
FEM-PrEP results
Partners PrEP & TDF2 results
FDA approval
VOICE-D Phase 1
VOICE-D Phase 2

# VOICE Outcomes

- Women enrolled in the trial: 5029 women in 21 months
- They kept coming back:

  95% of PY retained, 91% followed to termination visit
- They reported high adherence:

  90% adherence by FTFI, 88% by ACASI
- They returned the correct amounts of unused product:

  86% adherence by returned product counts
- Their blood told a different story:

  25-30% of quarterly samples positive for tenofovir

  >50% never had drug detected at any quarterly visit

Marrazzo, NEJM, 2015

# Adherence Counseling in VOICE

- Focus on empowerment of women to make their own decisions and on overcoming individual barriers and challenges
- Evolved during study
  - Initially based on reconciling product returns and reported use
    - Focus on correct product use and reminder tools
  - Changed to a client-center counseling approach midway through study (VASP initiated in May 2011)
    - Focus on individual support needs and life context
    - Did not allow consideration of reported adherence
    - Sought to encourage honest reporting of product use

van der Straten, AIDS and Behavior, 2015

# So what happened?

- Could not do PK testing until after study completion
  - Fear of unblinding
- Did not adequately address:
  - Lack of desire or willingness to use products
  - Other motivators to join a trial
  - Impact of outside influences
  - Degree of stigma

# What was VOICE-D?

- Ancillary study conducted after VOICE
- Phase 1: 88 women
  - IDIs
  - Anal sex, reasons to join trial and barriers to product use
- Phase 2: 127 women
  - IDIs and focus groups
  - Showed women their drug detection category

## High adherence/ High-level drug detection

A

B

## Inconsistent adherence/ Occasional drug detection

C

D

## Non adherence/ No drug detection

E

*Note: Each tea pot represents the average overall adherence for a participant, based on all samples tested. Each tea cup represents a specimen/ time point and each group of tea cups depicts a representative adherence pattern for a sample participant. Full cups represent detectable drug, empty cups represent no drug detected.*

# What did we hope to learn from VOICE-D?

- Reasons women joined the trial
- Reasons women wanted to appear adherent
- What happened to the unused product
- Biggest challenges to adherence
- Best motivators for adherence

# What did we learn from VOICE-D?

- Phase 1
  - A lot about anal sex attitudes and practice
    - 3 papers published, lead author Zoe Duby
  - What “other women” in the study did
    - Discarding of products in pit latrines and trash
    - Use of gel as a skin and hair product
  - Challenges to product use
    - Rumors in waiting rooms (product “rotting” uterus and liver)
    - Impact of stigma, particularly for the tablets
    - Gel being too wet, causing accusations of infidelity

# What did we learn from VOICE-D?

- Phase 2
  - Provision of individual PK results worked well
    - Acceptable
    - Understood
    - Promoted open discourse on product non-use
  - Motivators for enrollment were identified
    - Access to high quality health care, contraception, HIV/STI testing
  - Women openly discussed
    - How they counted and discarded “correct” amount of product
    - Why they wanted to stay in trial
  - Fear of side effects was most common adherence challenge reported, often fueled by:
    - Waiting room gossip/rumors
    - Medical research mistrust

van der Straten, JAIDS, in press

# What did we learn from VOICE-D?

- Why did women hide non-adherence?
  - Fear of being terminated from trial early
    - Fear of being labeled as HIV+
    - Did not want to lose access to health care services
  - Not wanting to disappoint clinic staff or be reprimanded by them
  - Not wanting to be labeled as a “failure”
  - It was easier than admitting non-use
    - No one would know it wasn’t true
    - Reduced time in clinic due to decreased counselling pre-VASP
    - There were no negative consequences

# What did we learn from VOICE-D?

- Common themes
  - Biologic monitoring of adherence with feedback was strongly recommended
    - Both phases of VOICE-D
    - All sites
    - All adherence categories
  - Participation in the trial was highly valued, product use was not
  - Stigma and fear of side effects were major barriers to product use
  - Using independent interviewers away from the trial site did not result in more honest reporting of product use in Phase 1
  - Providing women their own drug detection data triggered more open reporting and discussion in Phase 2

# How did VOICE impact future trials?

- Biologic measures of adherence are crucial
  - While trial is ongoing
  - With feedback to sites (blinded)
- Desire to participate in trial is distinct from desire to use product
  - Women need to “desire” both HIV prevention and the products tested
- Women have many competing priorities
  - Products that require less effort may compete better
- External influences are key drivers
  - Empowering individual women isn’t enough (even with covert product)
  - Need to address peer, family and community attitudes and pressures
  - Male partner engagement/involvement is important and desired