MTN-001
Adherence and Pharmacokinetic Study of Oral and Vaginal Preparations of Tenofovir

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Primary Objectives

- Comparison of oral tenofovir, vaginal tenofovir, and simultaneous use of both products

- Adherence
- Acceptability
- Pharmacokinetics
  - Blood
  - Cells in blood
  - Female genital tract

Study Schema

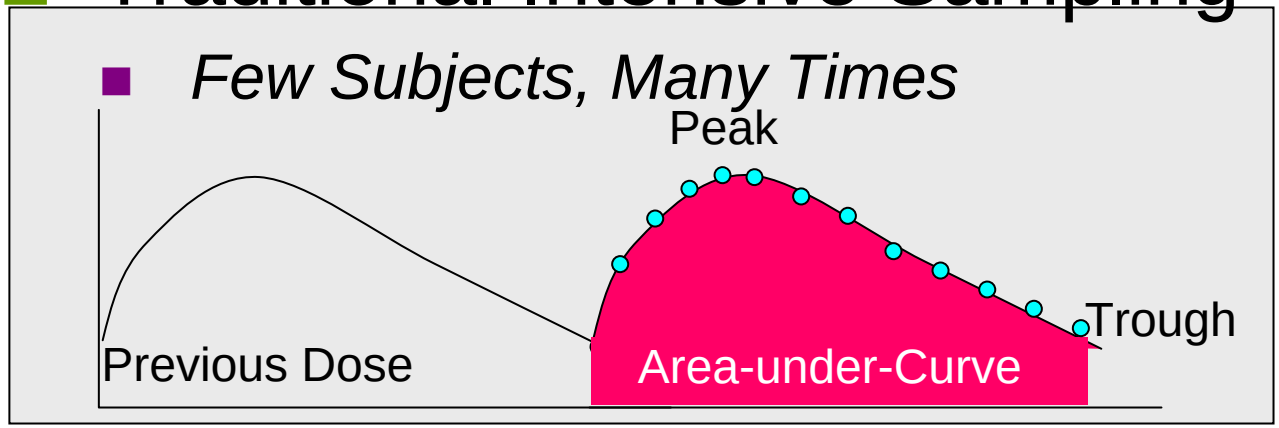
Sequence	N	Period A: 6 WEEKS	1 WK Wash out	Period B: 6 WEEKS	1 WK Wash out	Period C: 6 WEEKS	1 WK Wash out
1	24	Oral		Vaginal		Oral + Vaginal	
2	24	Vaginal		Oral		Oral + Vaginal	
3	24	Oral + Vaginal		Oral		Vaginal	
4	24	Oral + Vaginal		Vaginal		Oral	
5	24	Oral		Oral + Vaginal		Vaginal	
6	24	Vaginal		Oral + Vaginal		Oral	

PK DOT PK AA PK DOT PK AA PK DOT PK AA

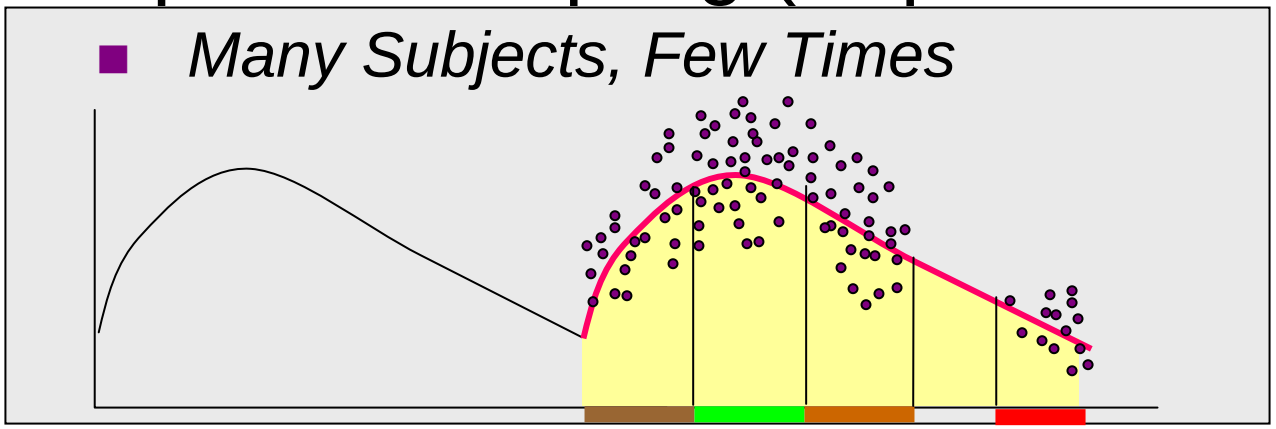
PK blood, intracellular ; unobserved dose
DOT PK blood, intracellular, CVL; observed dose
AA adherence assessment

PK Sampling Scheme

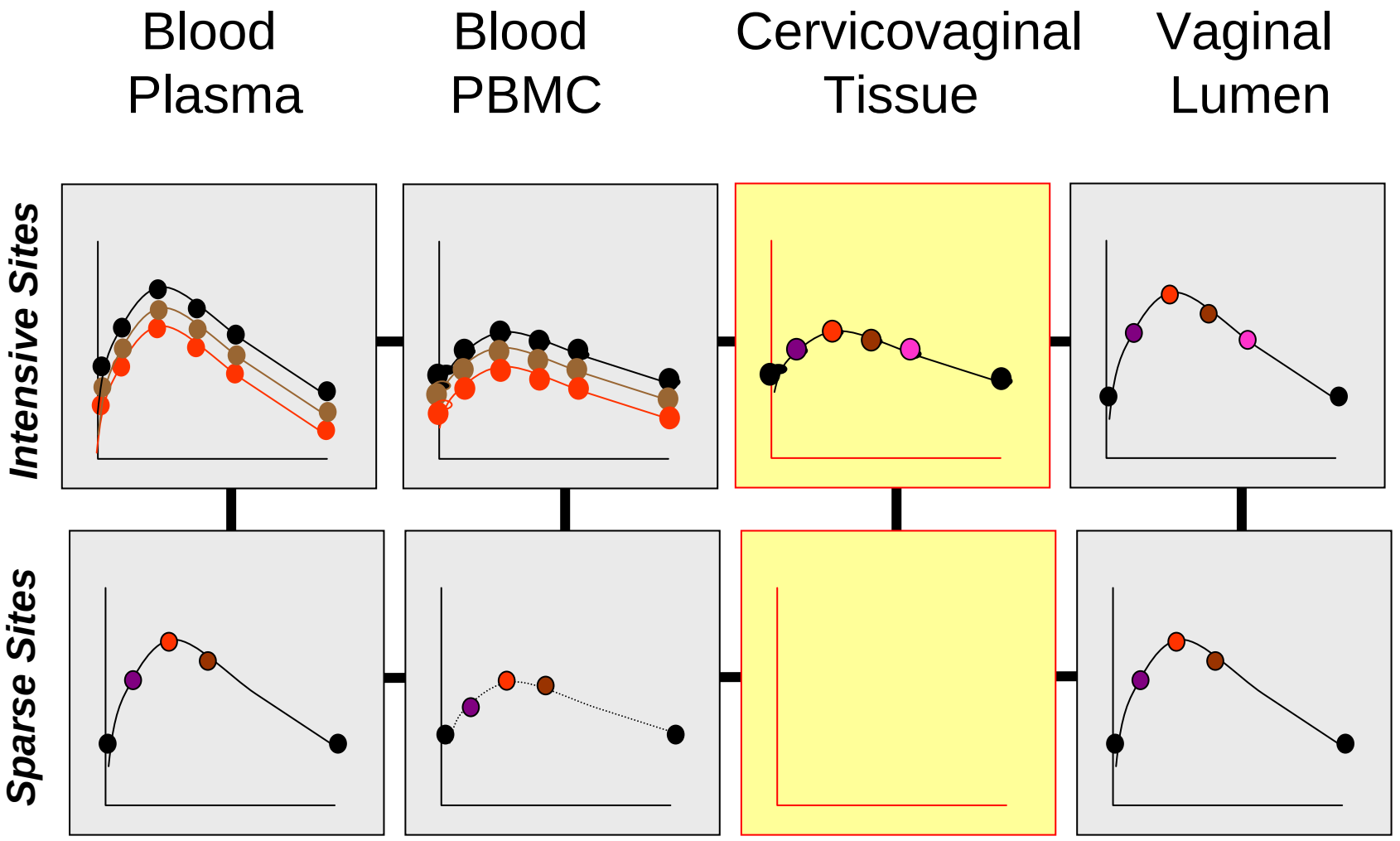
- Traditional Intensive Sampling
  - *Few Subjects, Many Times*



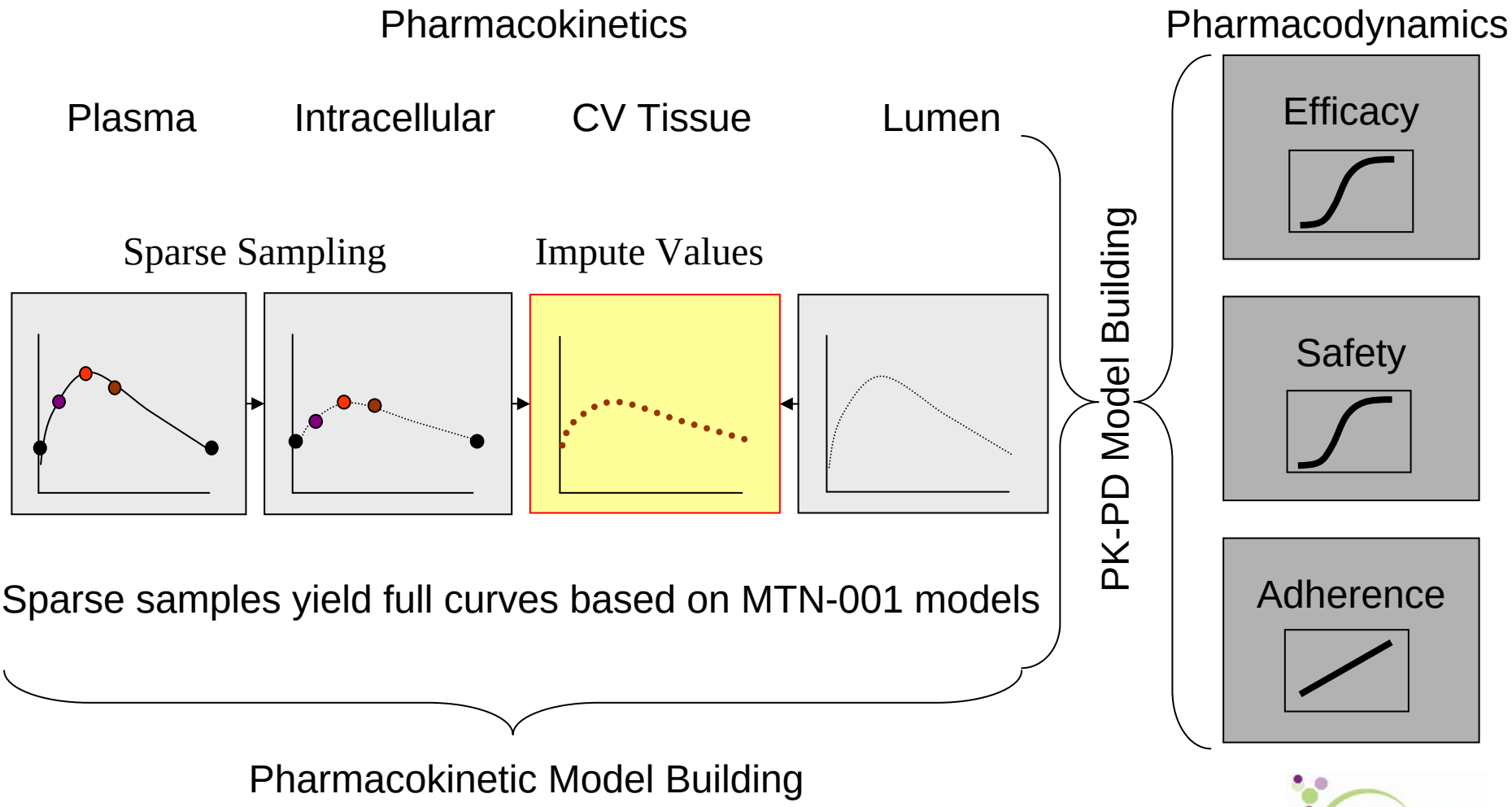
- Sparse Sampling (Population PK)
  - *Many Subjects, Few Times*



PK Multi-Site Model Building



MTN-003 Linkage: PK-PD Model



Unique Contributions

- Compare oral v. vaginal product adherence
- Impact of second product on adherence
- Comparison of oral v. vaginal PK
- Integrated multi-compartment PK model after oral dosing (blood cells, tissue, lumen)
- Additive effect of dual route dosing
- Comparison of observed v. unobserved PK to assess adherence
- Simulation of VOICE tissue intracellular TDP kinetics

Current Protocol Status

- Protocol version 1.0 to sites 20 NOV
- FDA IND response sent 2 APR
- IRB Approvals
  - All sites have submitted to their IRB/EC
  - Pitt approved 6 MAR; Registration submitted 31 MAR
  - CWRU approved 28 MAR; Registration submitted 3 APR
- Study-Specific Training:
  - Pitt: 8 – 10 April
  - Cleveland: 29 April – 1 May
  - Durban, Kampala planned for June
- Enrollment anticipated to open late April

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Questions?