



HIV VACCINE  
TRIALS NETWORK

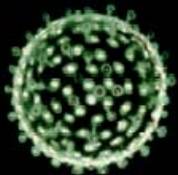


# Why we unblinded Phambili

Glenda Gray on behalf of HVTN 503(Phambili)

HVTN Full Group Meeting, Seattle

7<sup>th</sup>-9<sup>th</sup> November, 2007



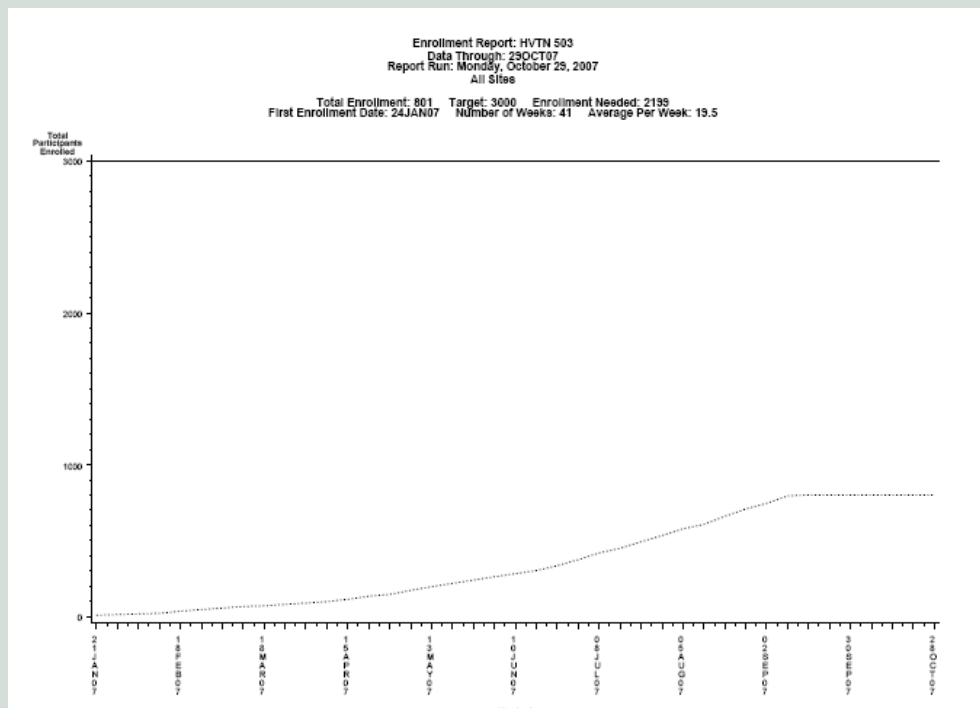


# Scope

- Phambili/HVTN 503 progress up to 19<sup>th</sup> September
- Events leading up to unblinding
- Phambili/HVTN 503 DSMB recommendations to the Oversight Committee (HVTN, NIAID and Merck)
- Process of unblinding



# 19<sup>th</sup> September: Stopping the steam train



801 enrolled (45% female):

- 3 vaccinations/placebo: 58
- 2 vaccinations/placebo: 501
- 1 vaccination/placebo: 215

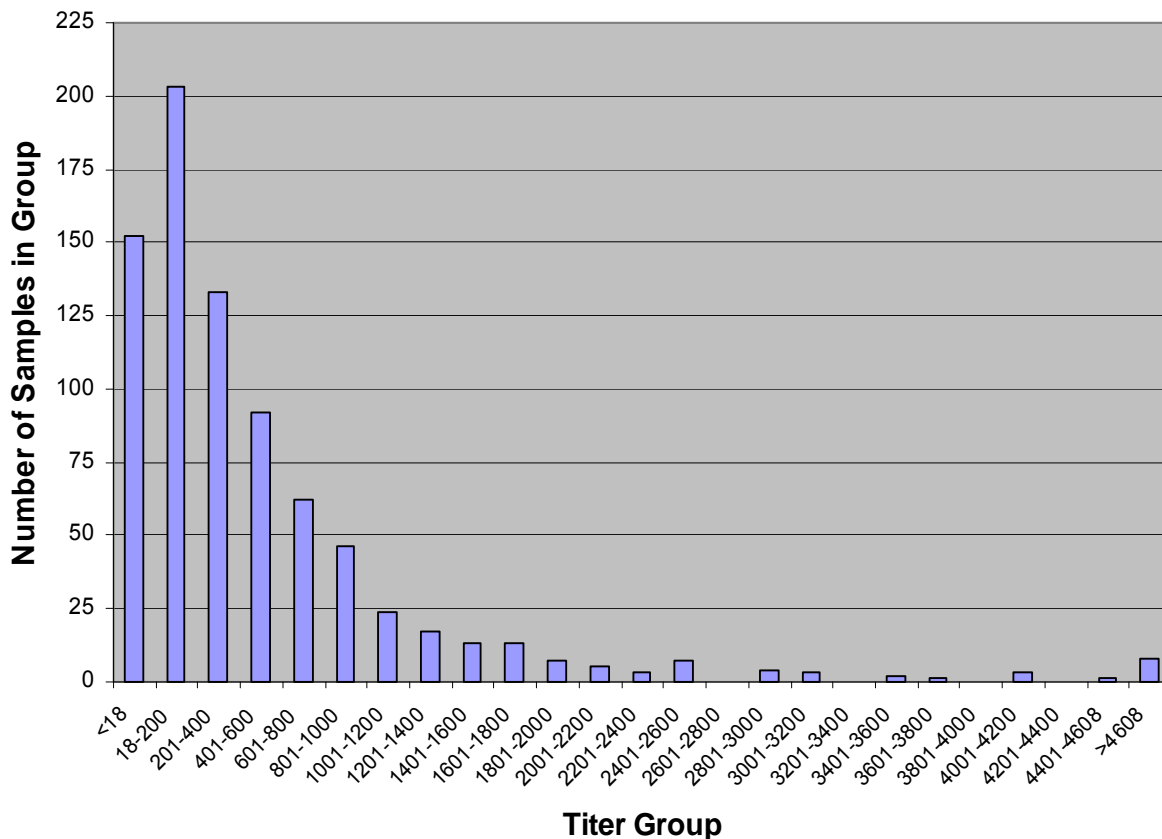
Age range:

- 18-20yrs: 30%
- 21-30yrs: 60%
- 31-35: 10%



# HVTN 503: Ad5 Neut AB titers

## HVTN-503 Ad5 Neut Ab Titer Distribution



791 total

Ad5<18: 19.2%

Ad5≤200: 44.8%

titer group	# in group
<18	152
18-200	203
201-400	133
401-600	92
601-800	62
801-1000	46
1001-1200	24
1201-1400	17
1401-1600	13
1601-1800	13
1801-2000	7
2001-2200	5
2201-2400	3
2401-2600	7
2601-2800	0
2801-3000	4
3001-3200	3
3201-3400	0
3401-3600	2
3601-3800	1
3801-4000	0
4001-4200	3
4201-4400	0
4401-4608	1
>4608	8



## Events leading up to the unblinding

- September 19 -- Paused enrolment and further vaccinations following recommendation of STEP study/HVTN 502 DSMB to halt immunizations in STEP
- September 28 -- Special meeting of Phambili/HVTN 503 DSMB convened; DSMB requested additional information from STEP sponsor
- October 8 -- Phambili DSMB convened again
- October 10 -- DSMB presented their recommendations to the Oversight Committee



# Phambili/HVTN 503 DSMB

- The 503 DSMB reviewed STEP data:
  - Lack of efficacy for both endpoints
  - More infections in the vaccine than placebo arms
- STEP DSMB recommended no further immunization and 503 DSMB concurred.
- 503 DSMB recommended to
  - Suspend enrollment and study injections
  - Unblind participants
  - Counsel participants about possible increased risk of HIV acquisition in the vaccine arm, based on data from STEP
- The OC concurred with this assessment



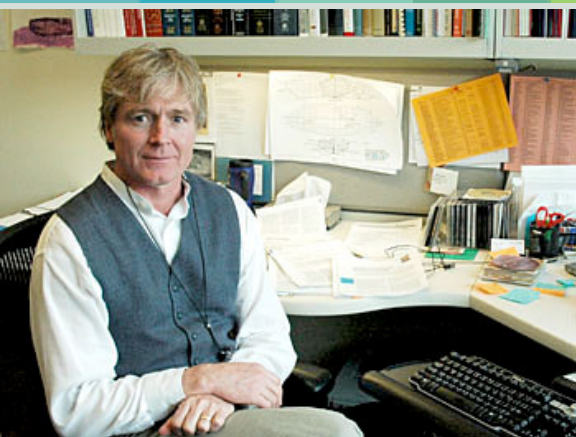
# Summary

- 502 showed the possibility that the vaccine might increase susceptibility to HIV acquisition.
- Key questions pertaining to safety and longer term effects might be answered in 502 due to its advanced state (almost everyone already immunized)
- 503 was in its infancy and would not yield substantial information without additional immunizations.
- It seemed prudent to err on side of caution, halt 503, unblind and counsel participants.



HIV VACCINE  
TRIALS NETWORK

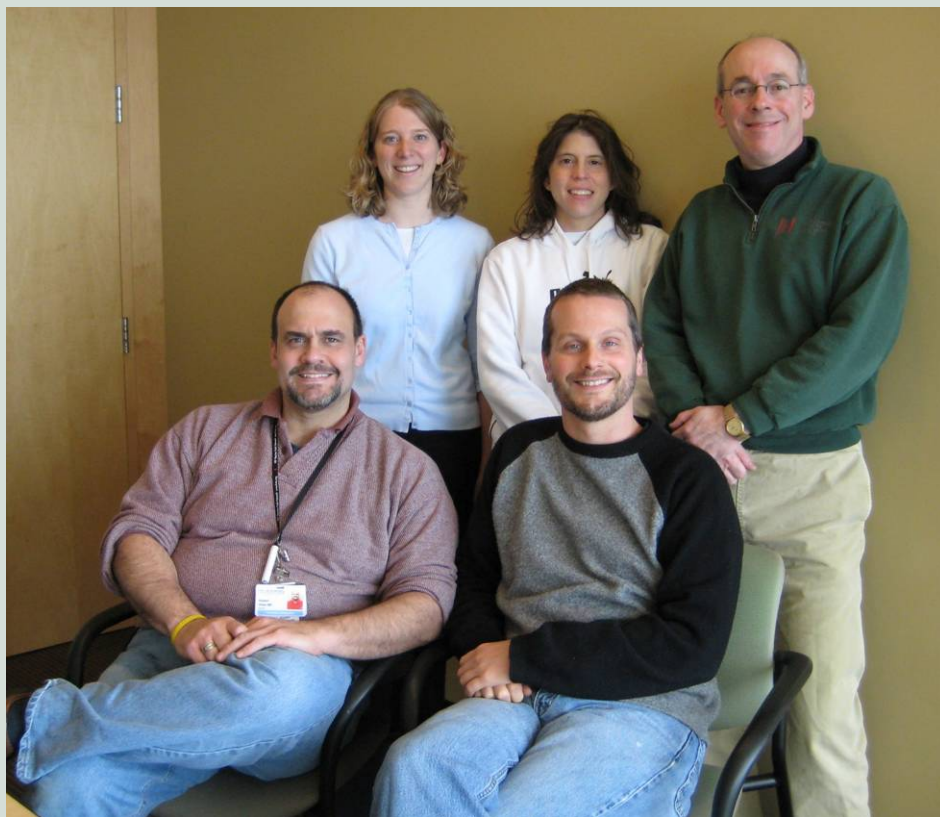
# STEPS NEEDED TO UNBLIND





# STEPS NEEDED TO UNBLIND

A team from Seattle



....Mary Allen



....and DAIDS Regulatory  
Affairs Branch



# STEPS NEEDED TO UNBLIND

October 15-22<sup>nd</sup>

- CABS consulted with decision, CABS input on participant information leaflet
- IRBS consulted on execution of DSMB & OC recommendations
- MCC, IBC, GMO & National Ethics Committee informed on October 22<sup>nd</sup>
- MOH and key government stakeholders informed
- Public announcement & unblinding on 23<sup>rd</sup> October
- Logistics (unblinding codes, CRFs, LOA) etc needed to be developed



# Unblinding: The Process

- Day 1: DAIDS approves LOA in one day
  - Day 10: 3 out of the 4 IRBS approved LOA
- Day 2 (7 am): Unblinding documents available
- Day 2: Unblinding begins:
  - Participants called via phone/ bulk SMS/ radio
- Day 5: ~200 participants unblinded
- Day 8: ~700 participants unblinded
- Day 16: Total unblinding complete



# Unblinding: Challenges

- Huge challenge contacting and getting participants in at such short notice
- Had to sort out new procedures on the job
- Staff anxiety about participant reaction
- Staff anxiety about jobs
- Participants studying for exams
- Medical officer resigning (MEDUNSA)



# Unblinding: Challenges with Press

- In RSA: winning Rugby world cup overshadowed the announcement
- One inaccurate report in local newspaper
- Washington Post: distorted reporting





# Conclusions

- CABS and key governmental stakeholders crucial in process of executing DSMB & OC recommendation
- SAAVI key to process in RSA
- Precise communication with participants & staff facilitated smooth unblinding & counselling re potential harm



# Acknowledgements:

**AIDS will be stopped by South Africans like you!**

CAPE TOWN:  
Tel: +27 (021) 633 4035

DURBAN:  
Tel: +27 (031) 260 1940

KLERKSDORP:  
Tel: +27 (018) 406 4200

MEDUNSA:  
Tel: +27 (012) 521 5906

SOWETO:  
Tel: +27 (011) 989 9907

**PHAMBILI**

Looking forward to a better future

[www.phambili.org.za](http://www.phambili.org.za)



Deaths in Women

