Clinical Trials: Rapporteur Session

AIDS Vaccine 2008
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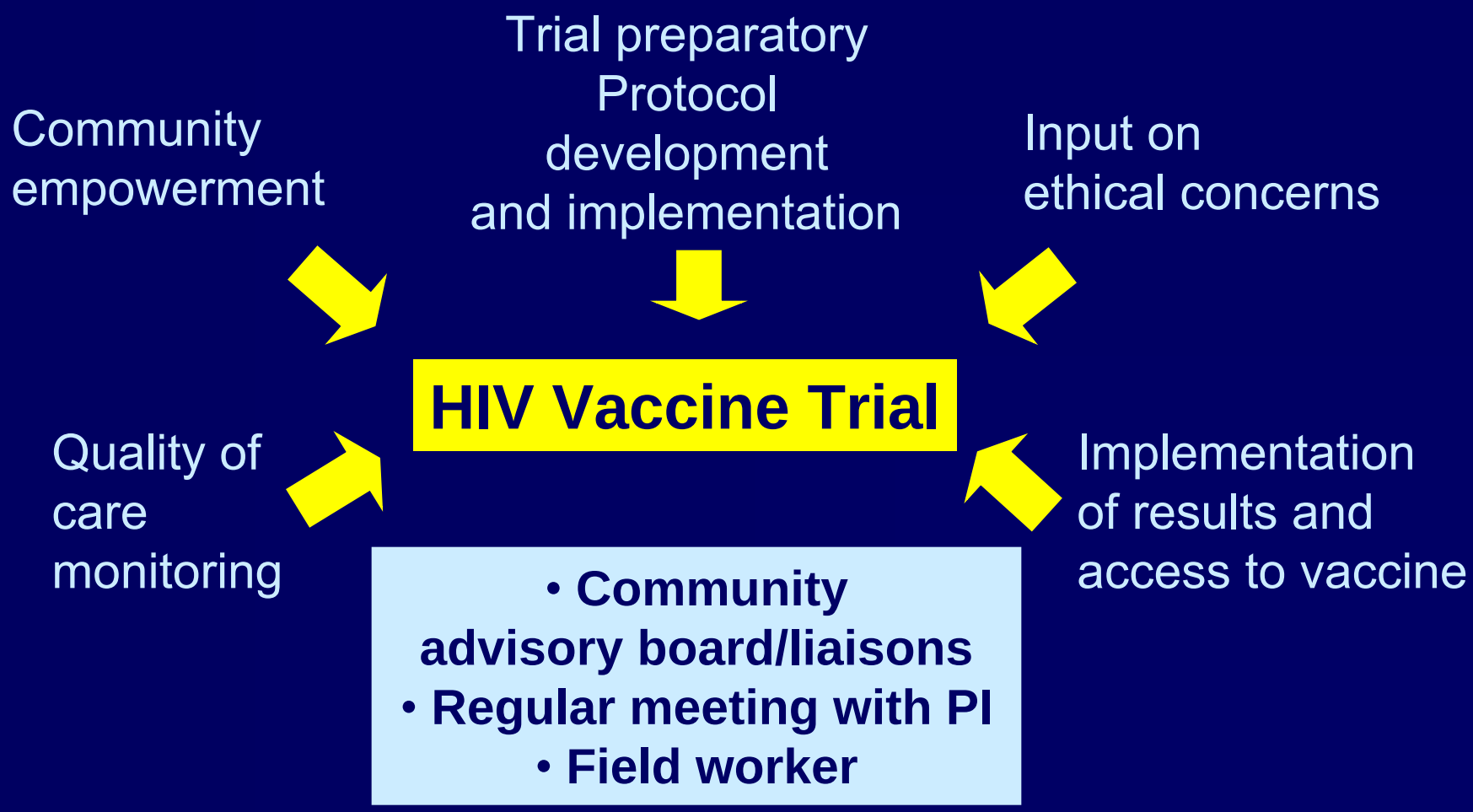
Jintanat Ananworanich, MD, PhD
Mark de Souza, PhD, MPH (AFRIMS)
Jerome H. Kim, MD (WRAIR)
Philip Renzullo, PhD, MPH (NIAID)

Outline

- Community involvement
- Preparing for HIV vaccine trials
- Lessons learned from the STEP trial
- Traditional/proposed trial development pathways
- The way forward

Community Involvement (Immediate, Larger, National, Global)



P. Goicochea (PL01-02), R. Twine (P06-11)

Preparing for HIV Vaccine Trials

- Community participation
- Knowing and identifying ways to improve acceptability to HIV vaccine intervention
  - Increase female participation in Western Kenya[1], Rwanda[2] and US (minority)[3] by intensified recruiting strategy
- Involve adolescents in HIV vaccine trials[4,5]

[1]A. Adega (P06-19, P06-18), [2]K. Kayitenkore (OA08-05), [3]P. Frew (OA08-02),
[4]H. Jaspan (OA08-04), [5]L. Bekker (RT01-05)

Preparing for HIV Vaccine Trials

- Using technology as a tool for enrollment and retention (free mobile phone minutes[1], radio[2], email[3])
- Importance of regional reference ranges[4]

[1]N. Chimbindi (P06-16), [2]A. Sangowawa (P14-15), [3]K. Louis (OA08-08), [4]A. Kamali (P13-13)

Maintaining Vaccine Research Agenda in the Absence of Vaccine candidates

- 20 years of cohort and vaccine preparedness in Uganda but no vaccine is ready for efficacy trials
- Maintain existing cohorts, community interest and well-trained staff by
  - Long term research investment
  - Multidisciplinary approach to research and prevention
  - Integration of prevention and care
  - Human capacity and infrastructure development
- Diversification of research portfolio to non-HIV

P. Kaleebu (SP01-02)

Lessons Learned from the STEP Trial

- Scientific issues[1]
  - Lower HIV viral load in Ad5 naive vaccinees with more IFN-γ-secreting T cells and those with more Gag CD8+ T cells
  - Beneficial effect of protective HLA alleles observed in HIV+ cohorts particularly in vaccine recipients
  - Further investigations
    - Role of Ad5 immunity in HIV acquisition
    - Potential confounders

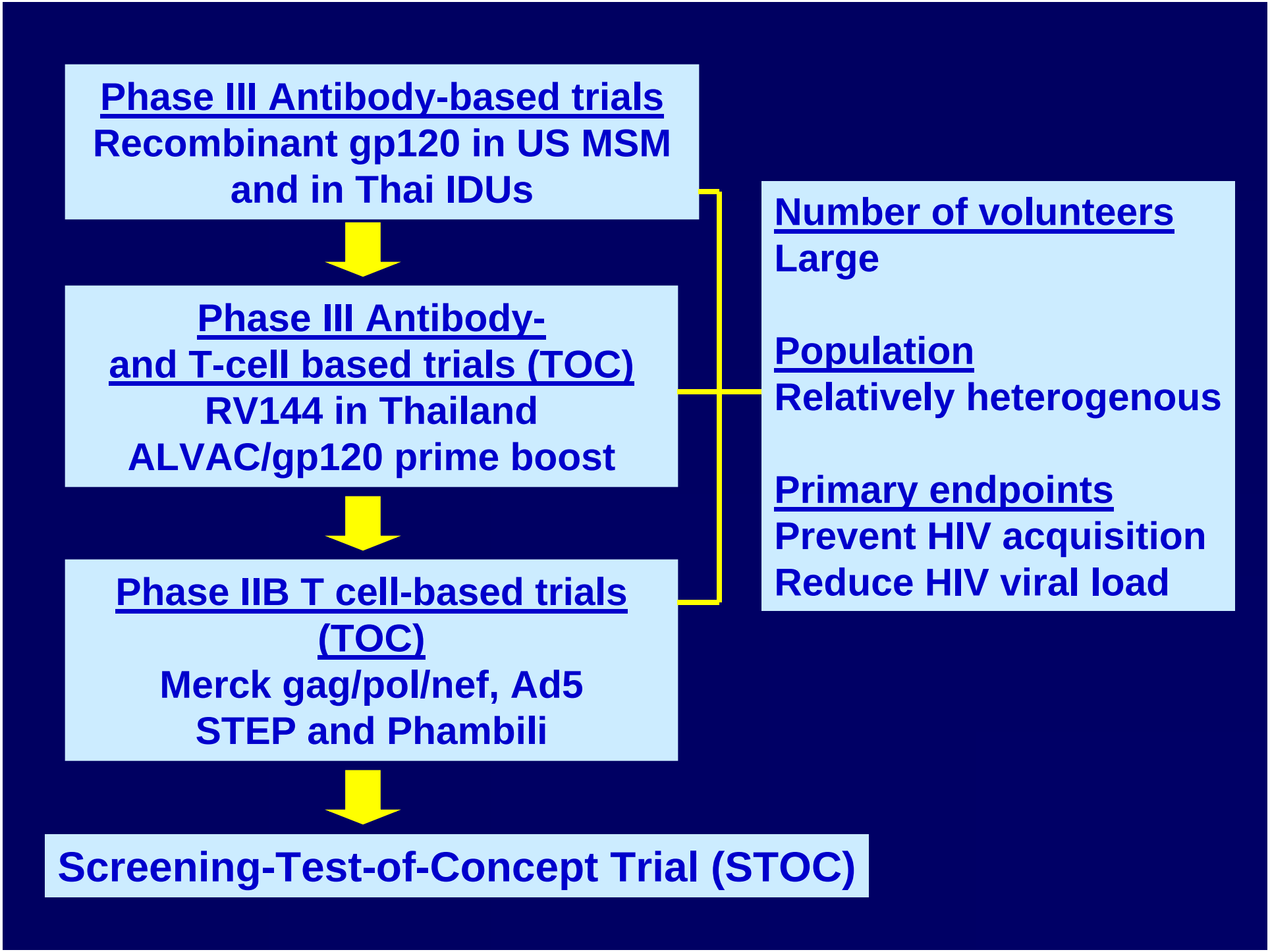
- Regulatory issues[2]
  - Issues with use of live viral vectors
  - Little guidance from FDA, EMEA, WHO and national regulatory authorities
  - Clear stopping rules
  - FDA advisory consultation

[1]J McElrath (PL01-01), S Buchbinder (PL 02-03), [2]H. Rees (SP01-05)

Lessons Learned from the STEP Trial

- Ethical issues
  - Trial-related harm
    - Obligation to provide monitoring and ARV without time limit
    - No obligation to provide monetary compensation unless stipulated in advance
  - Impact on future HIV vaccine trials
    - Inform volunteers on STEP trials
      - Factors that enhance HIV susceptibility
      - Similarities/differences of vaccine products/risk factors compared to STEP
    - Circumcision as required vs. encouraged

R. Macklin (PL02-02), N.Naicker (P13-27)


Phase III Antibody-based trials
Recombinant gp120 in US MSM
and in Thai IDUs
Phase III Antibody-
and T-cell based trials (TOC)
RV144 in Thailand
ALVAC/gp120 prime boost
Phase IIB T cell-based trials
(TOC)
Merck gag/pol/nef, Ad5
STEP and Phambili
Screening-Test-of-Concept Trial (STOC)
Number of volunteers
Large
Population
Relatively heterogenous
Primary endpoints
Prevent HIV acquisition
Reduce HIV viral load

Screening-Test-of-Concept Trial (STOC)

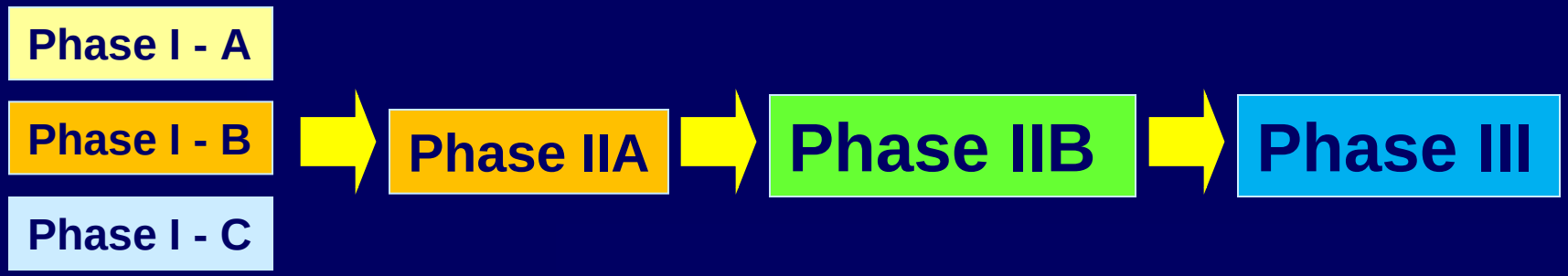
- Screen vaccine candidates for evidence of impact on HIV viral load set point
  - Consider advancing candidate if ≥ 1.0 $\log_{10}$ viral load reduction observed
  - Averaging at least 2 viral load measurements from a set window period (pre-ARV)

- Randomized 1:1 vaccine vs. placebo trial
  - 34 evaluable viral load endpoints required for 80% power against 1.0 $\log_{10}$ viral load change
  - Total sample size of around 1000
  - Around 3 years in duration
  - Relatively homogenous population

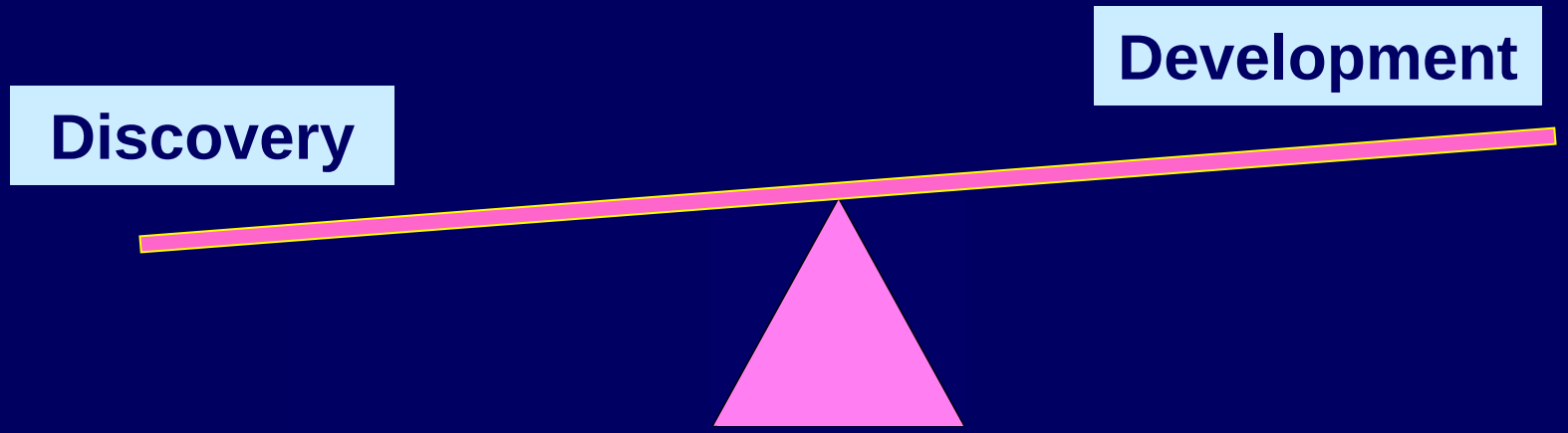
- Not designed to directly assess HIV acquisition/enhancement and immune correlates

F. Priddy (SP01-03), S. Self (SP01-04)

Traditional Trial Development Pathway



Proposed Trial Development Pathway



Phase I and/or II preventive clinical vaccine trials

- MVA - CRF01_AE[1]
- DNA/MVA Multiclade[2]
- F4co/AS01- HIV subtype B p17/p24 gag, RT and Nef[3]
- ADVAX – Clade C/B'[4]
- Tiantan Vaccinia – CRF07 B'/C[5]
- CD4 Multiepitope polypeptide (EP1043) alone

or in combination with CTL multiepitope DNA[6]

[1]OA05-06, [2]P13-01, [3]OA05-02, [4]P13-20, [5]P13-18, [6]P13-12

HIV Vaccine
as Part of Combination HIV Preventive Approach

Harm reduction

Circumcision

Condoms

STI treatment

ARV

Microbicides

UNAIDS/WHO Ethical Guidance 2007

HIV prevention trial participants have access to <u>all</u> state of the art HIV risk reduction methods