MDP301

AN INTERNATIONAL MULTI-CENTRE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF 0.5% AND 2% PRO 2000/5 GELS FOR THE PREVENTION OF VAGINALLY ACQUIRED HIV INFECTION

FUNDED BY UK MRC AND DFID

PRESENTED BY

GITA RAMJEE

HIV PREVENTION RESEARCH UNIT

MEDICAL RESEARCH COUNCIL

MTN REGIONAL MEETING

CAPE TOWN 18-22 OCTOBER 2009

MDP301 PARTNERS

ENDO
Pharmaceuticals
Boston
US

LSHTM
MRC CTU
St George's Hospital
Imperial College
London, UK

York/Hull University
York
University of Southampton
Southampton
UK

CRESIB/University of
Barcelona
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MRC UK, Masaka/Entebbe,
Nsambya Hospital, Kampala
Uganda

AMREF/NIMR/LSHTM
Mwanza
Tanzania

UNZA, Lusaka,
Illovo Sugar, Mazabuka
Zambia

Fundacio Clinic/Mavalane
Hospital/FDC
Manhica/Maputo
Mozambique

The Africa Centre, Mtubatuba
MRC, Durban
RHRU, Johannesburg
South Africa

MDP 301 GOVERNANCE

- Independent Data Monitoring Committee
  - Chair Professor Sir Alasdair Breckenridge(UK)
  - Statistician Professor Catherine Hill (France)
  - Clinician Dr Florence Mirembe (Uganda)
  - Public Health Physician Dr Isaac Malonza (Kenya)

- Trial Steering Committee independent members
  - Chair Professor Anna Glasier (UK)
  - Clinical epidemiologists
    - Professor Anne Johnson (UK), Dr Alwyn Mwinga (Zambia)
  - Clinicians Dr Mike Chirenje (Zimbabwe)
  - Community Mrs Angelina Wapakabulo (Uganda)

MDP301 IDMC AND TSC MEETINGS

- March 05 1st IDMC with TSC to review protocol; TSC followed IDMC thereafter for 1st-6th reports to the IDMC in
  - June 06
  - January 07
  - March 07
  - June 07
  - November 07
  - June 08
  - December 08
- Format is open session with data provided by site and MDP investigators in attendance followed by closed session with data by treatment group with IDMC and trial statistician only
- Since March 07, HPTN035 has held parallel DSMC
- February 08 IDMC advised to continue 0.5% and placebo but to stop 2% gel

MDP301 DESIGN

- 9389 Participants Screened and Enrolled
  - 0.5% PRO2000/5
  - 2% PRO2000/5 (stopped Feb 08, enrolment without 2% = 6,664)
  - or placebo
- Each followed for 12m (24m in Masaka)
- Primary endpoints = HIV infection and grade 3 or above clinical and laboratory adverse events
- Secondary endpoints
  - HSV2, NG, CT
  - Also syphilis, TV, BV and candida
- All Adverse Events

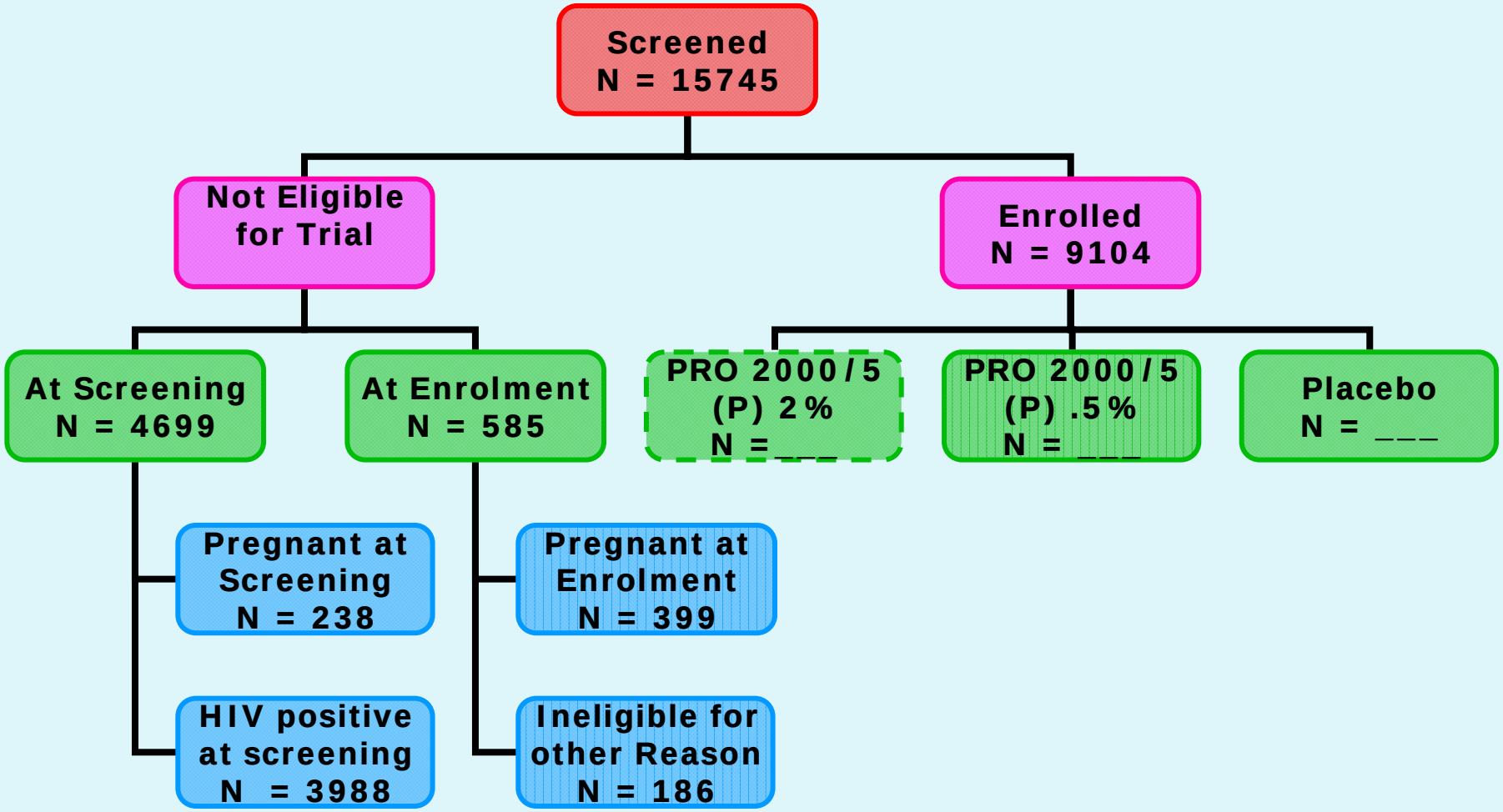
PRO2000/5 GEL PROPERTIES

- PRO2000/5 Gel (P), 0.5% and 2%
- API: Synthetic polymer prepared by acid-catalyzed condensation of 2-naphthalene sulphonic acid and formaldehyde, followed by neutralization and molecular weight fractionation
- Weight average molecular weight: 5±1 kDa and narrow molecular weight distribution
- Aqueous gel formation containing PRO2000/5 (0.5% or 2%), carbomer 1382, lactic acid, trolamine, and the preservatives methylparaben, propylparaben, and sodium benzoate (indicated by the “P” suffix)
- Buffered to pH 4.5
- 0.5% dose = 10mg PRO2000/5
- 2% dose = 40 mg PRO2000/5

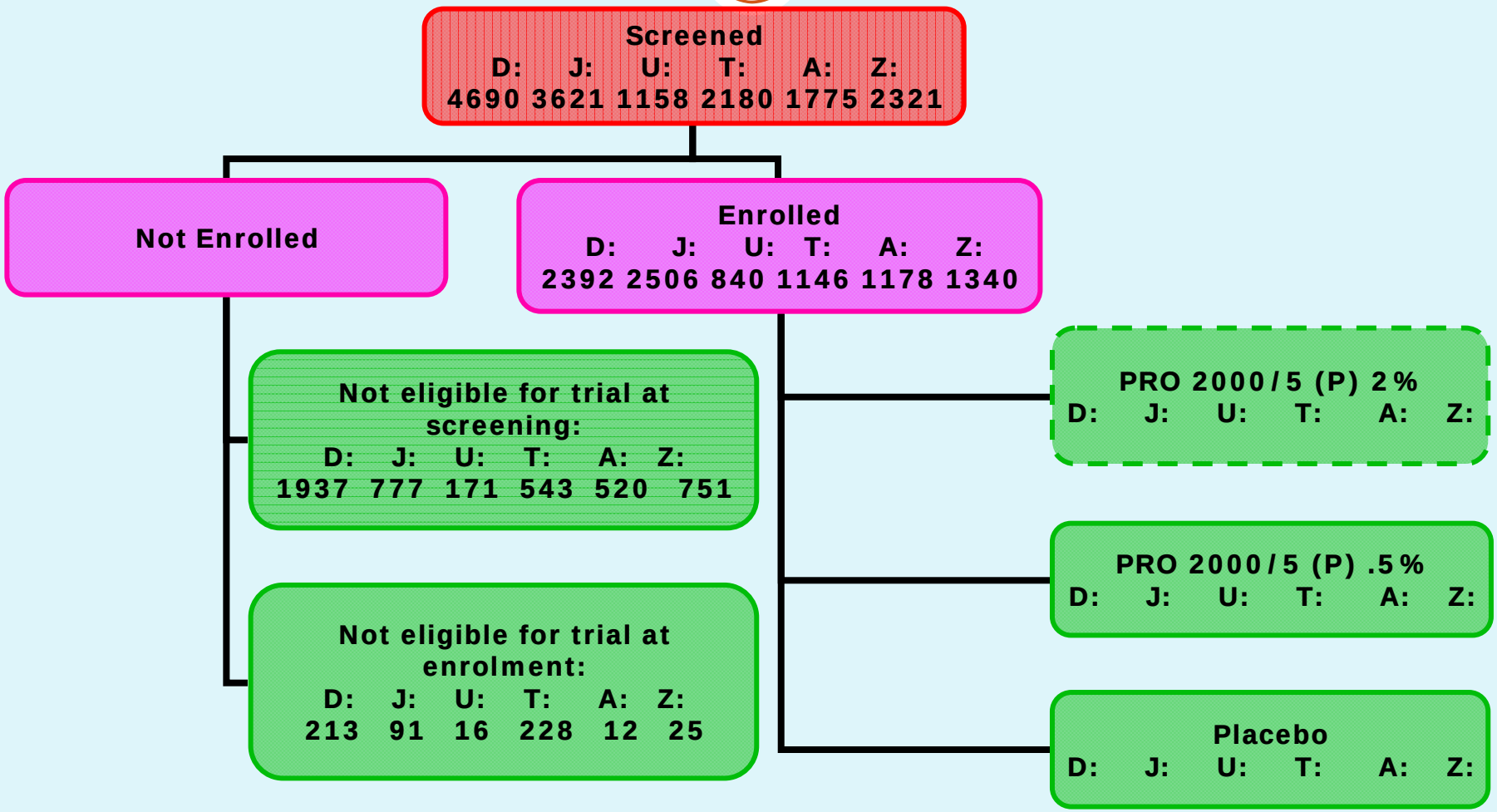
MDP 301 Special features

- Blood levels of PRO 2000 checked at the final visit
- Returned used and unused applicators every 4 wkly visit
- Asked about last sex act at every 4 wkly visit
- Social science subset (1,866 datasets on 747 women)
  - Completed coital diaries on 3 occasions during the trial
  - Participated in 3x In depth interviews during which information from clinic reports, gel returns and coital diaries were reconciled
  - Questioned about sensitive topics, and comprehension of informed consent and details of acceptability
  - Subset of self-selected male partners also interviewed

ENROLMENT FLOWCHART



SCREENING AND ENROLMENT BY SITE



Key- D: Durban J: Jo'burg U: Masaka T: Mwanza A: Africa Centre Z: Mazabuka

Three scenarios for result

- Safe but not effective
- Safe and effective, cautious stream
  - Proof of concept
  - Modest effect
  - Inconsistencies
- Safe and effective, encouraging stream
  - Long awaited breakthrough
  - At or greater than the moderate protection considered worthwhile
  - Greater protection in consistent users defined by self-reports
  - Absence of toxicity in women that were high gel users defined by the number of used applicators returned

PREPARATION OF DISSEMINATION

- Dissemination Working Group – Gita Ramjee, Roger Tatoud, Sheena McCormack, Joyce Wood
- MMCI and GCM communications – Mitzy Gafos and Neetha Morar
- Documentation for outcome scenario documents, e.g. press release, Q&A and background info
- Investigators' Meeting – end of November 2009
- Release date - unknown