

Overview of Microbicide Development Programme

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Microbicide Development Programme (MDP)



- Partnership for development of vaginal microbicides
- Collaboration between African and European Partners
- 6 clinical Sites in 4 African Countries.
- Funded by Dept for international development (Dfid).
- Managed by UK Medical research Council clinical trials unit.

MDP Partners



MRC SSHPU
Glasgow

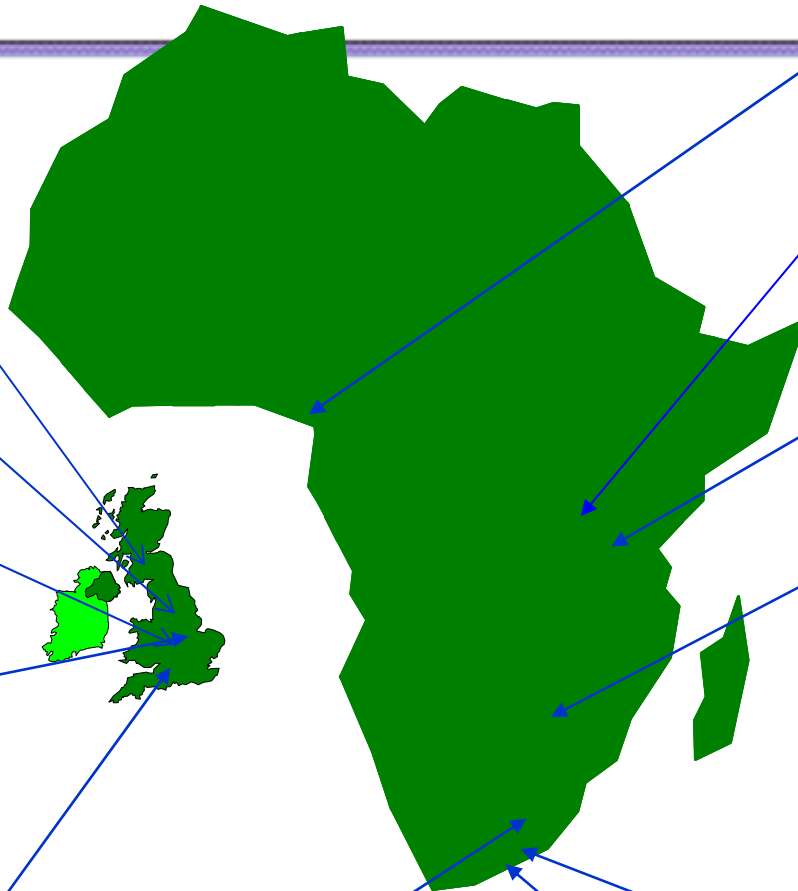
York/Hull University
York

Oxford University
Oxford

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

University of Southampton
Southampton, UK

University of Barcelona
Barcelona, Spain



Laboratoire de Santé Hygiène Mobile
Cameroon Red Cross
Yaoundé, Cameroon

Nsambya Hospital, Kampala
MRC UK, Masaka/Entebbe,
Uganda

AMREF/NIMR/LSHTM
Mwanza, Tanzania

UNZA, Lusaka,
Illovo Sugar, Mazabuka
Zambia

RHRU
Johannesburg, SA

Population Services International
Europe

The Africa Centre
Mtubatuba, SA

MRC SA
Durban, SA

How was mutual respect/support achieved within MDP?



- Input to scientific decision making
 - Protocol development
 - Representation in programme management board.
- Input to financial and performance decisions
 - Site PIs managed their own budgets from outset.

How was mutual respect/support achieved with communities?



During Feasibility:

- o Mapping to define community and identify key stakeholders
- o Formation of CAB/CAG with terms of reference
- o Consultation on key messages and dissemination

CLO workshop at start of trial:

- o Community representatives from 4 sites as well as MDP community and social science staff
- o Worked together across sites to solve scenarios that may arise during the trial
- o Specific communication skill training



International Scientific Advisory Group

**Data
Monitoring
Committee**

Independent members
of ISAG and
Investigators from PMB

**Trial
Steering
Committee**

Trial Management Group monthly

Programme Management Board (PMB) annual

PMB Executive quarterly

Programme Liaison Group alternate months

Institutional Partners

**Budgets
Actual
Forecasts
Workplans
Targets**

**Other science
Publications
PR issues**

Annual report

Scientific Disciplines
**Clinical
Social
Laboratory
Data management
Statistical
Community**

**Annual
report**

Objectives of MDP



Overall goal is to complete phase III effectiveness trials of candidate microbicides in Africa.

- Determine scientific mechanisms of action for microbicide agents.
- Conduct pre-clinical evaluation (in vitro models)
- Site assessment and preparation for phase III trials through feasibility and pilot studies.

MDP Objectives (cont)



- Social science research into acceptability of products
- Capacity building of African scientists and researchers.
- Facilitate marketing and access to a successful microbicide.

MDP301 pre-trial activities

2001-04 in 6 sites (aim ~770 pyrs):

❖ Feasibility study to assess

- o HIV incidence and prevalence
- o retention of women in follow-up when having repeated genital examinations
- o behavioural characteristics including condom uptake with counselling

2004-05 in 6 sites (n=~50 per site):

❖ Pilot Study using placebo gel to assess

- o barriers to gel use
- o the tools and procedures planned for the trial including informed consent

Insight from Feasibility: incidence

Populations	Clinics & communities				Bar/food	Discord ^{dnt}
					Facilities	Couples
	Dbn	Jhb	ACS	Mz/Za	Mw/Tz	Ms/Ug
Recruitment period (m)	14	15	12	18	14	2
Person yrs FU	499.2	531.4	158.1	356.4	717.4	31.2
Sero-conversions	37	21	20	13	25	4
HIV incidence	7.4	3.9	12.6	3.6	3.5	12.6
95% CI	5.4, 10.2	2.6, 6.1	8.2, 19.6	2.1, 6.3	2.4, 5.2	4.8, 34.1

...hence decision to use 4% in sample size calculation

Insight from Feasibility: retention

Populations	Clinics & communities				Bar/food	Discor ^{dnt}
	Dbn	Jhb	ACS	Mz/Za	Facilities	Couples
Start date	Aug02	Oct02	Jul03	Mar03	Mw/Tz	Ms/Ug
N screened	1263	1088	755	1974	1573	1370
HIV+ baseline	47%	20%	50%	30%	25%	(7%)
pregnant	1%	4%	1%	4%	10%	-
N enrolled	608	757	373	590	716	50
FU (% of enrolled)						
3m	94%	84%	76%	87%	83%	90%
6m	88%	79%	61%	79%	79%	84%
9m	82%	83%	47%	70%	70%	86%
12m	67%	87%	-	63%	71%	86%

...hence decision that primary efficacy endpoint be 9m

Insight from Feasibility: condom uptake

% last sex acts protected by condom

Populations	Clinics & communities				Bar/food Discor ^{dnt} Facilities Couples	
	Dbn	Jhb	ACS	Mz/Za	Mw/Tz	Ms/Ug
	At baseline	57%	58%	11%	15%	16%
At 6m	72%	76%	17%	16%	17%	29%
Difference	+15%	+18%	+6%	+1%	+1%	+11%

...this could increase further in trial

STI prevalence at week 0

%

Populations	Clinics & communities				Bar/food	Discord ^{dnt}
					Facilities	Couples
	Dbn	Jhb	ACS	Mz/Za	Mw/Tz	Ms/Ug
Chlamydia	10%	4%	6%	2%	4%	1%
Gonorrhoea	4%	2%	3%	1%	4%	2%
HSV2 +ve	61%	55%	69%	61%	73%	84%
h/o sores/ulcers	3%	7%	23%	5%	10%	55%
Syphilis (RPR)	3%	4%	7%	3%	8%	5%
TV	7%	6%	11%	2%	7%	7%

MDP301 Phase III Trial design

9,673 HIV negative women randomised to

0.5% PRO2000/5

2% PRO2000/5

or placebo in ratio of 1:1:1

each followed for 12m (-24m in Masaka)

Primary endpoint = HIV infection (modified ITT) and safety

Secondary endpoints = HSV2, NG, CT

(Also syphilis, TV, BV and candida)

Progress of MDP 301

- Enrollment started in October 2005.
- Total recruitment is 6000
- The DSMC has met 3 times to review safety data and with about half the expected endpoints achieved there are no safety concerns
- Enrollment complete by July 2008
- Trial results by end 2009

How is MDP doing i.t.o objectives



- Site participation in protocol development
- Site development and Training
- Cross site monitoring
- 5 Investigators meeting
- EDCTP involvement

MDP EDCTP involvement



- Undertake a microbicide feasibility study in Mozambique
- Improve clinical site infrastructure at the RHRU Orange Farm site
- Capacity building in conduct of clinical trials in a **south to south collaboration** (RHRU and Mozambique)

EDCTP grant progress to date:

Site set up



- Mozambique site set up, and recruitment to start by November 2007
- RHRU clinicians, data managers and social scientist conducted site visit
- Mozambique site staff visited RHRU clinical site

EDCTP grant progress to date:

Capacity Building



- 2 epidemiology writing courses
- GCP courses
- Community Advisory Group training
- Clinical trials course
- Cross site clinical monitoring training
- Community Radio talk shows

Summary



- Comprehensive research programme to develop, test and integrate effective microbicides into public health programmes
- Sustainable capacity transferred through genuine partnership
- Feasibility Studies kick-started VCT, gave women care for STIs, contraception, PAP smears and accelerated access to ARVs
- Social science and marketing data will build the economic and epidemiological models that inform & accelerate access

Thank You

- MDP participants
- MDP Partners
- Organizers of the Fourth EDCTP Annual Forum.