

# microbicides 2008

February 24 - 27, 2008  
Hotel Ashok, New Delhi, India

Striving towards HIV Prevention



## Highlights of Monday 25<sup>th</sup> February, 2008

### Track A

A plenary lecture by Dr. Hope, set the stage for Track A activities and resulted in new understandings of the epithelial surface of the female reproductive tract. He addressed the interaction of HIV virus with human cervicovaginal explant tissues and in vivo in non-human primates showing that HIV will diffuse into epithelial cell layers, potentially penetrating to the region where HIV susceptible target cells dwell.

Track A on the first day has 4 sessions on Drug Discovery in which Drs. Springer and Mosier reviewed the industry and academic processes for HIV topical microbicide drug discovery and lead identification. They identified the need to incorporate focused pharmacokinetic and pharmacodynamic analysis of candidates as part of the selection process for advancement to clinical trials. This session was followed by an oral presentations (chaired by Drs. Mellors and Haase) where several microbicides early in the pipeline were discussed. Dr. Sassi presented a film formulation of the defensin inhibitor, RC101. RC101 was shown not only to associate with epithelial cells for a prolonged period, but also to penetrate deep into the tissues.

A discussion of the critical gaps in the tropical microbicide field was chaired by Dr. Bhan and moderated by Dr. Turpin. The panelists reviewed the progress on the critical gaps of biomarkers for safety and efficacy (Fichorova) animal models (NHP (Cheng-Mayer) and humanized mice (Garcia)) and the use of early clinical assessments to address effects of clinical candidates on female reproductive tract susceptibility to HIV and HSV and immune parameters (Keller).

The final session explored new innovations in vaginal ring development (Malcolm), vaginal film and rectal specific formulation (Rohan) and the development of vaginal tablets (Garg). Potential pros and cons were identified for each delivery method with a general consensus that acceptability and safety of the different formulations approaches should be priorities. Oral presentation illustrated the breadth and depth of activities in this area to produce different dosage form of TMC120 and UC781 among others.

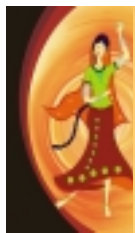
### Track B

#### Integration of behavioral science in microbicides research

- Contributions of behavioral science in microbicide research include assessing acceptability, assessing sexual behavior and adherence, improving and documenting behavioral measurement, understanding reasons for use and barriers to use and improving recruitment and screening processes.
- Newer friendly and computer-assisted technologies are being developed to assess acceptability and adherence
- Research needed on questions: nature [leading, confusing], order, wording, keeping recall period in mind
- Improving the quality of data in interviews: think aloud, verbal probing, behavioral coding

#### Opportunities and challenges in microbicide research in developing countries: Barriers to control HIV/AIDS

- Epidemic continues, global increase in no. of infections – most affected Africa, South east / South Asia are the hotspots. Increasing heterosexual spread in China
- Global burden 33 million – younger females on the rise
- Barriers to control: status of women, low condom acceptance, emphasis on treatment, dependence on external support, low awareness/ acceptability in vulnerable populations like women and youth, low acceptance of testing, stigma a barrier for testing, high proportion of uncircumcised men, very few female controlled strategies, vaccine distant
- Key elements of successful intervention: Political will and mobilization, good surveillance, unified national planning, multisector rapid response, focused intervention for high risk groups, risk-free testing, access to condoms, early education in schools, community involvement, reduce barriers to interventions, treatment for adults and pregnant women, development of effective vaccine and microbicides [ability to do efficacy trials, assess adherence and resistance]



# microbicides 2008

February 24 - 27, 2008  
Hotel Ashok, New Delhi, India

Striving towards HIV Prevention



## Opportunities and challenges in microbicide research in Africa

- Unsafe sex second most important factor to global health: STIs, abortions, genital mutilations, Africa contributing most women in HIV epidemic and also in microicide research
- Exponential growth in epidemic now showing signs of stabilization, but scaling up prevention essential
- Many major Phase II, IIb and III trials ongoing: Respect for women is the key
- Different kinds of women participate in microbicide trials: Addressing them is complex
- Media's portrayal bi-directional, challenge of bad news – product failures, political interventions in conduct of trials
- Why do women participate? Ancillary care or service, re-imburement as incentives,
- Regulatory issues: Ethics committees to deal with complex technical issues, heavy work burden and under-resourced - delays in processing requests
- Engagement with regulators, media and communities essential

## Its all about power

- Challenges for doing studies with enough power: phase III studies when a product believed to be effective in preventing HIV transmission
- Current trials do not measure efficacy: it is inferred that a woman has become infected after unknown number of sex acts: effectiveness trial more important
- Power depends on alpha level [study design], number of infections to be observed [incidence] and effectiveness [efficacy, adherence and route of exposure] of the product
- No. of outcomes decide precision
- Effectiveness = efficacy x adherence: do everything possible to see that the adherence is good
- Problems in power: Too few events, low adherence,
- Interim results can be used to calculate power to reject null hypothesis: more events might be targeted if efficacy low

## **SAVVY trial in Nigeria: PJ Feldblum**

Nigeria trial: pre-loaded single use applicator with placebo – Phase III study 2142 women” 1 yr follow up 12 visits

Early termination of trial: 75% completed the study  
High pregnancy rates, but equal in 2 arms”

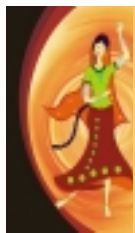
No evidence of effectiveness in preventing HIV infection

In future studies, more conservative HIV incidence estimations should be employed and more effective family planning measures should be advocated

## **Track C**

### **Plenary-behavioral contribution to trials**

Take lessons on adherence from FP field ie contraceptive use. Have to know which women are adherent and why. Evolution of concepts: risk reduction, acceptability framework and studies. There has been limited investigation of interpersonal and contextual factors. Acceptability is not the same as adherence of intention and behaviour. Reported adherence in phase 2 and 3- self report is high- but note Carraguard suggests 44% vs 96% self report. Need to move beyond acceptability to behaviour, adherence. Eg ACASI vs face to face, biomarkers. Fewer applicators used than biomarkers suggest. One fifth of those reporting no sex in 48 hrs had evidence of semen. ACASI gives more report of non use of gel. Improve style of questions eg asking non use first, avoid leading questions. Disentangle adherence and risk.



# microbicides 2008

February 24 - 27, 2008  
Hotel Ashok, New Delhi, India

Striving towards HIV Prevention



## Use of mixed methods approaches to measure intentions

Women do not use the terms planned, unplanned, unintended spontaneously. Variable interpretation of the terms when offered. Six item questionnaire based on qualitative work to identify intentions; More information at [www.lmup.org.uk](http://www.lmup.org.uk)

## Adherence

Planned framework, regular feedback from participants. Trying to find an adherence 'gold standard' may be unrealistic. Need to define what is an adequate degree of consistency for trial purposes, eg within 2 applicators, accepting plausible explanations for discrepancy. Triangulated data give the best consistency, where discrepancies are resolved at site using mixed methods. Most discrepancies are unintentional.

Identification of inconsistent users led to improved adherence, using an information, motivation and behavioural skills model. Encouraging disclosure was helpful.

Significant differences between trial and non trial participants in the associations observed.

Dose timing is very important in ARV microbicide use which has implications for behavioural tools.

## Behavioral and social science research tools

Interviews have revealed women's positive views of gel use. There was a big emphasis on the partner's satisfaction rather than women's sexual pleasure. Effects for women included wider impact on general wellbeing eg self confidence. This holistic perspective resonate with etic perspective of sexual health (as set out by WHO).

When undertaking international collaborative research it is necessary to have extended opportunities for tools development, translation, training and review of transcripts. Interviewers should be involved in the design of instruments. Employment opportunities can be enhanced by running projects consecutively.

Information technology gives added convenience and reliability to interviews for monitoring over time. The mode of data collection should be based on the study needs.

## Acceptability

Reliable scales for assessing acceptability were described such as the 'microbicide confidence scale'. Independent and mediator variables to predict willingness to use.

Disclosure was positively associated with relationship harmony but discovery was disruptive to relationships. Positive views of microbicides were linked to beliefs about cleansing, and with enhanced pleasure and intimacy. These benefits can be summarised as 'empowering in unanticipated ways'.

Differences in ease of use and sexual enjoyment were noted between different study sites, possibly explained by demographic and economic differences.

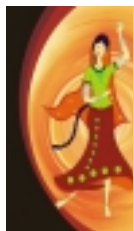
Gel was preferred to suppository for rectal use. Product substitution was common in a trial of the diaphragm and was associated with higher behavioural risk for HIV.

Lower adherence was seen in participants rating the praneem product as not easy to use.

## Track D

### Session: Defining the community and the importance of partnerships for HIV research

Speaker: Mangala Patil



# microbicides 2008

February 24 - 27, 2008  
Hotel Ashok, New Delhi, India

Striving towards HIV Prevention



- Community advisory board (CAB) has an important role to play to be the **bridge** between trial participants, broader community in the region, and researchers, scientists and clinicians.
- Dire **need for more communication** in easy-to-understand simple language about the objectives of the research and the research protocols or methods
- There are lot of **misconceptions** which trial participants or the community may have so it is another key role of CAB to communicate effectively to dispel such misconceptions or myths
- It is vital to maintain **transparency** between researchers and trial participants and broader community, and effective communication mechanisms will be key to keep the open information flow
- It is important to assess the **needs of a community before setting the research agenda**
- The **consent form** for trial participants should be **in local language** and written in a **simple to understand** manner and communicate clearly the key information about the research
- It is **critically important to get back to trial participants and share with them the results of the study/** trial – this **didn't happen** for female condom acceptability study, and trial participants still come to CAB members asking for the result and female condoms (Where are female condoms?)

## Session: Community involvement in microbicide trials

Speaker: *Morenike Upkong*

- **Community engagement strategies** are a key to ethical protocols in microbicide trials
- **Scientists may not see potential obstacles** in the study *from a community perspective*

Speaker: *M Nakimuli*

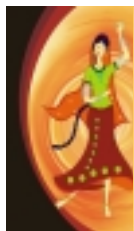
- Important to recruit effective **peer leaders** who belong the community where trial participants come from
- Peer leaders inform the CAB and form a vital link for information flow between CAB members and trial participants in their neighbourhood
- Peer leaders have important roles in effective mobilization, recruitment and retention of trial participants in the study

Speaker: *Winifred Nalukenge*

- Male partner involvement in the trial is often very helpful
- Important to effectively dispel misconceptions in the community about the microbicide trials especially after the trial closure or failure

## Session: Community involvement in microbicide trials (II)

- Microbicides Development Strategy (MDS) creates a blue print in microbicide-field's progress and highlight gaps in:
  - o Basic and pre-clinical science
  - o Clinical research
  - o Manufacturing and formulation
  - o Commercialization and access of microbicide products after they get through the trials later in the future
- The funding window: MDS proposes a funding mechanism to donor agencies to provide a window to key civil society organizations working on microbicides research, advocacy and development.
- Civil society engagement in microbicide trials is minimal. Civil society engagement helps the microbicide trials in many ways:
  - o Helps research to avoid pitfalls
  - o Maintain accountability between researchers and community
  - o Mobilizes new public resources
  - o Facilitates open and fair communication between different stakeholders thereby increasing accountability
  - o Increases trust in the communities



# microbicides 2008

February 24 - 27, 2008  
Hotel Ashok, New Delhi, India

Striving towards HIV Prevention



- Women's rights organizations are more involved with microbicides advocacy in South Africa. It should be happening in other countries as well. Feminist movement is completely disconnected from microbicides advocacy – this needs to change!
- Advocates themselves lack capacity to fully engage with the complexity of microbicide and clinical trials

## Session: Managing stakeholder expectations of trial results

- We need to strengthen communication strategies in the microbicides field. There is a lot of confusion after trial failures for trial participants of other microbicide candidate products who are left wondering: *'how is my gel different?'*
- We need to select effective community speakers and inform them routinely on developments and be informed from them as well. We need to conduct ongoing media training for these spokesperson
- Work closely with media agencies on an ongoing basis – so that media is well-verse with protocols of microbicides research and is an effective partner
- There will be different communication challenges when we do get a successful effective microbicides 7-10 years later
- Impact of microbicides is different on:
  - o Risk per sex act
  - o On individual risk if used overtime
  - o On HIV incidence in a controlled trial setting
  - o On population HIV incidence following widespread provision
- Messages should recognize frames of reference of audience:
  - o Family planning providers:
    - Make clear that HIV is akin to family planning technology development 20 years or so ago
    - Reference for judgement should be different:
  - o HIV policy makers
    - More appropriate to make comparisons with:
      - 87% for consistent condom use
      - 60% for imperfect condom use
      - 0% if a woman cannot use any current prevention option