HPTN 035

Phase II/IIb Safety and Effectiveness Study of the Vaginal Microbicides BufferGel and 0.5% PRO 2000/5 Gel (P) for the Prevention of HIV Infection in Women

MTN Regional Meeting

May 2007
HPTN 035 Study Sites

- Blantyre, Malawi
- Durban, South Africa
- Harare and Chitungwiza, Zimbabwe
- Hlabisa, South Africa
- Lilongwe, Malawi
- Lusaka, Zambia
- Philadelphia, USA
Some numbers: selected milestones

- 3 sites have completed accrual
- 4 current QC rate per 100 CRF pages
- 80% coital acts involve gel use currently
- 90% participants retained to date
- 2800 participants enrolled
- 5500 participants screened
- 30,000 lab specimens archived
- 177,000 CRFs completed
- 520,000 condoms shipped to sites
Selected Discussion Topics

- Adherence to gel use
- Informed consent process
- Reproductive health & pregnancy outcomes
Adherence to Gel Use

<table>
<thead>
<tr>
<th>Date</th>
<th>% Gel Use Overall</th>
<th>% Gel Use in Acts With a Condom</th>
<th>% Gel Use in Acts Without a Condom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct-05</td>
<td>73</td>
<td>84</td>
<td>47</td>
</tr>
<tr>
<td>Jan-06</td>
<td>72</td>
<td>80</td>
<td>53</td>
</tr>
<tr>
<td>Apr-06</td>
<td>74</td>
<td>82</td>
<td>57</td>
</tr>
<tr>
<td>Jul-06</td>
<td>75</td>
<td>82</td>
<td>60</td>
</tr>
<tr>
<td>Oct-06</td>
<td>77</td>
<td>83</td>
<td>64</td>
</tr>
<tr>
<td>Jan-07</td>
<td>78</td>
<td>83</td>
<td>68</td>
</tr>
<tr>
<td>Mar-07</td>
<td>79</td>
<td>83</td>
<td>71</td>
</tr>
<tr>
<td>May-07</td>
<td>81</td>
<td>83</td>
<td>78</td>
</tr>
</tbody>
</table>

NB: In May-07, when excluding visits on product hold, gel was used in 85% of acts with a condom and 83% of acts without a condom.
HPTN 035 Informed Consent Process

- Two step process — screening and enrollment
- Enrollment process is semi-standardized
- Common procedures manual followed at all sites
- Common materials developed for all sites
- Procedures and materials developed with site/community input
- Translated into local languages
Informed Consent Materials
Site SOPs define use of materials and steps in the process

At most sites, group counseling/education takes place first

At all sites, individual discussion – using the informed consent form and other materials – forms the basis of the informed consent process

At all sites, comprehension is assessed prior to enrollment
**HPTN 035 Enrollment Informed Consent Comprehension Checklist, Version 1.1 (12 April 2006)**

<table>
<thead>
<tr>
<th>PTID:</th>
<th>Date:</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Open-Ended Question/Statement</strong></td>
<td><strong>Required Points of Comprehension</strong></td>
<td>✔</td>
</tr>
<tr>
<td>1 Please describe your understanding of the purpose of the study.</td>
<td>study is testing two experimental gels</td>
<td></td>
</tr>
<tr>
<td></td>
<td>testing to learn if gels are safe</td>
<td></td>
</tr>
<tr>
<td></td>
<td>testing to learn if gels may prevent HIV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>study may not prove gels work</td>
<td></td>
</tr>
<tr>
<td>2 What do you understand that you are being asked to do in this study?</td>
<td>asked to use condoms and perhaps gel with each act of vaginal sex</td>
<td></td>
</tr>
<tr>
<td></td>
<td>have pelvic exams and HIV tests</td>
<td></td>
</tr>
<tr>
<td></td>
<td>come for monthly visits for up to 30 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>not get pregnant in next 30 months</td>
<td></td>
</tr>
<tr>
<td>3 What do you understand about possible risks that might happen as a result of being in the study?</td>
<td>gel may irritate skin inside or outside vagina</td>
<td></td>
</tr>
<tr>
<td></td>
<td>gel may have other side effects</td>
<td></td>
</tr>
<tr>
<td></td>
<td>possibility of social harms</td>
<td></td>
</tr>
<tr>
<td>4 What will happen if you do not join the study?</td>
<td>free to make her own decision about joining</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no effect on access to care when decide to join or not</td>
<td></td>
</tr>
<tr>
<td>5 Please tell me about the different groups of women in the study.</td>
<td>there are different gels</td>
<td></td>
</tr>
<tr>
<td></td>
<td>not everyone receives a gel</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no one knows who receives which gel</td>
<td></td>
</tr>
<tr>
<td>6 How will the information about you be protected?</td>
<td>participant information is kept under lock and key</td>
<td></td>
</tr>
<tr>
<td></td>
<td>only people working on the study have access</td>
<td></td>
</tr>
<tr>
<td>7 What are the benefits to you of participating in this study?</td>
<td>counseling, condoms, tests, clinical care, benefit to science or community (should mention at least one from ICF)</td>
<td></td>
</tr>
<tr>
<td>8 What should you do if you have any questions about what is happening in the study?</td>
<td>must articulate how to contact study staff</td>
<td></td>
</tr>
</tbody>
</table>

**Outcome:**
- Demonstrated comprehension of all required points, decided to enroll in study.
- Demonstrated comprehension of all required points, decided NOT to enroll in study.
- Demonstrated comprehension of all required points, deferred enrollment decision to another visit.
- Did not demonstrate comprehension of all required points (yet), needs more time/discussion, rescheduled for another visit.
- Unable to demonstrate comprehension of all required points, consent process discontinued.
- Other (specify): ________________________________

**Optional Comment Categories:**
- a. Answered correctly on first try
- b. Could not answer at first, but answered correctly after some probing/discussion
- c. Answered incorrectly at first, but answered correctly after discussion
- d. Not able to answer correctly at this time
- e. Other (describe)

**Staff Signature:** [Signature]
Each point is ticked when study staff determine the participant understands that point.

Additional open ended probing may be used to confirm/clarify comprehension of each point.

Enrollment may not occur unless/until comprehension of all points is demonstrated.

Multiple sessions may take place if needed.

Informed consent process overall has been successful, but is time-consuming.

Illiteracy & requirement for witness - challenge.
Reproductive health

- All participants are provided ongoing contraceptive counseling and encouraged to use highly effective contraceptive methods.
- Highly effective contraceptive methods are available free of charge at all sites, through direct provision or “nearby” referrals.
- Pregnancy rates declined over time, from ~20 per 100 py to ~13 per 100 py currently.
Pregnancy outcomes

- 243 pregnancies to date
- 97 participants still pregnant
- 146 pregnancy outcomes
  - 78 (53%) live births
  - 41 (28%) spontaneous abortions
  - 23 (16%) therapeutic/elective abortion
  - 6 (4%) fetal deaths/still births
Conclusion

- Study well on track
- Outstanding accomplishments
- Gel adherence in absence of condoms has improved steadily
- Consent process very detailed with comprehension assessment
- Monitoring pregnancy outcomes challenging but important