

***THIS PROTOCOL AND ALL OF THE INFORMATION RELATING TO IT ARE CONFIDENTIAL AND PROPRIETARY PROPERTY OF INTERNATIONAL PARTNERSHIP FOR MICROBICIDES, SILVER SPRING, MD, U.S.A***

**IPM 003**

**A PHASE I/II DOUBLE-BLIND, RANDOMIZED STUDY OF THE SAFETY, TOLERABILITY AND SYSTEMIC ABSORPTION OF TMC120 VAGINAL MICROBICIDE GEL (TMC120 GEL-002) AND MATCHING PLACEBO IN HEALTHY HIV NEGATIVE WOMEN**

**SPONSOR:**

**International Partnership for Microbicides  
1010 Wayne Avenue, Suite 1450  
Silver Spring, MD 20910 U.S.A.**

**Version 3.0  
January 16, 2006**

**PROTOCOL SYNOPSIS  
IPM 003**

**A PHASE I/II DOUBLE-BLIND, RANDOMIZED STUDY OF  
THE SAFETY, TOLERABILITY AND SYSTEMIC ABSORPTION OF  
TMC120 VAGINAL MICROBICIDE GEL (TMC120 GEL-002)  
AND MATCHING PLACEBO IN HEALTHY HIV NEGATIVE WOMEN**

**PURPOSE:** To assess the local safety and tolerability on vulval and cervicovaginal mucosa, plasma levels, and systemic absorption of 0.001% (10 µg/mL), 0.002% (20 µg/mL), or 0.005% (50 µg/mL) TMC120 vaginal microbicide gel (TMC120 Gel-002) compared with matching placebo gel in healthy HIV-negative women. Acceptability and compliance to TMC120 Gel-002, and occurrence of bacterial vaginosis in women who use TMC120 Gel-002 will be assessed.

**DESIGN:** Multicenter, double-blind, randomized phase I/II study in healthy female volunteers randomized in a 2:2:2:1 ratio to TMC120 Gel-002 (0.001%, 0.002%, or 0.005%) or matching placebo gel for 42 consecutive days. Volunteers will be monitored for safety, tolerability and compliance.

Approximately 10 women who have completed IPM 003 study product and 10 men who were partners of a woman who participated in IPM 003 at each of the 4 clinical sites will participate in separate focus group discussions for men and women approximately 8-10 weeks after completing study product. The purpose of the focus group discussions is to assess acceptability of the study product and to elicit opinions on study gel in a group setting.

**STUDY**

**POPULATION:** Healthy HIV-negative women ages  $\geq 18$  and  $\leq 50$  with no clinically detectable genital abnormality (including vulval, vaginal, cervical, and/or perineal ulcer and/or lesion), no abnormal or bloody Pap smear, or internal vaginal warts. Volunteers will be sexually abstinent from Day 0 until completion of Day 7 evaluations, at which time sexual activity may resume at the discretion of the volunteer.

**SAMPLE**

**SIZE:** 84 -112 (28 women per site at 3 to 4 sites)

## PROTOCOL SYNOPSIS (Cont.)

### TREATMENT REGIMEN:

Volunteers will be double-blind randomized to TMC120 Gel-002 (0.001%, 0.002%, or 0.005%) or matching placebo and will self-apply 2.5 mL of study product with pre-filled applicators twice daily (shortly after awakening and in the evening approximately 12 hours after morning application). On Day 0, the first gel application will be applied by the volunteer at the site under the supervision of the investigator, medical officer, or senior study nurse (direct observation is optional). The volunteer will remain in the clinic under observation for 1 hour after the first application. Application of the study product will continue twice daily through the day prior to their Day 42 visit, including during menses. Use of **study gel** in this study is not coitally dependent.

Condoms, panty liners, menstrual pads, and bags for return of used and unused applicators for compliance measurement will be provided. Treatment for urinary and genital infections (except HPV) will be provided. Volunteers diagnosed with abnormal Pap smears will be referred for treatment outside of the study. For volunteers with an active outbreak of HSV-2 after randomization, a single 7-day course of acyclovir will be provided.

### STUDY

#### DURATION:

It is anticipated that the study will accrue in approximately 6 months and follow-up completed in approximately 8 months. Each volunteer's participation will be a maximum of 56 ( $\pm 3$ ) days.

#### PRIMARY OBJECTIVES:

- To assess the local safety and tolerability on vulval and cervicovaginal mucosa of TMC120 vaginal microbicide gel (TMC120 Gel-002) when applied twice daily at three different concentrations (0.001%, 0.002%, and 0.005%) compared to matching placebo gel in HIV-negative women.
- To assess the plasma levels of TMC120 among HIV-negative women who apply TMC120 vaginal microbicide gel (TMC120 Gel-002) twice daily at three different concentrations of 0.001%, 0.002%, and 0.005%.

**PROTOCOL SYNOPSIS (Cont.)**

- To assess the systemic safety of TMC120 vaginal microbicide gel (TMC120 Gel-002) when applied twice daily at three different concentrations of 0.001%, 0.002%, and 0.005% compared to matching placebo gel in HIV-negative women.

**SECONDARY OBJECTIVES:**

- To assess the acceptability of TMC120 vaginal microbicide gel (TMC120 Gel-002) or matching placebo gel in HIV-negative women.
- To assess compliance to TMC120 vaginal microbicide gel (TMC120 Gel-002) or matching placebo gel in HIV-negative women.
- To assess the occurrence of bacterial vaginosis in HIV-negative women who apply TMC120 vaginal microbicide gel (TMC120 Gel-002) b.i.d. compared to women who apply matching placebo gel b.i.d.