

## Clinical Trial Outcomes for Potential Microbicide Products

Type of Trial/ Study Design	Participants and Location(s)	Date(s)	Main Outcomes
<b>Carraguard precursors</b>			
<b>PC-213 (iota-carrageenan)</b>			
<ul style="list-style-type: none"> <li>● Phase 1 safety (with colposcopic evaluation)</li> <li>● 7 days, 1x/day</li> <li>● Dose: 5mL</li> </ul>	<ul style="list-style-type: none"> <li>● 25 abstinent, HIV-negative women</li> <li>● 5 women per site:                             <ul style="list-style-type: none"> <li>● US (Los Angeles)</li> <li>● Finland</li> <li>● Australia</li> <li>● Chile</li> <li>● Dominican Republic</li> </ul> </li> </ul>	1995	No safety concerns
<b>PC-503 (lambda-carrageenan)</b>			
<ul style="list-style-type: none"> <li>● Phase 1 safety study (with colposcopic evaluation)</li> <li>● 7 days, 1x/day</li> <li>● Dose: 5mL</li> </ul>	<ul style="list-style-type: none"> <li>● 35 abstinent, HIV-negative women</li> <li>● 7 women per site:                             <ul style="list-style-type: none"> <li>● US (Los Angeles)</li> <li>● Thailand</li> <li>● Australia</li> <li>● Chile</li> <li>● Dominican Republic</li> </ul> </li> </ul>	1998	No safety concerns; volume too much (“too messy”) - volume reduced in next formulation

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Type of Trial/ Study Design	Participants and Location(s)	Date(s)	Main Outcomes
<b>Carraguard clinical trials (PC-515)</b>			
<ul style="list-style-type: none"> <li>● Expanded safety/acceptability (monthly pelvic exam)</li> <li>● ½ women received Carraguard; ½ received placebo (double-blinded)</li> <li>● 6-12 months, 3x/week, plus before sex</li> <li>● Dose: 4mL</li> </ul>	<ul style="list-style-type: none"> <li>● 400 HIV-negative women</li> <li>● Majority sexually active               <ul style="list-style-type: none"> <li>● Gugulethu, South Africa (200)</li> <li>● Ga-Rankuwa, South Africa (200)</li> </ul> </li> </ul>	1999-2002	No safety concerns; acceptable; feasible for phase 3 efficacy trial
<ul style="list-style-type: none"> <li>● Expanded safety/acceptability (monthly pelvic exam; colonoscopy at baseline &amp; month 1 for first 25 women)</li> <li>● ½ women received Carraguard; ½ received placebo (double-blinded)</li> <li>● 12 months, 3x/week, plus before sex</li> <li>● Dose: 4mL</li> </ul>	<ul style="list-style-type: none"> <li>● 165 HIV negative women</li> <li>● Majority sexually active               <ul style="list-style-type: none"> <li>● Chiang Rai, Thailand (1 site)</li> </ul> </li> </ul>	2000-2001	No safety concerns' acceptable
<ul style="list-style-type: none"> <li>● Expanded safety/acceptability (Women: monthly pelvic exam; cervico-vaginal lavages; oloposcopy as needed; Men: monthly genital exam)</li> <li>● ½ couples received Carraguard; ½ received placebo (double-blinded)</li> <li>● 6 months, before sex (at least 1x/week)</li> <li>● Dose: 4mL</li> </ul>	<ul style="list-style-type: none"> <li>● 55 HIV-negative, monogamous couples</li> <li>● Chiang Rai, Thailand (1 site)</li> </ul>	2001-2002	No safety concerns in men or women; acceptable among both men and women

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<b>Carraguard clinical trials (PC-515) <i>continued</i></b>			
<ul style="list-style-type: none"> <li>● Phase 1 safety study (pelvic/genital exam, plus vaginal lavages for women)</li> <li>● 7 days, 1x/day (men)</li> <li>● 14 days, 1x/day abstinent women</li> <li>● 14 days, before sex/1x day (sexually-active women)</li> <li>● Dose: 4mL</li> </ul>	<p>60 HIV-positive men and women in Durban, South Africa (1 site)</p> <ul style="list-style-type: none"> <li>● 20 abstinent men</li> <li>● 20 abstinent women</li> <li>● 20 sexually-active women</li> </ul>	2002-2003	No safety concerns in men or women; Carraguard not associated with increased genital shedding of HIV-1 RNA in women
<ul style="list-style-type: none"> <li>● Phase 1 safety study (pelvic exam, colposcopy, vaginal lavages)</li> <li>● Crossover design (Carraguard, placebo and no gel)</li> <li>● 7 days, 1x/day/arm, 1 month per arm (3 months total)</li> <li>● Dose: 4mL</li> </ul>	60 HIV-positive (abstinent) women in Chiang Rai, Thailand (1 site)	2003-2004	No safety concerns
<ul style="list-style-type: none"> <li>● Carraguard retention study (Vaginal lavages/Carraguard application)</li> <li>● Dose: 4mL</li> </ul>	15 female subjects recruited from the general population attending the clinic for reproductive health services (abstinent) in New York, NY. (1 site)	Aug-Dec 2004	Significant quantity of active carrageenan remains in the vagina for 24 hours; indicates potential for daily application of Carraguard

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<b>Carraguard Combination Products Clinical Trials</b>			
<b>Carraguard/levonorgestrel</b>			
<ul style="list-style-type: none"> <li>● Phase 1 safety study (Administration of E2: 50µg/d for 28 days/self-administration of CARRA/LNG: every other day for a 14-day period)</li> <li>● Dose of CARRA/LNG: 250µg</li> </ul>	<p>14 post-menopausal women were enrolled to obtain 12 women who complete study, aged 45-60, in Los Angeles, CA (1 site)</p>	<p>Jan-May 2006</p>	<p>No safety concerns</p>
<ul style="list-style-type: none"> <li>● Phase 1 safety study (PK) (administration of CARRA/LNG, wash-out periods)</li> <li>● Cross-over study design (Abstinent arm: couples abstain from sex for 48 hours post-application; samples taken from female at 0, 1, 2, 4, 8, 24 and 48 hours after both applications. Couples cross-over to sexually active arm, where they engage in sexual activity 2-4 hours after application. Blood samples taken from male partner before application and at 4, 8, 24 and 48 hours after the time of vaginal application in his female partner.)</li> <li>● Dose: 2 applications of 0.75 mg of CARRA/LNG</li> </ul>	<p>12 healthy sterilized female volunteers and their male partners. 6 couples in Santo Domingo, Dominican Republic and 6 couples in Santiago, Chile (2 sites)</p>	<p>Jan-June 2006</p>	<p>No safety concerns</p>