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CR #627

EVALUATION OF THE SAFETY, EFFECTIVENESS AND CLINICAL ACCEPTABILITY OF  
ORTHO CONTRACEPTIVE FOAMING VAGINAL TABLETS  
CONTAINING NONOXYNOL-9 VERSUS ORTHO CONTRACEPTIVE FOAMING TABLETS  
CONTAINING MENFEGOL

CONTRACEPTIVE TABLET STUDIES CONDUCTED IN BANGKOK, THAILAND AND IN ACCRA, GHANA

Prepared for  
Ortho Pharmaceutical Corporation

Centers: 0044, 0773, 4500

Study: 7798

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Center 0044, CR #617; Center 0773, CR #621; and Center 4500, CR #613.

## I. INTRODUCTION

Vaginal contraceptives are receiving a greater amount of attention because of the increasing dissatisfaction with IUDs and oral contraceptives and the need to provide a balanced array of methods. However, the scientific literature on these vaginal contraceptives is characterized by widely divergent reports of their effectiveness. While it is clear that differing results are primarily due to differences in study populations, the actual factors affecting compliance and successful use of vaginal contraceptives remain a matter of speculation. Family Health International (FHI) clinical trials of foaming vaginal tablets are designed to collect information on various objective and subjective side effects and to determine the rates of and reasons for discontinuation.

A study to evaluate the safety, efficacy and clinical acceptability of two types of contraceptive foaming vaginal tablets was initiated at the Korle-Bu Teaching Hospital in Accra, Ghana (Center 0044) in December of 1984, at Ussher Clinic in Accra, Ghana (Center 4500) in January 1985, and at the Chulalongkorn University Institute of Health Research in Bangkok, Thailand, (Center 0773) in September of 1985. Both tablets were obtained from Ortho Pharmaceutical Corporation, Raritan, New Jersey. One contained 100 milligrams of nonoxynol-9 (OVT-n) and the other 60 milligrams of menfegol (OVT-m). The clinical trials utilized a randomized, double-blind, parallel design. Four hundred women (300 from the Ghana sites and 100 from the Thailand site), were to be enrolled over a 12-month period. The following report combines the data from the studies conducted in the international sites and focuses on a comparison of the two tablets.

## II. METHODOLOGY

Volunteers had to be generally healthy women from 18 to 40 years of age who were sexually active. They could not be pregnant, or known to be sterile or infertile, nor could they have any anatomic abnormalities or allergies that might prevent successful use of the tablets. Volunteers must have had one menstrual period since termination of the last pregnancy. All women provided informed consent. Each woman was randomly assigned to use either OVT-n or OVT-m tablets throughout the course of the study as her sole means of contraception. She was instructed to insert the OVT-n or OVT-m tablet into her vagina and to wait at least 10 minutes before intercourse. She was to insert another tablet before each additional act of intercourse. If intercourse did not take place within an hour after insertion of the tablet, another tablet was to be inserted.

Follow-up was for one year, with follow-up visits scheduled at 1, 3, 6 and 12 months after admission. Tablets were supplied as needed at each follow-up visit. Pelvic examinations, Pap smears, and gonorrhea cultures were scheduled at admission and at the six-month and 12-month visits. Cervical conditions were analyzed by vaginal cytology tests. Cervical biopsies and conizations of the cervix determined medical discontinuations of cervical dysplasia cases; however, mild cervical dysplasia was not an exclusion or discontinuation criteria.

Women were recruited and followed in Accra, Ghana and in Bangkok, Thailand. A combined total of 279 women were admitted to the study; 143 were randomly assigned to the OVT-n group and 136 were randomly assigned to the OVT-m group. Four of the women participating in the study, (all from Center 0773), were

excluded by FHI from the analysis, three OVT-n users because of nonuse and one menfegol user who was considered infertile and not at risk of pregnancy because she did not have a menses during the course of the study. Admissions were begun in December of 1984 and were completed in November of 1986. Center 4500, in Accra, halted admissions after 12 months due to difficulty in recruiting volunteers to participate. Follow-up visits for the trial were completed in July of 1987. In Bangkok, a factory clinic admitted 14 women; a university clinic, 27 women; and a health clinic, 61 women. Women were provided product in nondescript packages labeled either, "A" or "B". The physicians and clinic staff provided the same information on the proper use of the tablets to all users. Both the staff and study participants were unaware of which tablet, type A or B, contained the nonoxynol-9 or menfegol.

Analysis is based on sociodemographic and medical data recorded by the clinic staff. Data were sent to FHI for scanning, keypunching and computer analysis. Chi-square, t-tests, and F tests were run on data when appropriate, but only statistically significant results are indicated.

Clinical acceptability of the product was inferred from reports of ease of enrollment, how well the study progressed, reported regularity of use of the tablets, reasons for irregular use, use of alternative or additional contraceptive methods, complaints, and reasons for discontinuation.

Product safety and effectiveness was determined by gross cumulative life table rates, reports of product-related problems, medical complications, serious or unexpected adverse experiences, and accidental pregnancies.

Accidental pregnancies were defined to be method failures if the tablets were reportedly used properly at every act of intercourse and, therefore, the pregnancy was due to a lack of efficacy of the method. If the tablets were misused or not used immediately prior to the time of conception, and the pregnancy was not planned, the pregnancy was considered as accidental due to use failure.

### III. USER CHARACTERISTICS

#### Sociodemographic Characteristics

Selected characteristics of the women (Table I) show the mean age of the OVT-n users (26.9 years) was slightly less, (but not statistically significant), than that of the OVT-m users (27.5). The level of education was not significantly different in both groups and averaged nearly nine years. The mean number of live births was not significantly different for both groups with a mean of approximately two children per woman. Women in both groups reported an average of nearly 2.5 intercourse acts per week at the time of recruitment.

#### Previous Contraceptive Practice

Fifty women in the OVT-n study group (35.7%) and 47 in the OVT-m study group (34.8%) had not been using contraceptives in the three months prior to admission (Table II). Fifteen percent of OVT-n users and 12.6% of the OVT-m users had experience with vaginal contraceptive methods in the three months prior to admission, whereas nearly one-third of all participants had used oral contraceptives. Twelve women (four OVT-n users and eight OVT-m users) had used Depo-Provera in the prior three months. Most of these 12 women were amenorrheal prior to admission while a few had some spotting. However, every

Depo-Provera user was due for her next injection (the dosage was 150 mg. every three months) at the time of her admission visit.

#### Medical History and Physical Examination

Upon admission, a medical history was taken and a pelvic examination was performed for each woman (Table III). Most were generally in good health with only a few abnormal conditions reported, none of which were considered serious enough to prevent study participation. Three OVT-m users were tested positive for gonorrhea at admission and were successfully treated by standard clinic procedures and then given study product. The incidence of cellular atypia on Pap smears was significantly different ( $p < .05$ ) between the two groups with 14.3% of OVT-n users and 5.9% of OVT-m users having cellular atypia.

#### **IV. CLINICAL ACCEPTABILITY**

Data on the regularity of use of both tablets as reported at all follow-up visits appears in Table IV. Approximately 70% of the women in both tablet groups reported using their method at every intercourse. The most common reasons given throughout the study for irregular use were patient neglect and male and female discomfort (Table V).

There were 38 reports of OVT-n users and 36 reports of OVT-m users using other contraceptive methods during intercourse at some point during study (Table VI). For various personal and medical reasons, seven of these women began using Depo-Provera or oral contraceptives and were subsequently discontinued from the study. The remainder reported that they primarily used withdrawal/rhythm or condoms as the alternative or additional methods of contraception.

### Product Evaluation

Method-related complaints refer to difficulties experienced by women or their partners or both during use of the product. Of the method-related complaints reported at any follow-up visits (Table VII), burning/stinging/warmth was reported most often by both groups of tablet users. Although infrequent, other reported complaints included inconvenient/troublesome/messy and that the tablet did not dissolve.

## **V. SAFETY AND EFFECTIVENESS**

### Medical Complications

Medical complications are defined as clinically significant conditions that develop during use of the assigned method. Regardless of whether OVT-n or OVT-m was used, very few medical complications were reported during follow-up (Table VIII). The most common complication reported was cellular atypia on Pap smear. A total of 45 women, (24 OVT-n users and 21 OVT-m users), were reported to have cellular atypia on Pap smear at a follow-up visit. (Six of these women also had cellular atypia on Pap at admission.) Sixteen of the 48 women who had reports of cellular atypia on Pap smear at follow-up were reported to have the same condition at a subsequent follow-up visit, while the condition resolved for 29 of the women. Since 22 of the 28 women who had cellular atypia on Pap at admission had normal Pap smears at follow-up visits, it is unlikely that the product causes cellular atypia on Pap smears.

### Serious Adverse Experiences

Serious adverse experiences are defined as any serious experience that suggests a significant hazard, contraindication, side effect, or precaution. With respect to human clinical experience that is fatal, or life-threatening,

is permanently disabling, requires in-patient hospitalization, or is a congenital anomaly, cancer, or overdose. With respect to results obtained from tests in laboratory animals, a serious adverse drug experience includes any experience suggesting a significant risk for human subjects, including any finding of mutagenicity, teratogenicity, or carcinogenicity.

One serious adverse experience was reported at center 0773 since it resulted in a conization of the cervix. An OVT-n user presented at admission with a dysplastic Pap smear. She used the nonoxynol-9 tablets for one month at which time a cervical biopsy and conization of the cervix indicated mild cervical dysplasia. The woman discontinued two months later due to the dysplasia. The investigator did not attribute the adverse experience to be related to the use of the tablets, since the woman presented with cervical dysplasia at admission.

One serious adverse experience was reported at center 4500. An OVT-n acceptor who had cervical dysplasia at admission, and who was later discontinued for this reason, experienced severe abdominal pains at her 6-month follow-up visit. The information given was inadequate for the medical assessment of this case. No additional information could be obtained by the center due to the woman being lost to follow-up after her discontinuation.

Center 0044 had three adverse experiences reported and all were among OVT-m users. One woman used the menfegol tablets for nine months at which time her Pap smear indicated adenocarcinoma in situ of her cervix. (A Pap smear was not performed at admission for this woman.) The woman was hospitalized for treatment. The adenocarcinoma in situ was not regarded by the investigator as being tablet-related but probably present before admission into the study.

One woman (Center 0044) discontinued menfegol tablets after nine months due to severe abdominal pains. The investigator categorized the reaction as severe and possibly related to the tablets. The condition resolved three months later. More specific information on her condition was unobtainable because the woman was lost to follow-up.

Another OVT-m user at Center 0044 complained of severe abdominal pains and vaginal discharge after four months of use. She continued using tablets for three more months after which time she was discontinued for these complaints. Her abdominal pains and vaginal discharge were not considered tablet-related but due to pelvic infection (acute salpingitis) for which she was treated and cured.

### Efficacy

Forty-one accidental pregnancies were reported after admission--22 in the OVT-n group and 19 in the OVT-m group (Table IX). In the OVT-n group, nine pregnancies were reported by the physician as method failures, while the remaining 13 were considered user failures. Of the 19 accidental pregnancies in the OVT-m group, seven were considered method failures and 12 were considered user failures. One pregnancy in each tablet group, both user failures, were not included in the life table analysis because the pregnancies occurred more than eight days after the last use of the product and thus were not considered to be study-related. (In effort to conservatively measure the efficacy of barrier methods, Family Health International has chosen to include any pregnancies which occur either one week before admission or one week after the date of last use of the method.) Twelve-month Pearl pregnancy rates (not shown), which include all accidental pregnancies reported and total

woman-months of use, were 22.2 per 100 women-years (1188.5 total women-months reported) for the OVT-n group and 19.3 per 100 women-years (1184.0 total women-months reported) for the OVT-m group. These rates were not statistically different.

Six-month discontinuation rates due to accidental pregnancy were  $8.3 \pm 2.5$  per 100 women for the OVT-n group and  $6.3 \pm 2.3$  per 100 women for the OVT-m group. At 12 months, these rates increased to  $19.3 \pm 3.8$  per 100 women and  $17.5 \pm 3.8$  per 100 women, respectively.

#### Discontinuation

Discontinuation during the study was analyzed by both the reason for discontinuation and by gross cumulative life table rates per 100 women at six- and twelve-months (Tables IX and X). (A gross cumulative life table rate was not generated for the discontinuation reason, "lost to follow-up".) Gross cumulative life table rates summarize the results of this study by grouping the time between admission and the end of the designated follow-up period into time intervals. Cumulative probability for each event of interest is estimated as a rate per 100 women.

Women discontinued for various reasons including pregnancy, vaginal/penile discomfort, medical, product-related, and other personal reasons. Forty-seven of the OVT-n users (33.6%) discontinued for known reasons while there were 43 (31.9%) known discontinuations in the OVT-m group. The most common reason for discontinuation was accidental pregnancy due to user failure.

Nine women in the OVT-n group discontinued for reasons of discomfort (seven for burning/stinging/warmth and one for unspecified male/female discomfort) and eight women did so in the OVT-m group (seven for burning/stinging/warmth and one for penile irritation). Twelve-month discontinuation rates due to discomfort were  $7.4 \pm 2.4$  per 100 women for the OVT-n group and  $6.7 \pm 2.3$  per 100 women for the OVT-m group.

There were nine women, (two OVT-n users and seven OVT-m users) who discontinued for other medical reasons. In the OVT-n group one woman discontinued due to vulvovaginitis and one due to dysplasia. In the OVT-m group, three women discontinued due to abdominal pain and one woman each discontinued for moniliasis, cervicitis, amenorrhea, and dysuria. At six and 12 months, the discontinuation rates for other medical reasons were  $1.7 \pm 1.2$  per 100 women in the OVT-n group. The discontinuation rate for other medical reasons in the OVT-m group increased from  $3.7 \pm 1.8$  at six months to  $7.0 \pm 2.6$  per 100 women at 12 months.

Two OVT-n users and one OVT-m user discontinued due to product-related reasons. Discontinuation rates for product-related reasons at 12 months were  $1.5 \pm 1.1$  and  $0.8 \pm 0.8$  for the OVT-n users and OVT-m users, respectively.

There were nine discontinuations in the OVT-n group and seven in the OVT-m group for other personal reasons. Discontinuation rates for other personal reasons at six months were  $4.9 \pm 2.0$  per 100 women among OVT-n users and  $5.9 \pm 2.2$  per 100 women among OVT-m users. While the 12-month discontinuation rates did not change for the OVT-m users, they increased to  $8.2 \pm 2.6$  per 100 women among the OVT-n users.

Seventeen OVT-n users (12.1%) were lost to follow-up and 13 OVT-m users (9.6%) were lost to follow-up. Lost to follow-up rates at 12 months were 43.6 per 100 women for OVT-n users and 40.0 per 100 women for OVT-m users. A total of 76 OVT-n users (54.3%) and 79 OVT-m users (58.5%) completed 12 months of their assigned tablets. Total woman-months of use in the OVT-n group was 1188.5 and 1184.0 in the OVT-m group.

## VI. SUMMARY

This report presents the results of a study to evaluate the safety, effectiveness and clinical acceptability of contraceptive foaming vaginal tablets containing nonoxynol-9 or menfegol as the active ingredient. The tablets were supplied by Ortho Pharmaceutical Corporation, Raritan, New Jersey, and the study was conducted at three international sites, two in Accra, Ghana and one in Bangkok, Thailand. Two hundred seventy-nine women randomly and blindly assigned to one of the two types of tablets were scheduled for follow-up visits at 1, 3, 6 and 12 months. One hundred forty OVT-n users and 135 OVT-m users are included in this analysis. Except in Center 4500, enrollment in the study progressed well and all of the women projected for enrollment were recruited. Over one-half of the women (159) returned for the 12-month clinic visit.

Although there was a difference between the two groups' gross cumulative 12-month life table pregnancy rates, the difference was not statistically significant. Seventy-six OVT-n users (54.3%) and 79 OVT-m users (58.5%) completed 12 months of tablet use. Approximately one-third of the women in each group discontinued use of their assigned method, most often because of accidental pregnancy. Twelve-month discontinuation rates for accidental

pregnancy were  $19.3 \pm 3.8$  per 100 women for the OVT-n group and  $17.5 \pm 3.8$  per 100 women for the OVT-m group. Twenty-five of the 41 total accidental pregnancies were attributed by the physician to be user failures. Twelve-month Pearl pregnancy rates were 22.2 and 19.3 per 100 women-years for the OVT-n group and OVT-m groups respectively.

This study indicates that with regular and proper use OVT-n or OVT-m tablets are comparable and safe means of birth control. Although few product-related or medical complaints were reported by both groups of the tablet users, the high incidence of user failures indicates tablets may not be suitable for these populations. Furthermore, the pregnancy rates might be conservative because 16.8% of the women at one or more follow-ups indicated use of other contraceptive methods, and also because 12 women had used Depo-Provera within the three months prior to admission. Long-term effectiveness of the tablets may not be adequately assessed by this data due to losing women to follow-up between their 6 and 12 month visits. The lost to follow-up rates at 12 months were 43.6 per 100 women for OVT-n users and 40.0 per 100 women for OVT-m users.

TABLE I

Selected Sociodemographic Characteristics of OVT-n and OVT-m Users  
at Three International Sites

Characteristic	OVT-n (N=140)		OVT-m (N=135)	
	No.	%	No.	%
<b>Age (years)</b>				
<20	12	8.6	7	5.2
20-24	41	29.3	40	29.6
25-29	42	30.0	41	30.4
30-34	34	24.3	28	20.7
35+	11	7.9	19	14.1
Mean	26.9 (SD=5.4)		27.5 (SD=5.7)	
<b>Education (years)</b>				
None	10	7.1	10	7.4
1-3	1	.7	2	1.5
4-6	31	22.1	28	20.7
7-9	15	10.7	16	11.9
10-12	55	39.3	47	34.8
13+	28	20.0	32	23.7
Mean	8.8 (SD=4.2)		8.9 (SD=4.4)	
<b>Total live births</b>				
None	33	23.6	26	19.3
1	38	27.1	32	23.7
2	28	20.0	38	28.1
3+	41	29.3	39	28.9
Mean	1.9 (SD=1.7)		2.0 (SD=1.7)	
<b>Average Frequency of Intercourse Per Week</b>				
	2.4 (SD=.9)		2.5 (SD=1.0)	

TABLE II

Prior Contraceptive Use Among OVT-n and OVT-m Users  
at Three International Sites

Characteristic	OVT-n (N=140)		OVT-m (N=135)	
	No.	%	No.	%
<b>Contraceptive method mainly used in three months prior to admission</b>				
None	50	35.7	47	34.8
Foam/jelly/suppository/ tablet	21	15.0	17	12.6
Orals	41	29.3	38	28.1
IUD	7	5.0	10	7.4
Condom	13	9.3	8	5.9
Rhythm/withdrawal	1	0.7	6	4.4
Depo-Provera (DMPA)	4	2.9	8	5.9
Diaphragm/Cervical Cap	2	1.4	1	0.7
Traditional herbs	1	0.7	0	0.0
<b>Primary experience with vaginal methods</b>				
None	107	76.4	109	80.7
Tablet	32	22.9	26	19.3
Foam	1	0.7	0	0.0
<b>Extent of experience with vaginal methods</b>				
None	107	76.4	109	80.7
Limited	26	18.6	16	11.9
Extensive	7	5.0	10	7.4

TABLE III

Gynecological Condition at Admission for OVT-n and OVT-m Users  
at Three International Sites

Characteristic	OVT-n (N=140)		OVT-m (N=135)	
	No.	% <sup>1</sup>	No.	% <sup>1</sup>
<b>Gynecological condition</b>				
None	130	92.9	126	93.3
Moniliasis	1	0.7	1	0.7
Trichomoniasis	0	-	1	0.7
Cervical erosion	6	4.3	3	2.2
Uterine fibroids	2	1.4	3	2.2
Ovarian cysts	0	-	1	0.7
Combination <sup>2</sup>	1	0.7	0	-
<b>Gonorrhoea smear</b>				
Negative	129	92.1	120	88.9
Positive	0	-	3	2.2
Not performed	11	7.9	12	8.9
<b>Pap smear</b>				
Normal	62	44.2	77	57.1 p<.05 <sup>3</sup>
Cellular atypia	20	14.3	8	5.9 p<.05
Cervical dysplasia	4	2.9	0	- p<.05
Not performed	54	38.6	50	37.0

1 Some percentages may not add to 100% due to rounding.

2 One woman had both uterine fibroids and cervical erosion.

3 Fisher's exact test

TABLE IV

Reported Regularity of Use Among OVT-n and OVT-m Users  
at Three International Sites

Characteristic	OVT-n (N=139) <sup>1</sup> No. <sup>2</sup>	OVT-m (N=129) <sup>1</sup> No. <sup>2</sup>
<u>Complete Use</u>		
Used method at each intercourse at every follow-up	95	91
<u>Irregular Use</u>		
Occasional nonuse	32	23
Frequent nonuse	14	14
Never used	2	4

1 Total N is number of women with follow-up data.

2 If a woman did not report complete use of the method she could appear in more than one of the irregular use categories, therefore totals are not additive.

TABLE V

Reported Reason for Irregular Use Among OVT-n versus OVT-m Users  
at Three International Sites\*

Reason	OVT-n (N=139) <sup>1</sup> No. <sup>2</sup>	OVT-m (N=129) <sup>1</sup> No. <sup>2</sup>
Regular use at every follow-up	95	91
Patient neglect	13	11
Too troublesome	3	2
Male discomfort	5	6
Female discomfort	6	8
Male and female discomfort	13	5
Out of supplies	2	3
Other reason	7	9
Unspecified	0	1

1 Total N is number of women with follow-up data.

2 If a woman did not report regular use of the method at every follow-up visit, she could appear in more than one of the reason for irregular use categories, therefore totals are not additive.

TABLE VI

Alternative or Additional Contraceptive Method Used at One or More  
Follow-Up Visits Among OVT-n and OVT-m Users:  
Three International Sites

Contraceptive Method	OVT-n (N=139) <sup>1</sup> No. <sup>2</sup>	OVT-m (N=129) <sup>1</sup> No. <sup>2</sup>
<b>Alternative<sup>3</sup> Method Used</b>		
Condom	8	8
Withdrawal/Rhythm	13	10
Depo-Provera	1	2
Oral Contraceptive	2	2
Foam	1	0
Unspecified	0	1
<b>Additional<sup>4</sup> Method Used</b>		
Condom	5	6
Withdrawal/Rhythm	8	6
Oral Contraceptive	0	1

1 Total N is number of women with follow-up data.

2 A woman may appear in more than one category, therefore totals are not additive.

3 Alternative method is any contraceptive method used when tablets were not used.

4 Additional method is any contraceptive method used when tablets were also used.

TABLE VII

Method-Related Complaints Among OVT-n and OVT-m Users  
at Three International Sites

Complaint	OVT-n (N=139) <sup>1</sup> No. <sup>2</sup>	OVT-m (N=129) <sup>1</sup> No. <sup>2</sup>
Vaginal burning/stinging/warmth	22	31
Male discomfort/irritation	4	5
Inconvenient/troublesome/messy	15	4
Tablet did not dissolve	10	1
Abdominal pain	4	3
Vaginal discharge	3	1
Too wet/watery vagina	6	1
Other	3	4
Women with one or more method- related complaints at follow-up	49	44

1 Total N is number of women with follow-up data.

2 A woman may appear in more than one category, therefore totals are not additive.

TABLE VIII

Medical Complications Ever Reported at any Follow-up Visit Among OVT-n and OVT-m Users: Three International Sites

Medical Complication	OVT-n (N=139) <sup>1</sup> No. <sup>2</sup>	OVT-m (N=129) <sup>1</sup> No. <sup>2</sup>
<b>Vaginal conditions</b>		
Moniliasis	3	2
Trichomoniasis	0	3
Vaginitis	2	0
Candidiasis	0	1
Gardnerella infection	1	0
<b>Cervical conditions</b>		
Cellular atypia	24	21
Cervical dysplasia <sup>3</sup>	2	0
Carcinoma <u>in situ</u> <sup>4</sup>	0	1
Cervical erosion	3	2
<b>Other medical conditions</b>		
Uterine fibroids	2	2
Endometritis	1	0
Dysuria	0	1
Amenorrhea	2	2
Irregular menses	1	1
Gonorrhea	0	1
Decreased menstrual bleeding	2	1
Postcoital bleeding	1	0

1 Total N is number of women with follow-up data.

2 A woman may appear in more than one category, therefore totals are not additive.

3 One woman who had mild cervical dysplasia at a follow-up visit also had dysplasia at admission. The other woman did not have a Pap smear at admission and was reported to have mild cervical dysplasia and was allowed to continue in the study.

4 A Pap smear was not performed at admission for this woman.

TABLE IX

Reasons for Discontinuation Among OVT-n and OVT-m Users:  
Three International Sites

Discontinuation Reason	OVT-n (N=140) No.	OVT-m (N=135) No.
<b>Pregnancy</b>		
Method failure	9	7
User failure	13	12
Planned pregnancy	3	1
<b>Vaginal/penile discomfort reasons</b>		
Vaginal burning/stinging/warmth	8	7
Penile irritation	0	1
Unspecified female/male discomfort	1	0
<b>Medical reasons</b>		
Moniliasis	0	1
Vulvovaginitis	1	0
Cervical dysplasia	1	0
Cervicitis	0	1
Amenorrhea	0	1
Abdominal pain	0	3
Dysuria	0	1
<b>Product-related reasons</b>		
Messy/inconvenient	1	1
Failure to dissolve	1	0
<b>Other personal reasons</b>		
Desires another method	0	1
Partner objects	4	1
Partner had vasectomy	1	0
Unable to continue follow-up visits	1	1
Outside the study protocol	1	0
Irregular intercourse	2	4
Loss to follow-up <sup>1</sup>	17	13
Completed 12 months of use	76	79

<sup>1</sup> A woman was considered a loss to follow-up if she did not return for her next scheduled follow-up visit within 12 months of her date of admission.

TABLE X

Gross Cumulative Life Table Rates<sup>1</sup> per 100 Women: OVT-n and Ovt-m Users  
Three International Sites

Event	OVT-n Users Rates/100 women (+ S.E.) <sup>2</sup>	OVT-m Users Rates/100 women (+ S.E.) <sup>2</sup>
<b>Accidental pregnancy<sup>3</sup></b>		
6 months	8.3 + 2.5	6.3 + 2.3
12 months	19.3 + 3.8	17.5 + 3.8
<b>Planned pregnancy</b>		
6 months	1.8 + 1.3	0.9 + 0.9
12 months	3.1 + 1.8	0.9 + 0.9
<b>Discomfort discontinuation</b>		
6 months	6.4 + 2.2	5.7 + 2.1
12 months	7.4 + 2.4	6.7 + 2.3
<b>Product-related discontinuation</b>		
6 months	1.5 + 1.1	0.8 + 0.8
12 months	1.5 + 1.1	0.8 + 0.8
<b>Other medical discontinuation</b>		
6 months	1.7 + 1.2	3.7 + 1.8
12 months	1.7 + 1.2	7.0 + 2.6
<b>Other personal discontinuation</b>		
6 months	4.9 + 2.0	5.9 + 2.2
12 months	8.2 + 2.6	5.9 + 2.2
<b>Lost to follow-up rate</b>		
6 months	8.6	8.2
12 months	43.6	40.0
<b>Total woman-months of use</b>		
12 months	1188.5	1184.0

1 Includes 9 women who subsequently became lost to follow-up

2 Standard error of rate

3 Accidental pregnancy rates do not include one OVT-n pregnancy and one OVT-m pregnancy which occurred eight or more days after last using the method.

4 The lost to follow-up rate was generated interactively and not by the gross cumulative life table rates. This rate is a calculation of the percentage of women lost to follow-up at each month listed in the follow-up schedule.