

PENILE APPLICATION OF DEXTRIN SULPHATE (EMMELLE) TO HIV+ AND HIV- MEN

Vicky Jespers, M.D.¹

Alan Chapman, B.Sc., Ph.D.²

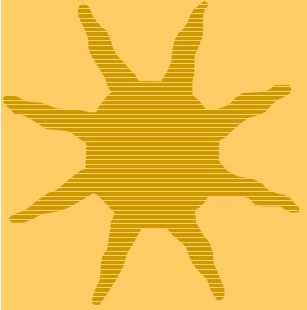
Lut Van Damme, M.D., M.Sc.¹

¹ *Institute of Tropical Medicine, Belgium*

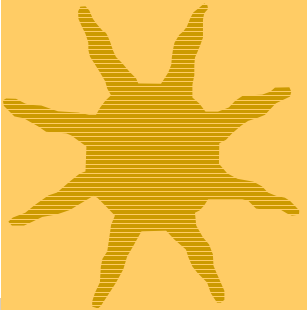
² *ML Laboratories plc, UK*



SAFETY STUDY

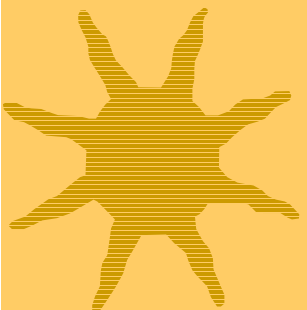


★ RANDOMISED DOUBLE-BLIND



★ PLACEBO-CONTROLLED

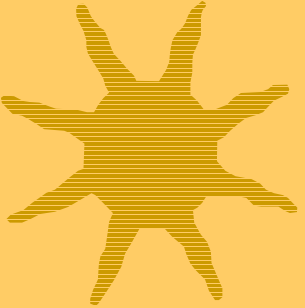
★ HIV+ AND HIV- MEN



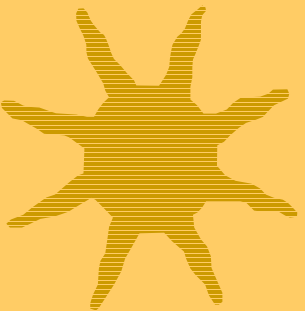
★ 4% DEXTRIN SULPHATE GEL



INCLUSION CRITERIA



1. Healthy or HIV+ with a CD4 > 200/ μ l



2. Abstain from using any other genital preparations



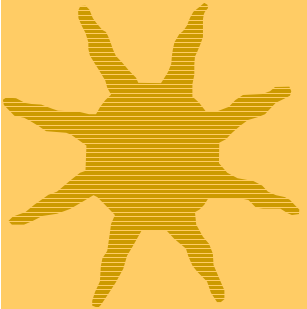
3. Have an HIV antibody test

4. Abstain from sex within 6h of daily gel application

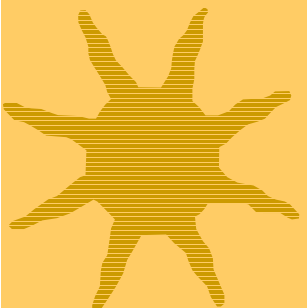
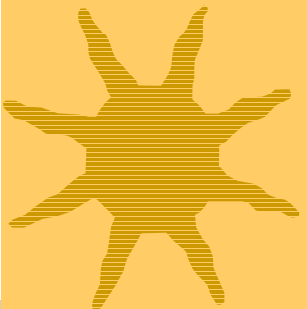
5. Use condoms for sex



EXCLUSION CRITERIA

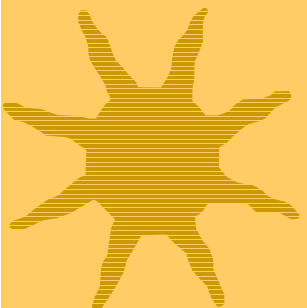
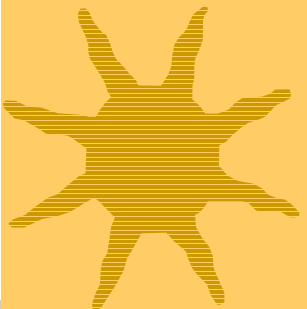
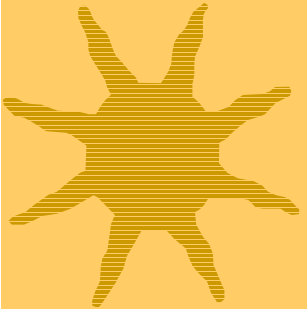


1. Untreated genital infection
2. Genital ulceration or warts
3. Pain or discomfort during sexual intercourse
4. No effective method of contraception
5. Intolerance to heparin or dextrin sulphate
6. History of a coagulation disorder
7. Likelihood of subject non compliance
8. Participation in any other clinical trial using a product not licensed in UK or Belgium.
9. At high risk of contracting HIV





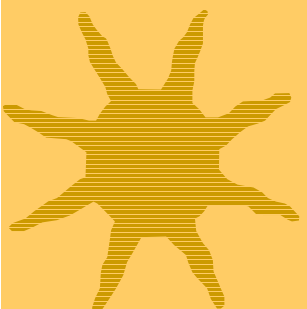
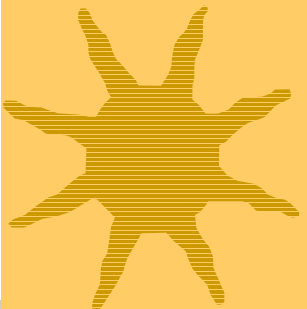
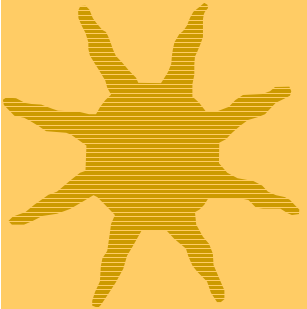
COMPOSITION GEL



	Dextrin sulphate gel	Placebo gel
Dextrin sulphate	4 % 80mg in 2g = approx 2ml	0
Carbopol	40 mg/g	40 mg/g
Lactic acid	0.48 mg/g	0.8 mg/g
Water	As required	As required



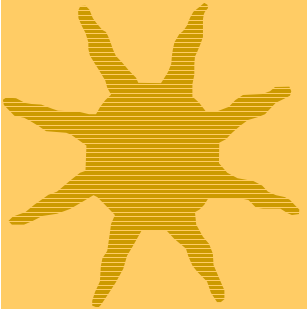
STUDY SCHEDULE



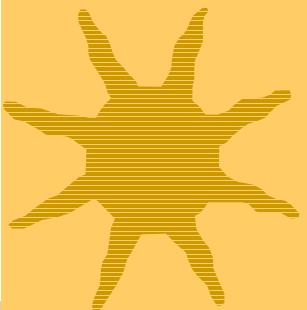
Visit	1 (Day -7)	2 (day 0)	3 (day 14)	4 (day 21)
Screening	x			
Consent	x	x		
Safety assessments	x		x	x
Gel use, diary card		x —————> ?		
Adverse events	x —————> ?			



BASELINE CHARACTERISTICS CANDIDATES



- ★ Apart from circumcision status: similar across treatment groups and HIV status

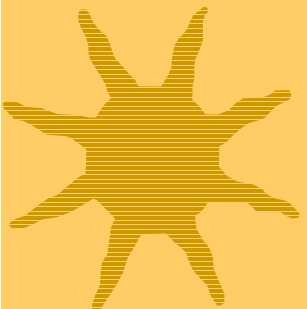


Total: 28	HIV+:16	HIV-:12
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DS	12 (6)	9 (1)
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Placebo	4 (1)	3 (0)
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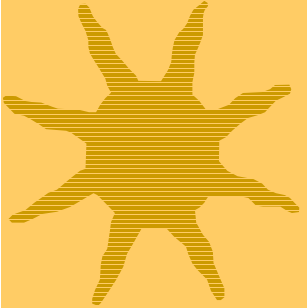
(number circumcised)



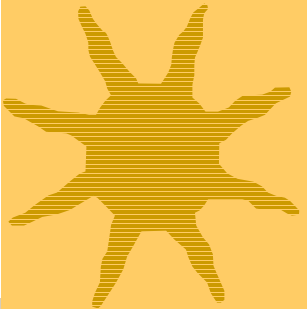
- ★ Average: 40 years, 177cm, 73 kg
- ★ Caucasian 25, Hispanic 2, Afro-Caribbean 1



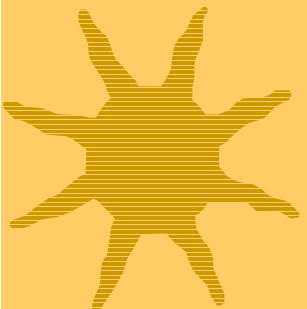
EXPOSURE STUDY MEDICATION



★ COMPLIANCE NEAR 100%



★ ONE APPLICATION FORGOTTEN

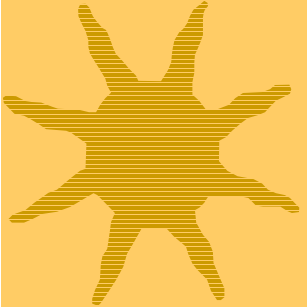


★ APPLIED TWICE SAME DAY: 2

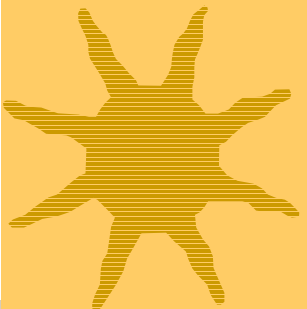
★ AVERAGE OF 8.2 HOURS



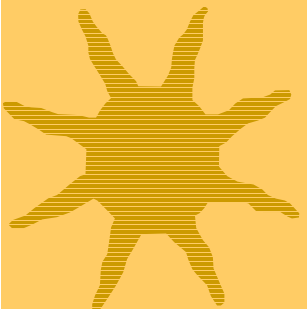
SEXUAL ACTIVITY



★ NO SEXUAL ACTIVITY: 25 %



★ VAGINAL INTERCOURSE: 32 %;
episodes 1-5

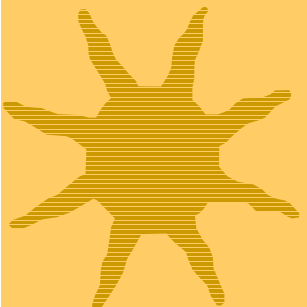
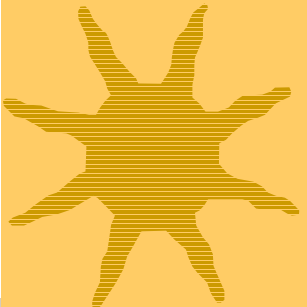
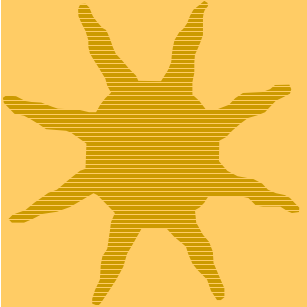


★ ANAL INTERCOURSE: 28 %;
episodes 2-8

★ MASTURBATION: 50%;
episodes 1-18



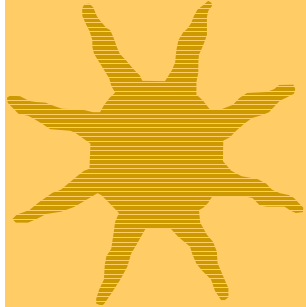
SUMMARY OF NON-SERIOUS REPORTS



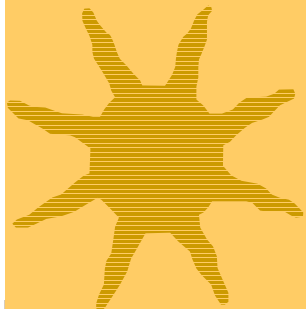
RELATION TO GEL USE	HIV-positive		HIV-negative		TOTAL	
	DS	Placebo	DS	Placebo	DS	Placebo
	N=12	N=4	N=9	N=3	N=21	N=7
ALMOST CERTAINLY	0	0	0	0	0	0
PROBABLY	0	0	4	1	4	1
POSSIBLY	6	1	1	1	7	2
NOT LIKELY	12	0	2	0	14	0
UNRELATED	9	3	8	2	17	5



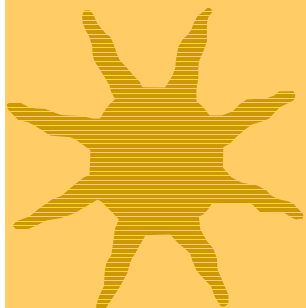
SUMMARY OF GENITAL EXAMINATION



★ OEDEMA	0
★ BLOOD IN URINE	0
★ PAIN DURING INTERCOURSE	0



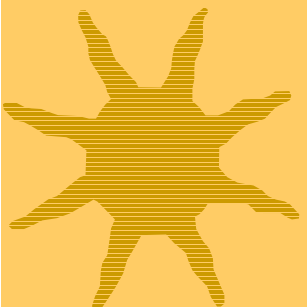
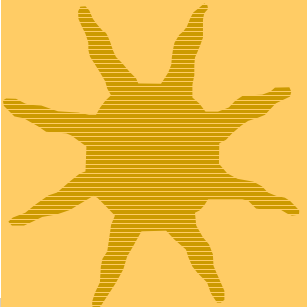
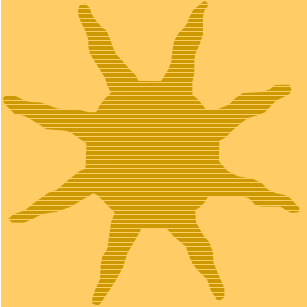
★ PAIN ON PASSING URINE	1
★ ITCH GENITAL AREA	3
★ BURNING GENITAL AREA	1



★ REDNESS-BLOODVESSELS INTACT	9
★ REDNESS-BLOODVESSELS DISRUPTED	1
★ SUPERFICIALLY DISRUPTED EPITHELIA	2
★ OTHER ABNORMALITIES	18



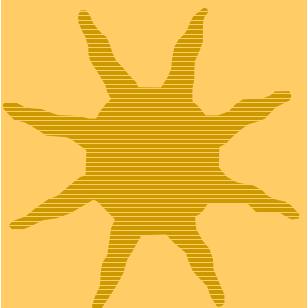
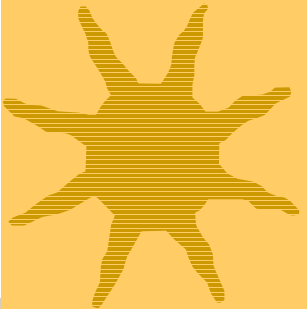
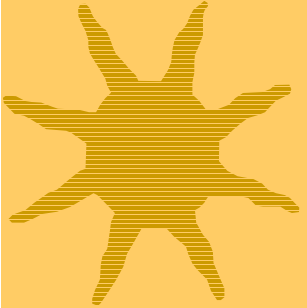
POSSIBLE CAUSES OF ERYTHEMA AND DISRUPTED EPITHELIA



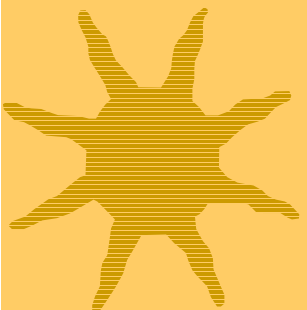
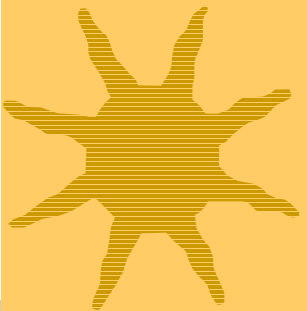
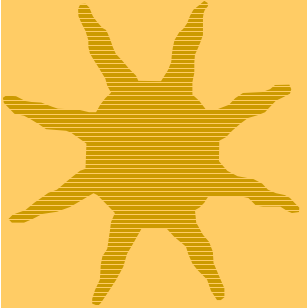
VISIT	DS	PLACEBO
1	1.ERYTHEMA PSORIASIS	
2	1.ERYTHEMA PSORIASIS 2.ERYTHEMA IRRITATED SEBACEOUS GLAND	3.ERYTHEMA CAUSE UNKNOWN 4.ERYTHEMA CAUSE UNKNOWN
3	1.ERYTHEMA IRRITATED SEBACEOUS GLAND 2.ECCHYMOSIS TRAUMA SEBACEOUS GLAND 3. DISRUPTED EPITHELIA AND ERYTHEMA HERPETIC LESIONS	4.ERYTHEMA CAUSE UNKNOWN
4	1.DISRUPTED EPITHELIA AND ERYTHEMA IRRITATED SEBACEOUS GLAND	



SUMMARY OF ABNORMAL APTT VALUES



	VISIT	HIV+	HIV-	TOTAL	%
PLACEBO	1	1	1	2	29
	3	1	2	3	43
	4	0	1	1	50
DS	1	1	0	1	5
	3	4	5	9	43
	4	2	0	2	25

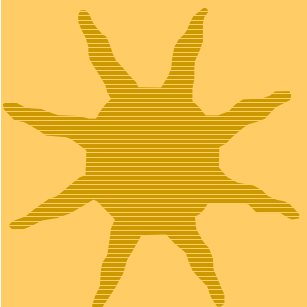
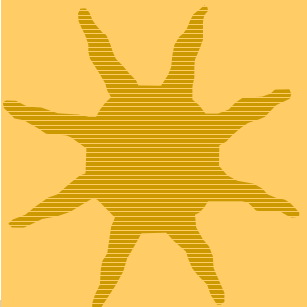
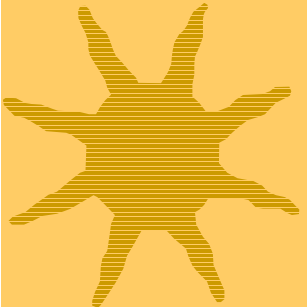


CONCLUSION

4 % DS GEL
ADMINISTERED TOPICALLY TO PENIS
IS WELL
TOLERATED AND ACCEPTED



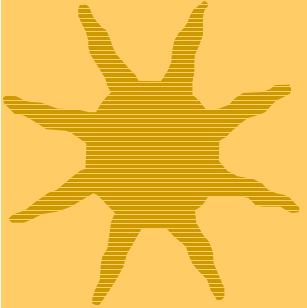
GRADING ADVERSE EVENTS



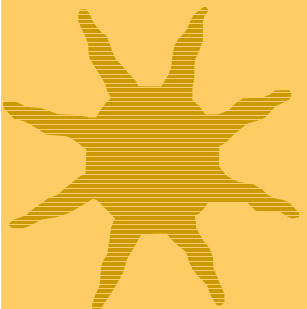
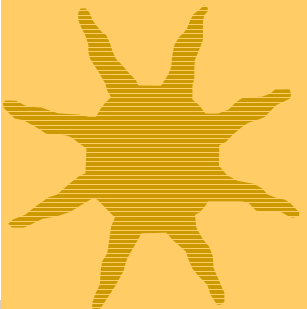
Grade	1	2	3
Symptoms	mild	moderate	severe
General definitions	Easily tolerated	Aware at most times of symptoms	Interrupting daily activities
Signs	*(swab tip is 5 x 10mm)		
Epithelial disruption	Superficial \leq 1 swab tip*	Superficial >1 , \leq 4 swab tips*	Deep or superficial, >4 swab tips*
Epithelium intact, blood vessels intact	Local-diffuse slight redness or local moderate-severe redness	Diffuse moderate-severe redness	Oedema or diffuse moderate-severe redness with Grade II symptoms
Epithelium intact, blood vessels disrupted	Single or multiple, < 1 swab tip*	Single or multiple, > 1 swab tip*	



GENITAL EXAMINATION

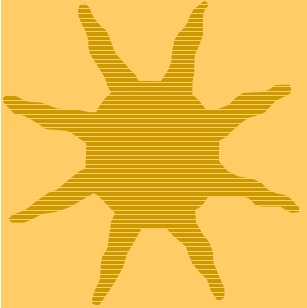


- ★ Oedema
- ★ Erythema
- ★ Disrupted epithelia (HSV specimen)
- ★ Superficial lesions and deep lesions
- ★ Other abnormalities
- ★ Redness; blood vessels intact and blood vessels disrupted
- ★ Symptoms
 - Pain on passing urine
 - Itching in genital area
 - Burning in genital area
 - Pain during intercourse



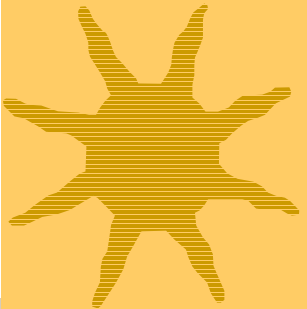


HAEMATOLOGY



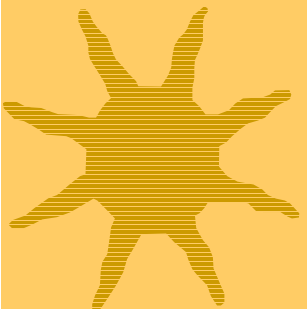
★ Full Blood Count

Haemoglobin, Haematocrit, Erythrocytes, Platelets, Leucocytes (and differential [Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils])



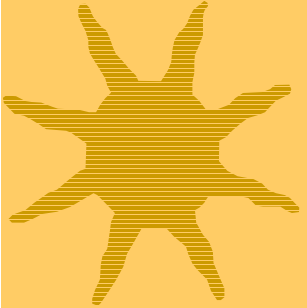
★ Coagulation Parameters

APTT and Thrombin time

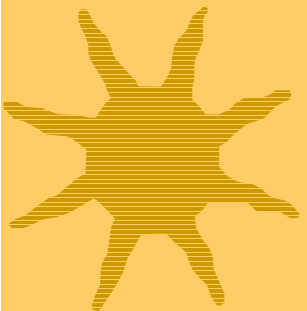
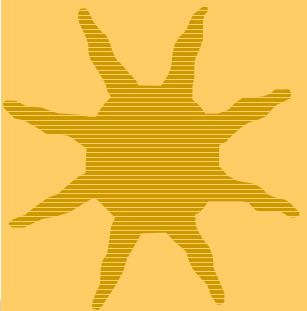




CLINICAL CHEMISTRY

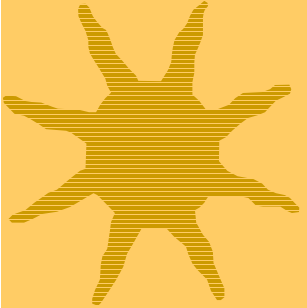


- ★ Sodium, Potassium, Bicarbonate, Urea, Creatinine, Bilirubin, AST or ALT, Total protein, Albumin, Calcium, Phosphate and Urate.

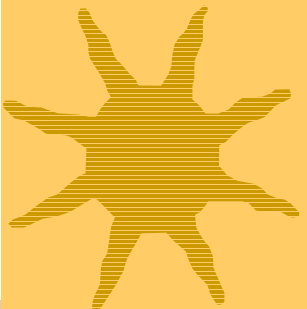




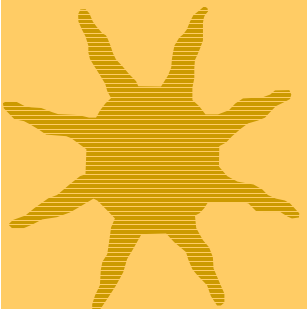
MICROBIOLOGY



Sexually Transmitted Disease Screen

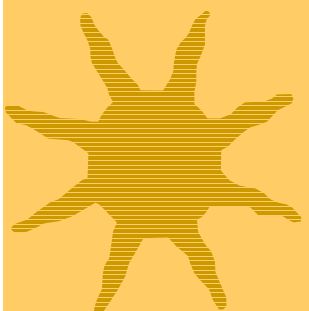
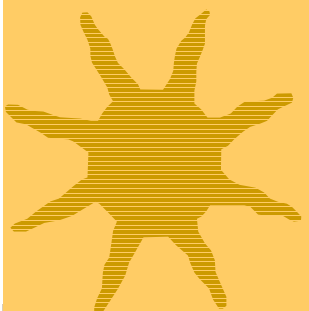
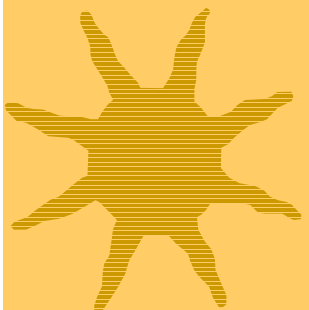


- ★ *Neisseria gonorrhoeae* – PCR
- Chlamydia trachomatis* (urethra) - PCR
- Syphilis serology - ELISA
- ★ Urine: Neutrophils
- ★ *Candida albicans* : sub-preputial swab





SUMMARY OF ABNORMAL APTT VALUES (normal 26-36 s)



	VISIT	HIV+	HIV-	TOTAL	%
PLACEBO	1	36.5	39.3	2	29
	3	36.2	52.5 42.2	3	43
	4	0	40.6	1	50
DS	1	38.4	0	1	5
	3	37.3,36.8, 40,38.3	40.2,42.8, 41.4,41.1, 36.1	9	43
	4	37.2 37.9	0	2	25