Medicines Control Authority of Zimbabwe

Clinical Trials Registry

PUBLIC TITLE/ACRONYM	CCNO17
Scientific Title	Clinical Evaluation of Daily Application of Nestorone® (NES) and Testosterone (T) Combination Gel for Male Contraception

Primary Sponsor Details

Sponsors *	National Institutes of Health Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

Secondary Sponsor Details

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Countries of Recruitment *

USA and Zimbabwe

Source of Funds	
Health Condition(s) or Problem(s) Studied *	Contraceptive Efficacy
Medicine Name *	IP Name: Nestorone® (NES) (international nonproprietary name segesterone acetate) and Testosterone combined gel • IP Codes: NES-8/T-62 and NES-8/T-74 • Active ingredients: Nestorone (0.19%), Testosterone (1.43%)
Quantity of medicine required *	The amount of medicine required will be determined by the number of participants enrolled.

7.0 PRINCIPAL INCLUSION CRITERIA *

Male Partner – **Inclusion Criteria**: Men who meet all the following criteria will be eligible for enrollment in the trial:

1. Good health as confirmed by medical history, physical examination, and clinical laboratory tests of blood and urine at the time of screening
2. 18 to 50 years of age, at the enrollment visit;
3. BMI < 33 kg/m2 ;
4. No history of androgen use in the six months prior to the first screening visit;
5. Agreement to use an effective method of contraception with his female partner (refer to Appendix 11 for acceptable forms of contraception) during the suppression and first 7 days of their recovery phase and only use the experimental method during the efficacy phase of the study;
6. . In the opinion of the investigator, the male subject is willing and able to comply with the protocol;
7. The subject is legally competent, has been informed of the nature, the scope and the relevance of the study, voluntarily agrees to participation and the study's provisions and has duly signed the informed consent form (ICF);
8. Sexually active with a female partner (as specified below) with whom he has been in a stable, mutually monogamous relationship for at least 1 year prior to screening and with whom he intends to remain in a relationship for the duration of the study;
9. No known infertility;
10. Normal reproductive state as demonstrated by: • Sperm concentration ≥15 million/mL in two semen samples and with no gross abnormalities of sperm motility and morphology on at least one semen sample assessment; • Screening Testosterone within the study site's local lab normal reference range for adult men;
11. Willingness to accept a low but unknown risk of conceiving a pregnancy for the duration of the trial.

Female Partner – Inclusion Criteria: Women who meet all the following criteria will

be eligible for enrollment in the trial:

1. Good general health with no chronic medical conditions that result in

periodic exacerbations which require significant medical care or are known

to affect fertility;

2. Aged between 18 and 34 years, inclusive, at the enrollment visit;

3. Have regular menstrual cycles of 21-35 days in duration, per patient report,

when not using hormonal contraception. If hormonal contraception has

been used, the following applies:

a. If recently used intramuscular Depo-Provera, must have had last

injection at least 3 months prior enrollment;

b. If using an IUD or an implant, she is planning to have this removed for

purposes unrelated to enrollment in the study prior to entering the

efficacy phase;

c. Completion of her last pack of oral contraceptives or completion of

effectiveness period for a monthly injection, patch or ring if any has

been used prior to entering the efficacy phase;

4. Have intact uterus and at least one ovary;

5. The subject is legally competent, has been informed of the nature, the

scope and the relevance of the study, voluntarily agrees to participation

and the study's provisions and has duly signed the informed consent form

(ICF);

6. Consistent use of effective contraception during the preceding cycle prior

to enrolling;

7. No known infertility;

8. Intends to remain in a monogamous relationship with male study partner

(as specified above). (Note: this study will not provide her contraception for

intercourse with any other male partners);

9. Be at risk for pregnancy with participating male partner (heterosexual

vaginal intercourse at least once per cycle and not sterilized);

10. Have a negative pregnancy test at enrollment;

11. Willingness to accept a low but unknown risk of pregnancy and able to understand the need for follow-up in case of pregnancy;

12. No medical contraindication to pregnancy;

7.1 PRINCIPAL EXCLUSION CRITERIA *

Male Partner – Exclusion Criteria: Men who meet any of the following criteria are not eligible for enrollment in the trial:

1. Men participating in another clinical trial involving an investigational drug within the last 30 days (or within five half-lives of the investigational drug, whichever is longer) prior to the first screening visit.
2. Men not living in the catchment's area of the study site or within a reasonable distance from the site.
3. Clinically significant abnormal findings at screening per the Investigator's medical judgment.
4. PSA levels ≥ 4 ng/mL

Abnormal serum chemistry values that may indicate clinically significant liver or kidney dysfunction.

6. Use of androgens or other anabolic steroids that may suppress gonadotropins within 6 months prior to the first screening visit.
7. Diastolic blood pressure (DBP) ≥ 85 and Systolic blood pressure (SBP) ≥ 135 mm Hg; (BP will be taken three times at approximately 5-minute intervals and the mean of the last two of the three measurements will be used to determine eligibility).
8. History of hypertension, including hypertension controlled with treatment.
9. Known history of primary testicular disease or disorders of the hypothalamic-pituitary axis.
10. Known hypersensitivity to progestins or testosterone or any excipient of the IP.
11. History of prostate, testicular or breast carcinoma.
12. Significant prostatic symptoms (IPSS > 15).
13. Known history of reproductive dysfunction including vasectomy or infertility.
14. Known history of significant cardiac, renal, hepatic, or prostatic disease.
15. History of thromboembolic disease.
16. A serious systemic disease such as diabetes mellitus (including diabetes controlled with treatment) or HIV.
17. Current active or ongoing hepatitis infection.
18. History of untreated sleep apnea.
19. Known or suspected current alcohol dependence syndrome, chronic marijuana use, or any illicit drug use that may affect metabolism/transformation of steroid hormones and study treatment

compliance.
20. Any skin condition that might interfere with absorption of gel.
21. Couples desiring fertility within the study participation period (approximately 70-90 weeks from screening to the 7th day of recovery).
22. PHQ9 score ≥ 10, a score ≥ 1 on Question #9 on the PHQ9, or history of severe depression or other serious mental health disorder, including ongoing use of an anti-depressant.
23. Men participating in competitive sports where drug screening for prohibited substances (including anabolic steroids) is routine. Exclusion is due to the potential of testing positive for androgens that may occur from their study participation coupled with the unknown efficacy (i.e., duration of positive testing) of a single application.
24. Use of sex steroids or medications which might interfere with steroid metabolism (i.e., ketoconazole, finasteride, oral corticosteroids, dutasteride and statins).
25. Use of anticoagulants.
26. Use of medications that will interfere or interact with Nestorone or Testosterone (see Appendix 2).

27. Use of oily cosmetic skin gels/products that would prevent absorption of steroids.
28. Previous participation in this clinical trial.
29. Any site staff member with delegated study responsibilities or a family member of a site staff member with delegated study responsibilities.
30. Have issues or concerns (in the judgment of the investigator) that may compromise the safety of the subject or confound the reliability of compliance and information acquired in this study.

Female Partner – Exclusion Criteria:

1. Desire to become pregnant from screening throughout the 7th day of recovery.
2. Breastfeeding.
3. Known or suspected current alcoholism or drug abuse.
4. Participation in another clinical trial involving an investigational drug within the last 30 days prior to the first screening visit.
5. Currently pregnant.
6. Known hypersensitivity to progestins or testosterone.
7. Previous participation in this clinical trial.
8. Any site staff member with delegated study responsibilities or a family

member of a site staff member with delegated study responsibilities.

9. Have issues or concerns (in the judgment of the investigator) that may compromise the safety of the subject or confound the reliability of compliance and information acquired in this study

7.2 PRIMARY END POINTS *

Twelve-month (365 days) cumulative contraceptive efficacy in couples, during the efficacy portion of the study, in which the male partner uses the product daily to suppress sperm production and the couple uses the method as their sole contraceptive method is the primary endpoint for this study.

9.0 DESIGN OF THE TRIAL

Type of trial *	Opened
If controlled	
Randomised	
Single Blind	
Double Blind	
Parallel group	
Cross over	
Other	
If yes to other, specify	A prospective, phase IIb, open label, single arm, multicenter study
If controlled, specify the comparator	
Other medicinal product(s)	
Placebo	
Other	
If yes to other, specify	
Other	

Expected Number of participants in Zimbabwe *	20
Total enrolment in each site: (if competitive enrolment, state minimum and maximum number per site.) *	30 -60 Couples
Total participants worldwide *	420

Time period for the trial *	The Sponsor estimates that the study will require approximately 104 weeks from the time the first participant provides documented informed consent/assent until the last participant's last study-related contact.