PHARMACOVIGILANCE AND CLINICAL TRIALS DIVISION

CLINICAL TRIAL APPLICATION PUBLIC ASSESSEMENT REPORT

PART 1: ADMINISTRATIVE DETAILS

Title of Study and Protocol Version: Assessing acceptability of Annovera contraceptive vaginal ring use (compared to other contraceptive method use) among women seeking family planning services. Version 5.4 dated 04 December 2024	**Study Ref:** CT282/2024
Date of receipt of the application: 28 October 2024	
Clinical trial Phase: IV	
Study Site(s): Mbare Poly Clinic, Mzengeli Way, Off Ardbennie Rd, Mbare, Harare and Matapi Clinic, Harare Rd South, Mbare, Harare	
Applicant/Principal Investigator name and address: Dr Gerald Hangaika, Médecins Sans Frontières (MSF) Mbare Project Office, No 33, 5th Avenue, Mbare, Harare	
Sponsor name and address: The Population Council, 1188 York Avenue, Weiss 5th Floor, New York, NY 10065, USA	
Study duration: 24 months	
Date of Commencement (Expected or Actual):	
Clinical trial authorisation validity period: 25 April 2025 to 31 July 2027	

PART 2: SUMMARY OF EVALUATION

Study design: A study evaluating acceptability of a contraceptive vaginal ring, Annovera, compared to other contraceptive methods specifically oral contraceptive pills (OCPs) or depot medroxyprogesterone acetate (DMPA) in women seeking family planning services using acceptability surveys and continuation rates. Women seeking family planning services at the study sites will be presented with their free choice, at no cost, of Annovera or other locally available contraceptive methods. Those selecting Annovera, and a subset of those selecting another contraceptive method will be given information on the study and if interested in participation, screened for eligibility.
Population: Women aged between 18-24 years who are not pregnant at screening or enrolment, are at risk for pregnancy and are seeking contraception. Total participants for the whole study are 400 participants and the expected number of participants to be recruited in Zimbabwe is 200 (100 Annovera users and 100 non Annovera users).
Study Objectives:

Primary objectives

1. To assess method satisfaction in Annovera users and to compare it with satisfaction among users of other contraceptive methods (non Annovera users) at 12 and 52 weeks of use.
2. To compare method continuation between Annovera users and users of other contraceptive methods at 4, 12, 24, 36, and 52 weeks.
3. To assess Annovera uptake by the proportion of women attending the site during the study period who initiated Annovera vs. initiated comparison (OC/DMPA) methods

Secondary objectives

1. To assess various dimensions of acceptability of Annovera at 4, 12, 24, 36 and 52 weeks
2. To determine characteristics associated with willingness to try Annovera (vs. to use other contraceptive methods)
3. To determine characteristics associated with satisfaction with Annovera (vs. with dissatisfaction with Annovera)
4. To assess reasons for contraceptive method selection and discontinuation in Annovera users and users of other contraceptive methods.

Eligibility Criteria:

Inclusion Criteria

1. Ages 18 through 24 (Zimbabwe) and 18 through 45 (Kenya) years old (inclusive) at screening, verified per site-specific SOPs
2. Fluent in spoken Shona (Zimbabwe) or Swahili (Kenya) and/or English
3. At risk for pregnancy (post-menarche, no prior sterilization, hysterectomy, oophorectomy, or menopause, per self-report)
4. Contraceptive intentions:
    a. for potential Annovera users, desiring to initiate a new contraceptive method or change from one currently being used; or
    b. for non-Annovera users, has initiated or changed to OC or DMPA use at enrolment
5. At least 12 weeks since last DMPA injection (per review of health record) if ever previously used DMPA
6. Sexually active, defined as having had penile-vaginal intercourse with a man within the three months before screening
7. Not pregnant at screening or enrolment (per negative pregnancy test)
8. Not trying to become pregnant or intending to become pregnant within the next year
9. No plans to move away from the study site in next 12 months
10. Able and willing to provide informed consent
11. Able and willing to provide adequate locator information
12. In the opinion of the site PI or designee, able and willing to comply with the protocol and all study procedures

Exclusion Criteria

1. BMI>29 (per exam at screening)
2. Known hypersensitivity to or prior complications with oestrogens, progestins, silicone or any of the other components of Annovera
3. Not eligible for combined hormonal contraception; this includes an assessment of the following:
    a. Breastfeeding
    b. Less than 6 weeks (<=42 days) postpartum
    c. For women 35 and older, currently smokes cigarettes
    d. History of deep vein thrombosis or pulmonary embolism
    e. Prolonged immobilization or anticipating major surgery in the next year
    f. Thrombogenic valvular or thrombogenic rhythm diseases of the heart
    g. Inherited or acquired hyper-coagulopathies
    h. Current or history of cerebrovascular disease, coronary artery disease, or ischemic heart disease

i. Uncontrolled hypertension or hypertension with vascular disease (self-report and clinic assessment)
j. Systemic lupus erythematosus with positive or unknown antiphospholipid antibodies
k. Migraines with aura
l. For women over 35 years old, migraines without aura (applicable to Kenya)
m. Current breast cancer or within 5 years of past breast cancer
n. Diabetes for > 20 years and/or with nephropathy, retinopathy or neuropathy
o. Symptomatic gall bladder disease
p. Liver tumour, acute hepatitis or severe cirrhosis
q. Undiagnosed abnormal vaginal bleeding
r. Known condition where steroid hormones are contraindicated

4. Use of medications that are contraindicated or believed to have a drug-drug interaction with Annovera
5. Current abnormal vaginal discharge, genital tract lesions, or active pelvic infections (for woman in whom the clinician suspects a genitourinary tract infection, treatment should be offered, and woman can enrol following resolution of symptoms)
6. History of genital tract surgery (including cervical polypectomy, dilatation and curettage, hysteroscopy, or laparoscopy) in the three months prior to the screening visit
7. History of toxic shock syndrome
8. Recurrent vulvovaginal candidiasis (defined as more than 3 episodes in the preceding year)
9. Current use of vaginal rings (such as Dapivirine ring) or any other instance, as per clinician judgement, where using Annovera along with other vaginally inserted products is not advised.
10. Any other condition the clinician feels would jeopardize the health and well-being of the participant
11. Previous enrolment in the trial as either an Annovera user or non-user

Vulnerable/High Risk Groups
None

Informed Consent, Decision-making & Confidentiality
Shona and English Informed Consent Forms were provided which were satisfactory.

Scientific and Technical Issues
The study design was found to be scientifically sound. The justification for the study was acceptable and follow up procedures were satisfactory. All scientific and technical aspects were satisfactory.

Other materials, documents and study instruments (Patient recruitment materials, Questionnaires)
Recruitment materials, patient information and questionnaires were satisfactory.

Clinical Trials/Study Medicines
Study medicine

1. Annovera® Contraceptive vaginal system, 103 mg segesterone acetate and 17.4 mg ethinyl oestradiol in each ring manufactured by Sever Pharma Solutions

Comparators

1. Oral contraceptive pills (OCPs) or
2. Depot medroxyprogesterone acetate (DMPA)

The justification for the study product and comparators was acceptable.

Summary of review of:

1. Quality
2. Safety

3. Efficacy

Quality, safety, efficacy and benefit risk analysis data were assessed and were satisfactory.

Application Review Process

The application was reviewed under the normal pathway.

Status after review:

The clinical trial was authorised on the 25th of April 2025.

PART 3: OVERALL COMMENTS AND CONCLUSION:

The Principal Investigator (PI) was required to address queries raised by the MCAZ Pharmacovigilance and Clinical Trials Committee after initial review of the application. The PI responded and addressed all the queries. The PI was subsequently authorised, with the approval of the Secretary for Health and Child Care, to conduct the trial subject to the contents of the application and the following conditions:

1. Reporting of all serious adverse events to MCAZ;
2. Submission of all amendments to the protocol for approval by MCAZ;
3. Submission of a progress report of the clinical trial by the 31st of January annually;
4. Submission of the final report and copy of any publication of the clinical trial prior to publication of results;
5. In compliance with the current Good Clinical Practices (cGCP) and all other relevant MCAZ guidelines;
6. Submission of the completed indemnity form for conducting clinical trials to the Director-General prior to commencement of the clinical trial;
7. Expiry date of this authorisation is 31 July 2027.

Name of 1st Evaluator: R. Manyevere Signature:  Date: 03/09/2025

Name of 2nd Evaluator: L. Chirinda Signature:  Date: 04/09/2025