RECKITT

CLINICAL INVESTIGATION TITLE

An open label, randomised, 3-way cross-over, single-centre, clinical investigation to evaluate the effectiveness of benzocaine in two NRL condoms compared with a standard NRL control without benzocaine in prolonging time to ejaculation in healthy adult men who feel they ejaculate too quickly during vaginal sex.

Short Investigation Title

A clinical investigation to assess the effectiveness of benzocaine in NRL condoms in healthy adult men who feel they ejaculate too quickly during vaginal sex.

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Confidentiality Statement:	The information contained in this document is privileged and confidential. Do not copy, circulate or otherwise distribute without written authority from Reckitt.
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SIGNATURE PAGE

[redacted]

INVESTIGATOR STATEMENT

I have read and understood this Clinical Investigation Plan (CIP) and agree:

- to conduct this clinical investigation in accordance with the CIP and to abide by all provisions of this CIP (including other manuals and documents referenced from this CIP). Amendments to the CIP are acceptable only upon mutual agreement with the exception of urgent safety measures that need to be taken to protect investigation subjects from any immediate hazard to their health and safety.
- to conduct this clinical investigation in accordance with the principles as set out in the Declaration of Helsinki and with ISO 14155:2020 and applicable national laws and regulatory requirements.
- to conduct this investigation only after a favourable opinion is obtained from the Ethics Committee and Regulatory Authority.
- to report all information or data in accordance with the CIP.
- to report any serious adverse events (SAEs) and device deficiencies that may have led to a SAE as defined in the "Safety Reporting" section of this CIP.
- to handle all medical device supplies provided by the Sponsor and collect and handle all clinical specimens in accordance with the CIP.

I understand:

- that information that identifies me will be used and disclosed as described in the CIP and that such information may be transferred to countries that do not have laws protecting such information.
- that since the information in the CIP and the references in the Investigator's Brochure (IB) (if applicable) are confidential, its disclosure to any third parties, other than those involved in approval, supervision or conduct of the investigation is prohibited. I will ensure that the necessary precautions are taken to protect such information from loss, inadvertent disclosure or access by third parties.

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LIST OF ABBREVIATIONS

Abbreviation	Abbreviation in Full
ADE	Adverse Device Effect
AE	Adverse Event
AEMT	Adverse Event Managment Team
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BS EN ISO	British Standard European Norm International Organisation for Standardisatio
CA	Competent Authority
CI	Confidence Interval
CIP	Clinical Investigation Plan
CRO	Clinical Research Organisation
DSO	Drug Safety Officer
eCRF	Electronic Case Report Form
EMSEX	Event-level Male Sexual
FAS	Full Analysis Set
GCP	Good Clinical Practice
GLMM	Generalized Linear Mixed Model
GMP	Good Manufacturing Practice
GP	General Practitioner
HIV	Human Immunodeficiency Virus
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IEC	Independent Ethics Committee
IELT	Intravaginal Ejaculation Latency Time
IMSU	Investigational Materials Supplies Unit
IP	Investigational Product
IPE	Index of Premature Ejaculation
IRB	Institutional Review Board
ISF	Investigator Site File
IUD	Intra-Uterine Device
IUS	Intra-Uterine System
MedDRA	Medical Dictionary for Regulatory Activities
MIR	Manufacturer Incident Report
NIP	Non-Investigational Product
NRL	Natural Rubber Latex
PABA	Para-aminobenzoic Acid
PCP	Primary Care Physician
PE	Premature Ejaculation
PGIC	Patient Global Impression of Change

Abbreviation	Abbreviation in Full
PP	Per Protocol
QA	Quality Assurance
RA	Regulatory Authority
R&D	Research and Development
REC	Research Ethics Committee
SABS	South African Bureau of Standards
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDV	Source Data Verification
SOP	Standard Operating Procedure
SPQ	Subject Perceived Questionnaire
STD	Sexually Transmitted Disease
STI	Sexually Transmitted Infection
TE ADE	Treatment-Emergent Adverse Device Effect
TE AE	Treatment-Emergent Adverse Event
USADE	Unanticipated Serious Adverse Device Effect
WHO	World Health Organization

CLINICAL INVESTIGATION SYNOPSIS

Investigation Title:	An open label, randomised, 3-way cross-over, single-centre, clinical investigation to evaluate the effectiveness of benzocaine in two NRL condoms compared with a standard NRL control without benzocaine in prolonging time to ejaculation in healthy adult men who feel they ejaculate too quickly during vaginal sex.
Reckitt Investigation Number:	5078401
Background and Rationale:	[redacted]
Objectives:	The primary objective of this clinical investigation is: • To determine the effectiveness of benzocaine, providing ancillary topical action to act as a male genital desensitiser and intended to delay male climax and prolonging the time to ejaculation, of the Test Condom A (5% benzocaine paste condom) compared with

	the Control NRL Condom (standard NRL condom) at prolonging time to ejaculation. The secondary objectives of this clinical investigation are: • To determine the effectiveness of benzocaine, providing ancillary topical action to act as a male genital desensitiser and intended to delay male climax and prolonging the time to ejaculation, of the Test Condom B (3% benzocaine paste condom) compared with the Control NRL Condom at prolonging time to ejaculation. • To determine the effectiveness of benzocaine, providing ancillary topical action to act as a male genital desensitiser and intended to delay male climax and prolonging the time to ejaculation, of the Test Condom A and Test Condom B compared with the Control NRL Condom at prolonging time to ejaculation for an increase of 2, 3 and 4 minutes. • To evaluate the sexual pleasure when using the Test Condom A or Test Condom B compared with the Control NRL Condom. • To evaluate the subject's improvement at "lasting longer" for both the Test Condom A and Test Condom B compared with the Control NRL Condom. • To evaluate the user acceptability of the Test Condom A, Test Condom B and Control NRL Condom. • To evaluate the in-use tolerability of the Test Condom A, Test Condom B and Control NRL Condom. • To evaluate the performance (slippage and breakage) of the Test Condom A, Test Condom B and Control NRL condom when used during vaginal intercourse. • To assess the safety of the Test Condom A, Test Condom B and Control NRL Condom.
Primary Endpoint:	The primary outcome measure is a change from baseline in the Intravaginal Ejaculation Latency Time (IELT) – the duration from the start of vaginal entry (vaginal penetration into the female partner) until the start of intravaginal ejaculation (release of semen), with the Test Condom A compared to the Control NRL Condom over a 4-week assessment period.
Secondary Endpoints:	The secondary outcome measures are: • Change from baseline in IELT with the Test Condom B compared to the Control NRL Condom, over a 4-week assessment period.

	• Proportion of subjects who achieve an increase of 2 minutes from baseline in IELT in each of the Test Condom A and Test Condom B compared to the Control NRL Condom. • Proportion of subjects who achieve an increase of 3 minutes from baseline in IELT in each of the Test Condom A and Test Condom B compared to the Control NRL Condom. • Proportion of subjects who achieve an increase of 4 minutes from baseline in IELT in each of the Test Condom A and Test Condom B compared to the Control NRL Condom. • A measure of EMSEX (Event-level Male Sexual) pleasure scale at the end of a 4-week assessment period when using Test Condom A compared with the Control NRL Condom. • A measure of EMSEX pleasure scale at the end of a 4-week assessment period when using Test Condom B compared with the Control NRL Condom. • A measure of Patient Global Impression of Change (PGIC) at the end of a 4-week assessment period when using the Test Condom A compared with the Control NRL Condom. • A measure of PGIC at the end of a 4-week assessment period when using the Test Condom B compared with the Control NRL Condom. • User acceptability, experience and preference asked at the end of a 4-week assessment period when using Test Condom A compared with the Control NRL Condom. • User acceptability, experience and preference asked at the end of a 4-week assessment period when using Test Condom B compared with the Control NRL Condom. • The in-use tolerability of Test Condom A, Test Condom B and Control NRL condom, evaluated through subject perceived questions asked at the end of each 4-week assessment period. • A measure of the total clinical failure rate of Test Condom A, Test Condom B and Control NRL condom. • Overall proportion of subjects with Adverse Events/ Adverse Device Effects (AEs/ ADEs), i.e. the occurrence of one or more AEs/ ADEs per subject.
Success Criteria:	A statistically significant difference ($p<0.05$) in mean IELT between the Test Condom A compared to the Control NRL Condom, in favour

	of Test Condom A. A difference of two minutes is considered clinically meaningful.
Design:	This is an open label, randomised, 3-way cross-over, single-centre, clinical investigation to evaluate the effectiveness of benzocaine in two NRL condoms versus a control NRL condom without benzocaine.
Subjects:	150 subjects who meet the inclusion/exclusion criteria will be enrolled into the clinical investigation to ensure that a minimum of 135 subjects complete the clinical investigation. **Inclusion Criteria** Only male subjects to whom all of the following conditions apply will be included: 1) Subjects and their female partners have provided written informed consent. 2) Subjects and their female partners that can follow investigation instructions and complete the investigation assessments. 3) Subjects and their female partners between the ages of ≥18 years and ≤60 years. 4) Subjects and their female partners must have no health condition in their medical history that, in the opinion of the investigator, would be considered as clinically relevant. 5) Subjects that are circumcised or uncircumcised. 6) Subject must be sexually active having regular intercourse (frequency of at least four times over a four-week period with a minimum frequency of once a week and may comprise twice in one week to account for female partner's menstrual period break). 7) Subjects must agree to use the test condoms provided for vaginal intercourse only in this clinical investigation. 8) Subjects in a stable, monogamous, sexual relationship with the same female partner for more than or equal to 3 months, who plan to maintain their relationship for the duration of the clinical investigation. 9) Subject's female partner should already be on an established other highly effective form of non-barrier contraception, unless post-menopausal (confirmed menopausal prior to screening, amenorrhea for at least 12 months after cessation of exogenous hormone treatment). Highly effective non-barrier contraception includes: oral contraceptive (oestrogen and progestogen or progestogen-only hormonal contraception associated with inhibition of ovulation), intra-uterine device (IUD) or intra-uterine system (IUS), hormonal implant, injectables, patch and vaginal

	ring or sterilization of at least one partner (i.e. bilateral tubal ligation, vasectomy deemed medically successful). 10) Both the male subject and female partner must be willing to avoid situations or activities that may have an effect on their sexual activity. 11) Subjects and their female partners with no history of reduced sexual desire. 12) Subjects and their female partners must agree to use only the condoms and lubricant(s) provided for the clinical investigation during the three assessment periods. 13) Subjects reporting a frequency of 'occasionally' to the Sexual Intercourse Self-Estimation Scale. **Exclusion Criteria** Male subjects to whom any of the following conditions apply must be excluded: 1) Subject with a pregnant or breastfeeding female partner or the female partner desires to become pregnant during the clinical investigation (Female partners must have a negative pregnancy test as part of screening). 2) Subject, or his female partner have received an investigational (unapproved) drug within 30 days of screening. 3) Subject or his female partner with a current history of alcohol or drug abuse (self-reported) per local definitions of abuse. 4) Subjects and their female partners with a history of or are suffering from anemia, coronary artery disease, impaired cardiac conduction, pulmonary disease, diabetes, and renal or hepatic disease. 5) Subjects and their female partners with a history of, suspected to have, or be at increased risk of methaemoglobinemia / complications related to ester anaesthetics which could trigger methemoglobinemia. 6) Subject and/or his female partner have a physical or psychological condition that would prevent them from following investigation procedures - including but not limited to the following: a) Urological disease (e.g. prostatitis, urinary tract infection) or genitourinary surgery within 8 weeks of screening. b) Ongoing significant psychiatric disorder (e.g. bipolar disease, depression / anxiety disorder or schizophrenia) not controlled by medication.

	c) History of surgery or injury to the pelvis, retroperitoneal surgery, radiotherapy, multiple sclerosis, spinal cord injury, chronic inflammation of the prostate or urethra. d) Relevant (in the opinion of the Investigator) previous or planned genital surgery (i.e lazer for abnormal smear). e) A female partner that has been diagnosed with or treated for vaginal complaints (including vaginal dryness) in the previous 3 months which, in the opinion of the investigator, deems the partner unsuitable for the investigation. f) Any broken skin or wounds in the genital area. 7) Subject with a female partner that has a decreased interest in sexual intercourse or other forms of female sexual dysfunction. 8) Subjects on medication that is contraindicated, which may affect erection including but not limited to priapism caused by certain anti-hypertensives (Hydralazine, Prazosin, Guanethidine) and antidepressants (Trazodone, Thioridazine, Chlorpromazine) or topical medication which may damage the condom. 9) Subject and/or his female partner have any medication which may, in the opinion of the investigator affect the safety of the subject, including but not limited to benzocaine drug interactions such as cholinesterase inhibitors. 10) Subject and/or his female partner is using or intends to continue to use antibiotics of the sulphonamide type (examples include Gantrisin (sulfisoxazole), Bactrim or Septra (trimethoprim and sulfamethoxazole), Sulfadiazine, Azulfidine (sulfasalazine) and Zonegran (zonisamide) or cholinesterase inhibitors (examples include Aricept (donepezil), Razadyne ER (galantamine), and Exelon (rivastigmine)) from 7 days prior to screening and for the duration of the investigation. 11) Subjects with Body Mass Index (BMI) >40kg/m^2. 12) Subject that has been diagnosed or received treatment for PE (premature ejaculation) caused by medical or surgical issues, e.g., anti-depressant therapy, local anaesthetic spray or has a history of confirmed diagnosis of PE. 13) Subjects with confirmed erectile dysfunction, hypo or hyperthyroidism, hypogonadism, hyperprolactinemia. 14) Confirmed diagnosis of male subjects with other forms of ejaculatory dysfunction e.g. retrograde ejaculation, anejaculation, painful ejaculation.

	15) Subjects that have had prior genital, prostatic or lower tract surgery (other than vasectomy or circumcision). 16) Subjects with haemorrhagic disorder, hepatitis B or C, HIV infection or having had penile implant surgery, at any time in their past. 17) Any condition that the male and/ or the female sexual partner may have that, in the opinion of the investigator, may compromise the data generated, put the subject at risk or may interfere significantly with the subject's ability to participate in the clinical investigation. 18) Subjects or their female partners who have any relevant history of untreated sexually transmitted disease (STD) which from the investigator opinion may jeopardise subjects' safety. 19) Either partner needed to use condoms for a specific STI protection e.g. discordance for HIV or herpes. 20) Subjects and their female partners who have any relevant history of allergy including local anaesthetics, parabens, PABA (Para-aminobenzoic Acid), commercial hair dyes, paraphenylenediamine, lubricants and latex. 21) Subjects and their female partners who are an employee of the Investigator's department at the site or a partner or first-degree relative of the Investigator. 22) Subjects and their female partners fail to satisfy the investigator of fitness to participate for any other reason.
Products to be Evaluated and Treatment Regimen:	The three condoms to be evaluated are: • Test Condom A: NRL condom with 5% benzocaine paste • Test Condom B: NRL condom with 3% benzocaine paste • Control NRL Condom: Standard NRL condom (non-medicated NRL condom.) Treatment regimen – subjects will be randomised to use each of the condom types according to the randomisation schedule. Following at least 4 entries of IELT duration record over a 4-week period, they will repeat the process using a second condom type followed by a third condom type as per the randomisation plan. Investigational lubricant will be provided to subjects that routinely use lubricant during intercourse.
Methodology:	The duration of the clinical investigation is anticipated to be a maximum of 19 weeks (from screening to follow-up).

	Subjects will attend the clinical site on 5 occasions (1 screening visit, 3 assessment period visits, and 1 follow-up visit). Subjects will be required to report at least 4 IELT duration records over a maximum period of 4 weeks (total length of condom assessment period). Potential suitable subjects and their female partners will be identified by the clinical site and will be invited to attend the clinical site for a screening visit. Written informed consent will be obtained from the male subject and his female partner prior to any pre-investigational screening procedures being carried out. **Visit 1 – Screening (Baseline Period):** Before undergoing any clinical investigation procedure, subjects and their female partners will be asked to provide written informed consent for their participation in the clinical investigation. The screening visit procedures will consist of inclusion/exclusion criteria, medical history, physical examination and vital signs recording. Urine pregnancy test for subject's female partner of childbearing potential will be carried out. Subjects and their female partners will be trained on the use of the stopwatch provided to measure the IELT and will be briefed on the completion of the IELT diary and various questionnaires (EMSEX pleasure scale, PGIC and subject perceived questionnaire (SPQ)). AEs and concomitant medications will be collected from the start of the screening visit until the follow-up visit. Subjects will be instructed to complete an IELT diary within 2 hours after each coital act and to report a minimum of 4 IELT duration records over the 4-week baseline period. Each coital act must be at least 24 hours apart. During this 24 hour interval, subjects and their female partners will be instructed to refrain from any sexual activity including masturbation. **Visit 2, 3, 4 (Assessment Periods 1, 2, 3):** Subjects who fulfil the eligibility criteria will return to the clinical site for the first assessment period, where eligibility for entry into the clinical investigation will be reconfirmed. At each visit, any concomitant medications and AEs will be recorded. Subjects will receive their first condom type as per the randomisation schedule. Subjects will be instructed to complete the IELT diary and EMSEX pleasure scale for each condom used within 2 hours after each coital act and to report a minimum of 4 IELT duration records over a maximum period of 4 weeks. Each coital act must be at least 24 hours apart. During this 24 hour interval, subjects and their female partners will be instructed to refrain from any sexual

	activity including masturbation. On completion of each condom assessment period, subjects will be required to complete questionnaires (PGIC and SPQ). A 3-day washout period, where no test condom will be used, is required before subjects attend the clinical site to return unused condoms and be supplied with their subsequent condom type. **Visit 5 – Follow-up Visit:** The follow-up visit will be conducted after the subject has reported a minimum of 4 IELT duration records in the third condom assessment period and will consist of a physical examination and vital signs recording. Subjects will be required to return unused condoms, lubricant (if applicable) as well as the stopwatch.
Statistical Evaluation:	The primary population will be the Full Analysis Set (FAS), defined as subjects who use at least one of the clinical investigation condoms and who have IELT recorded in at least one of the post-baseline study periods. A sensitivity analysis will be performed on the Per Protocol (PP) population, which will include data from a treatment period where subjects were compliant with the protocol. The PP population will take into consideration compliance with condom usage (IELT recorded for at least four condom uses). For each subject, a mean IELT will be calculated across all intercourse episodes within a period (baseline period, assessment period 1, assessment period 2 and assessment period 3) and used for analysis. The change from baseline in IELT will be analysed using a linear mixed model with comparisons between each of the 5% and 3% Benzocaine Condoms and the standard NRL Condom. The model will include terms for baseline IELT, treatment and period, with subject as a random effect. Differences between each of the 5% and 3% Benzocaine Condoms and the standard NRL Condom will be presented with 95% confidence intervals (CI) and an associated p-value. No adjustment for multiplicity will be made since there is a single primary comparison (5% Benzocaine Condom versus standard NRL Condom). In the event that the model assumptions are not upheld, a non-parametric alternative will be used.

1 BACKGROUND AND RATIONALE

1.1 Background for the Investigation and Rationale

[redacted]

1.2 Investigational Product

NRL male condoms of varying benzocaine concentration are to be evaluated in this clinical investigation:

- Test Condom A: NRL condom with 5% benzocaine paste
- Test Condom B: NRL condom with 3% benzocaine paste
- Control NRL Condom: Standard NRL condom (non-medicated NRL condom)

[redacted]

The 3 condom types to be investigated have been formulated using well recognised ingredients with good safety profiles and the risks associated with the design and formulation of the product have been judged to be acceptable. Furthermore, the condoms to be used in this clinical investigation have been manufactured in line with Good Manufacturing Practice (GMP) and have been designed to comply with BS EN ISO (British Standard European Norm International Organisation for Standardisation) 4074:2015 Natural latex rubber condoms – Requirement and test

method and BS EN ISO 13485:2016+A11:2021 Medical devices – Quality management systems – Requirement for regulatory purposes. The condoms have also been designed to meet individual country-specific condom standards for NRL condoms (e.g. Kite mark/ South African Bureau of Standards (SABS)).

1.3 Treatment Rationale

Before any test condom is used, a 4-week baseline period is set to obtain baseline data and allow subjects and their female partners to familiarise themselves with the use of the stopwatch method. In the assessment periods, the condom types will be tested in a three-way cross-over design where subjects will be randomised to use each of the three condom types in a defined order, according to the randomisation schedule. To minimise the impact of recall bias, condoms will be used over no more than a 4-week time period. Subjects will then repeat the assessment period for the 2 remaining condom types. All condoms must be used during vaginal intercourse. All condoms will be used as intended. Each coital act must be at least 24 hours apart. During this 24 hour interval, subjects and their female partners will be instructed to refrain from any sexual activity including masturbation.

1.4 Investigation Population and Indication

In order to limit the effect of disease on the endpoints and safety of the subjects, healthy male subjects and their female partners with an interest in trialling the test condoms which can extend time to ejaculation during vaginal intercourse will be selected, based upon the inclusion and exclusion criteria presented in the clinical investigation. The criteria considered for the subject selection will involve: age, Body Mass Index (BMI), frequency of sexual activity per week, stable monogamous relationship, usage of acceptable contraceptive methods for subjects' female partners, medication history and medical history which may affect the remit of the clinical investigation.

1.5 Non-Clinical Evidence

[redacted]

[redacted]

1.6 Clinical Evidence to Date

[redacted]

1.7 Benefits / Risks Assessment

This clinical investigation has been designed to evaluate the effectiveness of the ancillary action of benzocaine in NRL condoms compared with a standard NRL condom without benzocaine at prolonging time to ejaculation. Subjects in this clinical investigation are healthy male volunteers who

are interested in trialling a condom that may prolong the time to ejaculation. The condom is not intended to treat any medically diagnosed erectile dysfunction or premature ejaculation (PE). Each subject will undergo a physical examination which will be conducted using standard clinical practice and focus on sexual health history. Further clinical examination will be conducted as deemed appropriate by the investigator. This will be performed as part of enrolment into the clinical investigation to confirm their health status as defined in this clinical investigation plan (CIP). The risks to the female partner are expected to be similar to that of the male subject, considering exposure to the latex condom, lubricant and possible exposure to benzocaine.

A healthy population (both male and female partners, due to exposure) will be included in the clinical investigation for the safety of subjects and to limit the effect of medical conditions on the efficacy evaluations.

Natural Rubber Latex (NRL) Condom

Male condoms made from NRL have a long history of safety and effectiveness and their performance during use is well established. The adverse reactions associated with NRL condoms are well known and documented in the IB. These include genital discomfort, genital burning, irritation and itching. More rarely, skin swelling, penile artery occlusion and penile vascular disorder may occur.

In addition to providing a barrier to human immunodeficiency virus (HIV), other infectious agents responsible for the transmission of sexually transmitted infections (STIs) and to spermatozoa, NRL condoms with benzocaine have been designed to deliver the ancillary function to prolong time to ejaculation.

Benzocaine

The adverse reactions associated with benzocaine are also well known and include local irritation and sensitisation and more rarely hypersensitivity, cyanosis and methemoglobinemia.

Benzocaine-induced methemoglobinemia

Benzocaine-induced methemoglobinemia (i.e. presence of an elevated circulating fraction of methaemoglobin within the erythrocytes) is a rare complication associated with topical anaesthesia which has been reported in the published clinical literature (Kane et al., 2007; Taleb et al., 2013; Hersh et al., 2005; Guay 2009; Jiwa et al., 2018; Currie et al., 1997) and can be life-threatening. Though most reports have occurred in young children and are associated with higher doses of benzocaine (Ash-Bernal et al., 2004), the study principal investigator and the project team will be trained to recognise the signs and symptoms of methemoglobinemia. They will, in turn, train the trial subjects to recognise and report it. Any subjects showing signs of methemoglobinemia will, therefore, be removed from the clinical investigation. This will be included as part of Investigator training and will be emphasised in any subject information sheet. Potential subjects or their partners with a history of, or suspected methaemoglobinaemia will be excluded from this clinical investigation.

Due to the nature of this clinical investigation, there is a likelihood that subjects may experience condom failure (slippage or breakage), in which case, subjects and their female partners who

believe they are at risk of pregnancy will be provided with access to emergency contraception and appropriate follow-up. Further to this, subjects or their female partners of childbearing potential should already be on a highly effective form of contraception as per inclusion 9. There is also the possibility of contracting an STI, in which case subjects will have access to the clinical site where appropriate measures will be taken. Additionally, subjects will also have access to sexual health information and consultation (if required) at the clinical site.

The clinical investigation includes safety measures expected of condom performance considering the safety profile of benzocaine in healthy subjects. Therefore, the overall benefit-risk profile for the use of the IP as defined in this CIP is considered acceptable.

1.7.1 Covid-19

For investigation subjects, all mandated hygiene measures and social distancing requirements will be followed in line with government guidelines and all relevant local guidelines will be monitored throughout the course of the clinical investigation and any changes implemented, when appropriate as the investigation progresses. Covid-19 control procedures required by the local regulations at the time of the investigation conduct to be followed by investigation subjects will be documented in the Investigator Site File (ISF).

If required per local regulation, investigation subjects and their female partners will be provided with additional information about Covid-19 and any additional requirements in relation to their participation. This information will be provided to them in written and verbal format and they will be asked to sign that they have understood this additional information before proceeding with their involvement in the clinical investigation. Investigation subjects and their female partners will be reminded that they can discontinue participation and withdraw their informed consent at any time. In case of travel restrictions for subjects and their female partners brought about by Covid-19 or additional calamitous circumstances which may prevent them from completing their on-site investigation visits, alternative methods to ensure continuity of investigation conduct and subject follow-up may be implemented. Prior to implementation, these alternative methods will be submitted to relevant authorities and Independent Ethics Committee (IEC) / Research Ethics Committee (REC) / Institutional Review Board (IRB) for approval, where needed, and the information will be provided in the Informed Consent Form (ICF) signed by the subjects and their female partners.

The risk benefit analysis for this clinical investigation has been performed to consider the potential impact of Covid-19 on the safety and wellbeing of investigation subjects and on the potential for the clinical investigation to be conducted appropriately. Risk assessments will be revisited throughout the course of the investigation and input from the Investigator will be used to identify the current local risk to the investigation, subjects and those at the site.

Oversight of monitoring and onsite/remote monitoring procedures, taking into account Covid-19 will be captured within the clinical monitoring plan for the clinical investigation.

1.8 Ethical Conduct of the Investigation

This clinical investigation will be conducted in accordance with this CIP and the principles set out in the Declaration of Helsinki. It will comply with International Council for Harmonisation (ICH) Good Clinical Practice (GCP), ISO 14155:2020 and applicable regulatory requirements.

2 INVESTIGATION OBJECTIVES AND ENDPOINTS

2.1 Investigation Objectives and Endpoints

The investigation endpoints based on the investigation objectives are provided in Table 2.1.

Table 2.1 Investigation Objectives and Endpoints

Objectives	Endpoints
Primary Objective:	**Primary Endpoint:**
To determine the effectiveness of benzocaine, providing ancillary topical action to act as a male genital desensitiser and intended to delay male climax and prolonging the time to ejaculation, of the Test Condom A (5% benzocaine paste condom) compared with the Control NRL Condom (standard NRL condom) at prolonging time to ejaculation.	Change from baseline in Intravaginal Ejaculation Latency Time (IELT) with the Test Condom A compared to the Control NRL Condom, over a 4-week assessment period.
Secondary Objectives:	**Secondary Endpoints:**
• To determine the effectiveness of benzocaine, providing ancillary topical action to act as a male genital desensitiser and intended to delay male climax and prolonging the time to ejaculation, of the Test Condom B (3% benzocaine paste condom) compared with the Control NRL Condom at prolonging time to ejaculation	• Change from baseline in IELT with the Test Condom B compared to the Control Condom, over a 4-week assessment period.
• To determine the effectiveness of benzocaine, providing ancillary topical action to act as a male genital desensitiser and intended to delay male climax and prolonging the time to ejaculation, of the Test Condom A and Test Condom B compared with the Control NRL Condom at prolonging time	• Proportion of subjects who achieve an increase of 2 minutes from baseline in IELT in each of the Test Condom A and Test Condom B compared to the Control NRL Condom. • Proportion of subjects who achieve an increase of 3 minutes from baseline in IELT in each of the Test Condom A and Test

to ejaculation for an increase of 2, 3, and 4 minutes.	Condom B compared to the Control NRL Condom. • Proportion of subjects who achieve an increase of 4 minutes from baseline in IELT in each of the Test Condom A and Test Condom B compared to the Control NRL Condom.
• To evaluate the sexual pleasure when using the Test Condom A or Test Condom B compared with the Control NRL Condom.	• A measure of Event-level Male Sexual (EMSEX) pleasure scale at the end of a 4-week assessment period when using Test Condom A compared with the Control NRL Condom. • A measure of EMSEX pleasure scale at the end of a 4-week assessment period when using Test Condom B compared with the Control NRL Condom.
• To evaluate the subject's improvement at "lasting longer" for both the Test Condom A and Test Condom B compared with the Control NRL Condom.	• A measure of Patient Global Impression of Change (PGIC) at the end of each 4-week assessment period when using the Test Condom A compared with the Control NRL Condom. • A measure of PGIC at the end of each 4-week assessment period when using the Test Condom B compared with the Control NRL Condom.
• To evaluate the user acceptability of the Test Condom A, Test Condom B and Control NRL Condom.	User acceptability, experience and preference will be evaluated through subject perceived questions: • User acceptability, experience and preference asked at the end of a 4-week assessment period when using Test Condom A compared with the Control NRL Condom. • User acceptability, experience and preference asked at the end of a 4-week assessment period when using Test Condom B compared with the Control NRL Condom.

• To evaluate the in-use tolerability of the Test Condom A, Test Condom B and Control NRL Condom.	• The in-use tolerability of Test Condom A, Test Condom B and Control NRL condom, evaluated through subject perceived questions asked at the end of each 4-week assessment period.
• To evaluate the performance (slippage and breakage) of the Test Condom A, Test Condom B and Control NRL condom when used during vaginal intercourse.	• A measure of the total clinical failure rate of Test Condom A, Test Condom B and Control NRL condom.
• To assess the safety of the Test Condom A, Test Condom B and Control NRL Condom.	• Overall proportion of subjects with Adverse Events/ Adverse Device Effects (AEs/ ADEs), i.e. the occurrence of one or more AEs/ ADEs per subject.

2.2 Success Criteria

A statistically significantly greater increase in mean IELT of at least two minutes in the Test Condom A compared to the Control NRL Condom.

3 INVESTIGATIONDESIGN AND RATIONALE FOR DESIGN

3.1 Investigation Design

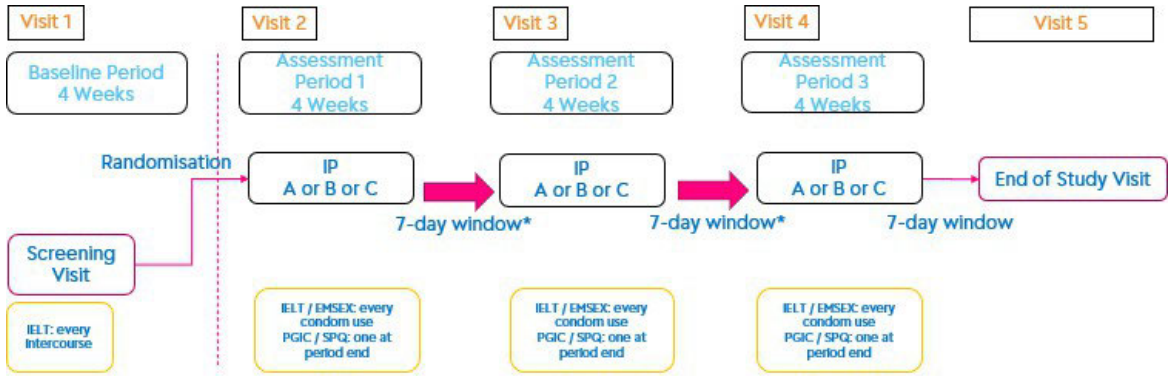
The investigation design is an open label, randomised, 3-way cross-over, single-centre clinical investigation evaluating the effectiveness of benzocaine in two NRL condoms in prolonging time to ejaculation compared with a standard NRL condom control in healthy male subjects who feel they ejaculate too quickly during vaginal sex.

The teat of Test Condom A and Test Condom B contains benzocaine so Test Condom A and Test Condom B are visually different from the Control NRL condom. As a result of the inherent appearance of these benzocaine condoms, subjects and their partners may notice a difference between condom types provided in each condom assessment period. The clinical investigation is therefore designed to be an open label investigation. To avoid data collection bias, each individual condom will be debranded and each set of condom types will be put in an identical box and tamper sealed. Subjects and the clinical site will not know the condom type from its primary pack and kit box. Only one condom type will be given to subjects for use in each assessment period so subjects will not be able to compare condom type side by side. The randomisation schedule will be kept only with Sponsor IMSU (Investigational Materials Supplies Unit), a CRO (Clinical Research Organisation) statistician, who is responsible for randomisation and is not involved in the analysis, and delegate site staff until database lock. Other Sponsor/CRO team members, subjects and their female partners, investigators and clinical site staff will not be provided the information of which condom type subjects have been randomised to receive.

Subjects will attend the clinical site on 5 occasions: one screening visit, three assessment period visits and one follow-up visit. Screening includes a 4-week baseline period, which allows the subject and his partner to familiarise themselves with the use of the stopwatch method and completing IELT diaries. Eligible subjects will return to the clinical site, where they will be randomised and receive the first of the three condom types (according to the randomisation schedule). Subjects will be provided with 8 condoms per condom type. The process will be repeated until all three condom types have been used. The follow-up visit will occur within 7 days after the completion of the final condom assessment period. At least a 3-day washout period, where no test condom will be used, is required before subjects attend the clinical site for visit 3 and visit 4. The 3-day washout period is to mitigate the effects on any residual benzocaine across condom types.

The investigation design is outlined in the schematic below (Figure 3-1).

Figure 3-1 Investigation Design Schematic



*A 3-day washout period is required before next visit.

3.2 Rationale for Investigation Design

The benzocaine test condoms will be compared with a standard NRL condom (as a control). Each condom type, benzocaine (5% and 3%) and the NRL condom will be debranded and will be provided to the subjects, in a randomised manner, to use over a 4-week period. Following use of the first condom type the subjects will then receive the second condom type, followed by the third condom type at their subsequent visit.

Measurement of the ejaculation latency time using the stopwatch method has been suggested as the most appropriate primary efficacy endpoint in PE interventional clinical trials (Waldinger et al., 2005; McMahon 2016). Change in IELT has been chosen as a primary outcome measure in order to evaluate the ancillary effectiveness of 5% benzocaine paste in delaying time to ejaculation in those men who ejaculate sooner than they would like. Secondary outcome measures include patient reported outcome measures to evaluate impact on sexual pleasure and sexual satisfaction, and patient global impression of change, in order to demonstrate the clinical benefit.

3.3 Determination of Sample Size

In a publication titled “A Multinational Population Survey of Intravaginal Ejaculation Latency Time (Waldinger et al., 2005)”, 500 couples were studied in a non-interventional setting over a 4-week period. The mean IELT was 8 minutes (SD = 7.1). Assuming this will be representative of the IELT of men using the standard NRL condom, and that the correlation between repeated measurements within the same subject in the 3 periods of the crossover trial will be 0.5, the table below shows the number of subjects required to detect a clinically meaningful difference of 2 minutes in mean IELT between the Test Condom A (5% Benzocaine paste) and the Control NRL Condom at 90% power, with a significance level of 5% using a two-sided paired t-test.

IELT (mins)		**Number of Subjects**	
Control NRL Condom	Test Condom A (5% Benzocaine paste)	Number to complete	Number randomised (10% drop out)
8	10	135	150

A sample size of 135 subjects will be sufficient to detect a difference of 2 minutes in mean IELT between the Test Condom A and the Control NRL Condom. Allowing for a dropout rate of 10%, 150 subjects will be randomised.

A 2 minute difference in IELT is considered clinically meaningful based on previous studies identified in the published literature. Shabsigh et al (2019) conducted a randomised controlled trial of topical 4% benzocaine wipes for the management of PE defined as self-reported poor control over ejaculation and an IELT of 2 minutes or less. Results showed a statistically significant increase in mean IELT of 164.80 (±11.40 SE) seconds after 1 month of treatment compared to placebo (110.10 s ±9.90 SE). The clinical benefit of a difference in IELT of 1 minute or larger compared to placebo is demonstrated via a patient reported outcome known as the Index of Premature Ejaculation (IPE) whereby the men in the treatment group reported significantly higher sexual satisfaction and greater improvement in distress related to intercourse. For the purposes of relevance to the target population, a larger 2-minute difference in IELT has been selected as the relevant effect for this clinical investigation based on the subjects being healthy adult men as opposed to only men with PE (IELT <2 minutes).

4 SELECTION AND WITHDRAWAL OF SUBJECTS

4.1 Investigation Population

A sufficient number of healthy male subjects will be recruited from the clinical site.

The expected duration of each subject’s participation is a maximum of 19 weeks (from screening to follow-up). There will be 1 clinical site in Germany participating in the clinical investigation.

4.2 Inclusion Criteria

Only male subjects to whom all of the following conditions apply will be included:

1) Subjects and their female partners have provided written informed consent.
2) Subjects and their female partners that can follow investigation instructions and complete the investigation assessments.
3) Subjects and their female partners between the ages of ≥18 years and ≤60 years.
4) Subjects and their female partners must have no health condition in their medical history that, in the opinion of the investigator, would be considered as clinically relevant.
5) Subjects that are circumcised or uncircumcised.
6) Subject must be sexually active having regular intercourse (frequency of at least four times over a four-week period with a minimum frequency of once a week and may comprise twice in one week to account for female partner's menstrual period break).
7) Subjects must agree to use the test condoms provided for vaginal intercourse only in this clinical investigation.
8) Subjects in a stable, monogamous, sexual relationship with the same female partner for more than or equal to 3 months, who plan to maintain their relationship for the duration of the clinical investigation.
9) Subject's female partner should already be on an established other highly effective form of non-barrier contraception, unless post-menopausal (confirmed menopausal prior to screening, amenorrhea for at least 12 months after cessation of exogenous hormone treatment). Highly effective non-barrier contraception includes: oral contraceptive (oestrogen and progestogen or progestogen-only hormonal contraception associated with inhibition of ovulation), intra-uterine device (IUD) or intra-uterine system (IUS), hormonal implant, injectables, patch and vaginal ring or sterilization of at least one partner (i.e. bilateral tubal ligation, vasectomy deemed medically successful).
10) Both the male subject and female partner must be willing to avoid situations or activities that may have an effect on their sexual activity.
11) Subjects and their female partners with no history of reduced sexual desire.
12) Subjects and their female partners must agree to use only the condoms and lubricant(s) provided for the clinical investigation during the three assessment periods.
13) Subjects reporting a frequency of 'occasionally' to the Sexual Intercourse Self-Estimation Scale.

4.3 Exclusion Criteria

Male subjects to whom any of the following conditions apply must be excluded:

1) Subject with a pregnant or breastfeeding female partner or the female partner desires to become pregnant during the clinical investigation (Female partners must have a negative pregnancy test as part of screening).
2) Subject, or his female partner have received an investigational (unapproved) drug within 30 days of screening.
3) Subject or his female partner with a current history of alcohol or drug abuse (self-reported) per local definitions of abuse.

4) Subjects and their female partners with a history of or are suffering from anemia, coronary artery disease, impaired cardiac conduction, pulmonary disease, diabetes, and renal or hepatic disease.
5) Subjects and their female partners with a history of, suspected to have, or be at increased risk of methaemoglobinemia / complications related to ester anaesthetics which could trigger methemoglobinemia.
6) Subject and/or his female partner have a physical or psychological condition that would prevent them from following investigation procedures - including but not limited to the following:
    a) Urological disease (e.g. prostatitis, urinary tract infection) or genitourinary surgery within 8 weeks of screening.
    b) Ongoing significant psychiatric disorder (e.g. bipolar disease, depression / anxiety disorder or schizophrenia) not controlled by medication.
    c) History of surgery or injury to the pelvis, retroperitoneal surgery, radiotherapy, multiple sclerosis, spinal cord injury, chronic inflammation of the prostate or urethra.
    d) Relevant (in the opinion of the Investigator) previous or planned genital surgery (i.e lazer for abnormal smear).
    e) A female partner that has been diagnosed with or treated for vaginal complaints (including vaginal dryness) in the previous 3 months which, in the opinion of the investigator, deems the partner unsuitable for the investigation.
    f) Any broken skin or wounds in the genital area.
7) Subject with a female partner that has a decreased interest in sexual intercourse or other forms of female sexual dysfunction.
8) Subjects on medication that is contraindicated, which may affect erection including but not limited to priapism caused by certain anti-hypertensives (Hydralazine, Prazosin, Guanethidine) and antidepressants (Trazodone, Thioridazine, Chlorpromazine) or topical medication which may damage the condom.
9) Subject and/or his female partner have any medication which may, in the opinion of the investigator affect the safety of the subject, including but not limited to benzocaine drug interactions such as cholinesterase inhibitors.
10) Subject and/or his female partner is using or intends to continue to use antibiotics of the sulphonamide type (examples include Gantrisin (sulfisoxazole), Bactrim or Septra (trimethoprim and sulfamethoxazole), Sulfadiazine, Azulfidine (sulfasalazine) and Zonegran (zonisamide) or cholinesterase inhibitors (examples include Aricept (donepezil), Razadyne ER (galantamine), and Exelon (rivastigmine)) from 7 days prior to screening and for the duration of the investigation.
11) Subjects with BMI >40kg/m^2.
12) Subject that has been diagnosed or received treatment for PE (premature ejaculation) caused by medical or surgical issues, e.g. anti-depressant therapy, local anaesthetic spray or has a history of confirmed diagnosis of PE.

13) Subjects with confirmed erectile dysfunction, hypo or hyperthyroidism, hypogonadism, hyperprolactinemia.
14) Confirmed diagnosis of male subjects with other forms of ejaculatory dysfunction e.g. retrograde ejaculation, anejaculation, painful ejaculation.
15) Subjects that have had prior genital, prostatic or lower tract surgery (other than vasectomy or circumcision).
16) Subjects with haemorrhagic disorder, hepatitis B or C, HIV infection or having had penile implant surgery, at any time in their past.
17) Any condition that the male and/ or the female sexual partner may have that, in the opinion of the investigator, may compromise the data generated, put the subject at risk or may interfere significantly with the subject's ability to participate in the clinical investigation.
18) Subjects or their female partners who have any relevant history of untreated sexually transmitted disease (STD) which from the investigator opinion may jeopardise subjects' safety.
19) Either partner needed to use condoms for a specific STI protection e.g. discordance for HIV or herpes.
20) Subjects and their female partners who have any relevant history of allergy including local anaesthetics, parabens, PABA (Para-aminobenzoic Acid), commercial hair dyes, paraphenylenediamine, lubricants and latex.
21) Subjects and their female partners who are an employee of the Investigator's department at the site or a partner or first-degree relative of the Investigator.
22) Subjects and their female partners fail to satisfy the investigator of fitness to participate for any other reason.

4.4 Investigation Restrictions

4.4.1 General Restrictions

General investigation restrictions for subjects and female partners are listed in Table 4-1 below:

Table 4-1 General Restrictions

Restriction	From	To	Applicable to male subjects	Applicable to female partners
Enrolment into another clinical investigation/ study once participating in this clinical investigation	30 days prior to Screening	Follow-up	Yes	Yes

Restriction	From	To	Applicable to male subjects	Applicable to female partners
Use of anaesthetic medication	3 days prior to Screening	Follow-up	Yes	Yes
Use of antibiotics of the sulphonamide type (examples include Gantrisin (sulfisoxazole), Bactrim or Septra (trimethoprim and sulfamethoxazole), Sulfadiazine, Azulfidine (sulfasalazine) and Zonegran (zonisamide) or cholinesterase inhibitors (examples include Aricept (donepezil), Razadyne ER (galantamine), and Exelon (rivastigmine))	7 days prior to Screening	Follow-up	Yes	Yes
Unprotected sexual intercourse	Screening	Follow-up	Yes	Yes
Use of anti-hypertensives or antidepressants or any medication which affects erection	Screening	Follow-up	Yes	No
Use of topical medication in the intimate area	Screening	Follow-up	Yes	Yes
A change of partner	Screening	Follow-up	Yes	Yes
Use of sexual performance enhancer	Screening	Follow-up	Yes	Yes

All non-compliance will be recorded as a deviation.

If the Investigator (or delegate) becomes aware of an investigation restriction being contravened by a subject and/or his female partner, this will be recorded. An assessment will be made and recorded by the Investigator to determine whether this affects their safety or data integrity, and whether the subject may continue participating in the investigation.

4.5 Discontinuation / Withdrawal and Replacement of Subjects

The Investigator may withdraw the subject from the clinical investigation at any time. Reasons for removing a subject from the clinical investigation include, but are not limited to:

- AEs/ADEs that in the judgement of the Investigator may cause severe or permanent harm (significant clinical deterioration is a Serious Adverse Event (SAE)/ Serious Adverse Device Effect (SADE)).
- Violation of the CIP, which in the judgement of the Investigator affects subject's/female partner's safety or data integrity.
- In the Investigator's judgement, it is in the subject's/female partner's best interest (this includes inadequate device performance).
- Subject and/or female partner declines further clinical investigation participation.

The primary reason for withdrawal will be documented in the electronic Case Report Form (eCRF).

If a subject or his female partner chooses to prematurely stop the clinical investigation at least 2 documented attempts should be made to contact the subjects for follow-up assessments which will include assessments as described for the follow-up visit (Section 7.5).

In the event of any abnormalities (e.g. STI) considered to be clinically significant, subjects and/or their female partners will be followed up with appropriate medical management. Referral or collaborative care will be organised if considered necessary.

150 subjects will be randomised into the clinical investigation. Subjects withdrawn from the clinical investigation before receiving any IP will be replaced (i.e. prior to randomisation).

5 INVESTIGATION TREATMENT

5.1 Medical Device

The IPs to be used for this clinical investigation are listed in Table 5-1 below. All the IPs are made of NRL.

Table 5-1 The Condom key Dimensions

Condom Type	[redacted]					
Test Condom A	[redacted]					
Test Condom B	[redacted]					
Control NRL Condom	[redacted]					

[redacted]

5.2 Non-Investigational Product (NIP)

5.2.1 Lubricant

Lubricant is applied to the Test Condom A and B and Control NRL Condom before packaging. However, some subjects may desire additional lubrication, in which case Durex Real Feel Silicone Based Lube (50 ml) will be supplied. This is a silicone oil-based lubricant, which is compatible with NRL condoms.

[redacted]

5.2.2 Stopwatch

Stopwatches for measuring IELT will be supplied and shipped directly from IMSU to the clinical site.

5.3 Concomitant Therapies

Any treatment considered necessary for subject's and their female partner's welfare may be administered and / or continued under the supervision of the Investigator.

Concomitant therapy, including prescription and non-prescription over-the-counter drugs, including vitamins, herbal and dietary supplements medication and non-pharmacological treatments such as physiotherapy, will be captured in the concomitant therapies page of the eCRF from the date of informed consent for subjects and their female partners. Any changes in concomitant therapy during the clinical investigation will be documented, including cessation of therapy, initiation of therapy and dose changes. The Investigator will record the AE for which the concomitant therapy was administered in the eCRF.

5.4 Packaging and Labelling and Supply / Resupply

A kit per subject will be assembled by the IMSU. Each kit will contain three cartons: one carton containing 8 of the Test Condom A, one carton containing 8 of the Test Condom B, and one carton containing 8 of the Control NRL Condom. Each condom will be individually foil wrapped in plain packaging (debranded). In addition to the kits, the clinical site will be supplied with a bulk supply of

debranded lubricant to be provided to subjects that routinely use/desire to use lubricant during coitus.

The kits, cartons, individual condoms, lubricants and stopwatches will be labelled in accordance with directive 2003/94/EC as amended, BS EN ISO 15223-1:2021 – Medical Device and including any other applicable national / state legislation or standards. The IPs and NIPs will be labelled with German text.

5.5 Storage Conditions

Kits, condoms and lubricants should be kept in a cool, dry place away from direct sunlight at a temperature not above 30°C. At the clinical site all investigational supplies should be kept in a secure area with restricted access. The correct storage conditions will be monitored and recorded weekly. Any excursions from the correct conditions should immediately be reported to the Sponsor.

5.6 Debranding

Each condom will be contained within an individual foil packet on which all branding has been covered. All the condom types will be debranded in the same manner and identical boxes will be used for the Test Condom A and B and Control NRL Condom.

To avoid data collection bias, the access to the randomisation schedule will be kept only with Sponsor IMSU, a CRO statistician, who is responsible for randomisation and is not involved in the analysis, and delegate site staff until database lock. Other Sponsor/CRO team members, subjects and their female partners, investigators and clinical site staff will not be provided the information of which condom type subjects have been randomised to receive.

5.7 Emergency Unblinding Procedures

The emergency unblinding procedures are not applicable as it is an open label investigation. Because the Investigator is not informed of test product allocation, upon request and according to the CRO standard operating procedures (SOPs) or a working instruction, the randomisation code can be provided to the Investigator for a subject in an emergency such as SAE/ SADE that requires knowledge of which condom was used so that the SAE/ SADE can be treated appropriately. If the code for a subject is given to the Investigator during the investigation, the Investigator must document the details of the event and promptly inform the Sponsor.

5.8 Accountability of Medical Device

The Investigator will keep all of the investigation supplies in a secure storage facility, accessible to those individuals authorised by the Investigator to dispense the condoms.

Upon completion of the condom assessment period, subjects will be required to return their unused condoms to the clinical site at their next visit.

The Investigator (or delegate) will maintain an inventory using kit numbers as a reference. This will include the description and quantity of kits received during the course of the clinical investigation, as well as the record of materials that are dispensed and returned (i.e. how much, to whom and

when). This inventory will be subject to review by the clinical investigation monitor during monitoring visits.

5.9 Return and Destruction

The Investigator (or delegate) will conduct a full IP/NIP supply reconciliation and will record the results of this reconciliation. Following review of this reconciliation documentation the CRO will arrange for the return of all unused Test Condom A, Test Condom B, Control NRL Control, used/unused lubricants and all supplied stopwatches to the Sponsor. Condoms and lubricants will be destroyed at the end of the clinical investigation (upon finalisation of the Clinical Investigational Report) by the Sponsor. Sponsor reconciliation will be completed to confirm destruction. Details will be documented in an IP handling Manual.

6 INVESTIGATION PROCEDURES BY VARIABLE

6.1 Informed Consent

Prior to conducting any investigation-related activities, written informed consent must be obtained from the subject and his female partner. No subject can enter the clinical investigation before informed consent of the subject and his female partner has been obtained. Upon signing the ICF by the subject and his female partner, the subject is enrolled into the clinical investigation.

All subjects and their female partners will be provided with oral and written information describing the nature and duration of the clinical investigation and the procedures to be performed. Sufficient time needs to be given to the subject and his female partner to review all information provided, ask questions for clarification of clinical site staff and decide whether to participate or not. The Investigator must explain to each subject and his female partner the nature of the clinical investigation, its purpose, the procedures involved, the expected duration, the potential risks and benefits involved, and any potential discomfort. Each subject and his female partner must be informed that participation in the clinical investigation is voluntary and that he / she may withdraw from the clinical investigation at any time and that withdrawal of consent will not affect his / her subsequent medical treatment or relationship with the treating physician. The subject and his female partner must be informed that their medical records may be examined by authorised individuals other than their treating physician.

The subject and his female partner should understand the information provided before signing and dating the ICF. The Investigator or person obtaining consent must also sign and date the form. Each subject and his female partner will be given a copy of the signed informed consent and written information.

The original signed ICF for each subject and his female partner will be verified by the monitor and kept in the clinical site ISF.

If new information should become available during the investigation of which subjects and their female partners need to be aware, an updated ICF will be provided and the above process will be followed to confirm subjects and their female partners are happy to continue with the clinical

investigation. For subjects who have completed the clinical investigation, the Investigator will decide if this new information needs to be provided to them.

6.2 Randomisation

Subjects will be allocated to a condom use regime (one of six treatment sequences in a fixed block size) according to a computer-generated randomisation schedule produced by the CRO.

A randomisation schedule will be generated for 204 kits to account for dropouts, overage, replacement and additional randomisation codes for IMSU retention samples (which will be retained at Reckitt).

Randomised subjects will be numbered sequentially.

6.3 Administration of Medical Device

Subjects will not be given the full condom kit to take away with them. Following randomisation each subject will be given one of the condom cartons from their kit (as per randomisation schedule). This will contain 8 condoms. Each condom must be used for penile-vaginal intercourse only. To mitigate double exposure to benzocaine, subjects will be instructed to use one investigational condom for each coital act. Each coital act must be at least 24 hours apart. During this 24-hour interval, subjects and their female partners will be instructed to refrain from any sexual activity including masturbation. In the situation of condom breakage or condom slippage, subjects may continue to have intercourse without the investigational condom only if they believe they are not at risk of an STI or pregnancy.

On return to the clinical site for the subsequent visit, subjects should return all unused condoms. They will then be given the second condom carton from their kit according to the randomisation schedule, containing 8 condoms of the second condom type to be used during the second condom assessment period (4 weeks). This is to be repeated for subjects to complete use of their third condom type.

Subjects will be trained in the use and handling of the condoms (verbally and written format). Subjects will be instructed to record IELT, the duration from the start of vaginal entry (vaginal penetration into the female partner) till the start of intravaginal ejaculation (release of semen), for each condom used.

During the clinical investigation, subjects are permitted to use lubricant if needed. Subjects should make the clinical site aware of this through questioning by the clinical site staff. Any use of lubricant will be recorded in the IELT diary.

6.4 Demographics

Baseline characteristics and demographic information will be recorded. This will include:

1. For male subjects and their female partners:
    - Sex
    - Age
2. For male subjects only:

- Ethnicity
- Height (in metres to the nearest cm)
- Weight (kg to the nearest 0.1 kg; in indoor clothing and without shoes).

BMI will be calculated as follows: Body weight (kg)/ [Height (m)]^2.

6.5 Medical History and Prior Therapies

Details of all relevant current and historical medical diseases, conditions or surgeries, including duration, will be recorded for subjects and their female partners. All prior therapies such as prescription or non-prescription drugs, including vitamins, herbal and dietary supplements and non-pharmacological treatments such as physiotherapy will also be recorded. Medical history for all prior therapies should be recorded, regardless of being relevant. In addition, the contraception method will also be recorded.

6.6 Physical Examination

For male subjects, a complete physical examination, including a penile examination, will be performed by the Investigator or a medically qualified delegate (e.g. Principal Investigator/ Co-Investigator). The Investigator or delegate may conduct physical examination of female partners in any case of AE/ ADE or in the opinion of the Investigator.

The examination will include at least general appearance, skin/ subcutaneous tissue, ears/ eyes/ nose/ mouth/ throat, head/ neck, respiratory/ chest, cardiovascular, gastrointestinal, musculoskeletal, neurological, lymph nodes and penile examination. Other body systems can be examined if required, at the discretion of the Investigator or delegate. The Investigator or delegate will provide an interpretation of the results. Clinically significant abnormalities will be recorded on the medical history at screening or AE/ ADE page of the eCRF.

6.7 Vital Signs

For male subjects, vital signs will be measured after the subject has been seated for approximate 5 minutes and include the following:

- Blood pressure (systolic and diastolic; mmHg)
- Heart rate (radial pulse counted for 30 seconds; beats/ minute)
- Oral or tympanic body temperature (ºC)

The Investigator or delegate will provide an interpretation of the results. Clinically significant abnormalities will be recorded on the AE/ ADE page of the eCRF.

6.8 Pregnancy Test

Urine samples for pregnancy testing (for subject's female partner of childbearing potential only) will be collected and prepared according to the test kit instructions.

6.9 Sexual Intercourse Self-Estimation Scale

Subjects will be asked to verbally rate the scale. The question and the scale are:

Thinking of any sexual intercourse you have had over the past 12-months, how often do you feel intercourse ended early due to earlier than desired ejaculation?

- 1 = Never
- 2 = Occasionally (now and then/irregularly)
- 3 = Frequently (often/regularly)
- 4 = Every time

Subjects that rate a score of 2 (Occasionally) would meet the inclusion criterion. Anyone who selects the score of 1 (Never), 3 (Frequently) or 4 (Every time) would not meet the inclusion criterion of the investigation. Those who answer 3 (Frequently) or 4 (Every Time) will be advised to seek opinion from his healthcare provider as there may be a missed diagnosis of PE.

6.10 Diary and Questionnaires

6.10.1 Intravaginal Ejaculation Latency Time (IELT) Diary

Each subject will be asked to complete an IELT diary to record the IELT duration record for each condom use within 2 hours after each coital act (per condom type). Subjects will also be instructed to record condom failure (breakage or slippage) and any use of lubricant in the diary.

6.10.2 EMSEX Pleasure Scale

Each subject will be asked to complete an EMSEX pleasure scale for each condom use within 2 hours after each coital act (per condom type). EMSEX pleasure scale is a 11-item scale which assesses sexual pleasure at the event level (Aaron et al, 2018). For each item, the range spans the entirety of the potential range from 0 (zero) to 100 (one hundred).

6.10.3 Patient Global Impression of Change (PGIC)

Upon completion of each condom assessment period, each subject will be required to complete a PGIC. PGIC is a patient-reported scale which assesses the subject's perception of improvement in terms of 'lasting longer' since using the condoms (Althof et al, 2010). The PGIC is a 7-point response scale (Very much better, Better, Little better, No change, Little worse, Worse, Very much worse) to ask subjects how they describe the change in their ejaculation time in each assessment period.

6.10.4 Subject Perceived Questionnaire (SPQ)

Upon completion of each condom assessment period, each subject will be required to complete a SPQ. The questionnaire will collect the following information (including, but not limited to): experience with condom use, acceptability, preference and tolerability.

6.11 Adverse Events

During visits to the clinical site non-leading questions will be used to collect any AEs/ ADEs. In addition, spontaneously reported AEs/ ADEs will be collected.

The observation period for an individual subject and his female partner will start after giving informed consent and will finish at the last visit (follow-up visit). All AEs/ ADEs that arise during the observation period will be recorded and an assessment of the AEs/ ADEs will be performed as per Section 8.2 by a medically qualified Investigator. If a subject or his female partner has an AE/ ADE that is still ongoing at the last visit, an attempt will be made by the Investigator to follow this up as per Section 8.4.

If an untoward medical occurrence happens after the subject has signed the consent form but before administration of the device, it should be reported as an AE, including those associated with investigation procedures.

7 INVESTIGATION PROCEDURES BY VISIT

7.1 Investigation Flow Chart / Table of Investigation Procedures and Assessments

Table 7-1 Schedule of Assessment

Visit	Visit 1	Visit 2	Visit 3 & 4	Visit 5
Period	Screening Baseline Period	Assessment Period 1	Assessment Period 2 & 3	Follow-up
Procedure / Day	Within 28 days prior to Day 1	Day 1	Within 7 days after each condom assessment period	Within 7 days after 3rd condom assessment period
Informed consent	X			
Inclusion / Exclusion[1]	X	X	X	
Demographics	X			
Medical history & prior therapies	X			
Concomitant medication	X	X[9]	X[9]	X[9]
Vital signs	X			X
Physical examination[2]	X	X	X	X
Pregnancy test[3] (subject's female partner)	X	X	X	X
Randomisation		X		

Visit	Visit 1	Visit 2	Visit 3 & 4	Visit 5
Period	Screening Baseline Period	Assessment Period 1	Assessment Period 2 & 3	Follow-up
Day / Procedure	Within 28 days prior to Day 1	Day 1	Within 7 days after each condom assessment period	Within 7 days after 3rd condom assessment period
Provide investigation stopwatch	X			
Dispense Investigational Product[4]		X	X	
Collect returned Investigational Product[5]			X	X
Collect returned investigation stopwatch				X
Stopwatch measure and condom use training[6]	X	X	X	
Provide IELT diary, EMSEX pleasure scale, PGIC and SPQ	X[7]	X	X	
Completion of IELT diary	X	X	X	
Completion of EMSEX pleasure scale, PGIC[8] and SPQ[8]		X	X	X
Review for extent of completion of diary and questionnaires		X[7]	X	X
Adverse Events & Adverse Device Effects and Device Deficiencies	X[9]	X[10]	X[10]	X[10]

1. Eligibility will be confirmed at visit 1 as part of the screening visit. Continued eligibility will be confirmed at each assessment visit (visit 2, 3 and 4).
2. At visit 1, subjects will undergo a penile examination as part of the physical examination. At visit 2, 3, 4 and 5 (assessment period visits and follow-up visit) these will only be performed if necessary in the opinion of the Investigator. The Investigator may conduct physical examination of female partners in any case of AE/ ADE or in the opinion of the Investigator.

3. Subject's female partner of childbearing potential must have a negative pregnancy test at Screening. In cases where subjects have experienced a condom breakage or slippage, their female partner may be subject to a pregnancy test, if deemed necessary by the investigator.
4. Subjects will be provided their allocated condoms (condom type in accordance with the randomisation schedule) at visits 2, 3 and 4. Lubricant will also be supplied, if requested by subjects.
5. Any unused condoms will be returned to the clinical site on visits 3, 4 and 5. All used and unused lubricant will be returned to the clinical site on visit 5.
6. At visit 1, subjects and their female partners will be trained on the stopwatch process and the correct use of the condoms. At visit 2, 3 and 4 (assessment period visits) the training will only be performed if necessary in the opinion of the Investigator.
7. IELT Diary only.
8. PGIC and SPQ can be completed at home or at the next visit.
9. Excludes ADEs and Device Deficiencies.
10. In additional to male subjects' data collection, concomitant medication and AE/ ADE of female partners will be collected through spontaneous reporting or in response to non-leading question to the subject on visit 2, 3, 4 and 5 or observation by the Investigator.

7.2 Visit 1: Screening Visit and Baseline Period

At the screening visit, which will be carried out within 28 days prior to subjects receiving their first condom type, subjects and their female partners will be asked to provide written informed consent (separately) for the participation in the clinical investigation.

Once informed consent has been obtained, the subjects will be issued a screening number. Clinical assessments consisting of demographics, medical history, prior therapies, vital signs recording, physical examination, concomitant medication, AEs will be carried out for each subject. Medical history, prior therapies, concomitant medication and AEs for the female partners will be assessed as well as urine pregnancy test for women of childbearing potential.

Clinical site staff will explain to each subject and his female partner the stopwatch process and how to measure the IELT i.e. that the duration of the IELT is calculated from time of vaginal entry (vaginal penetration into the female partner) until the start of intravaginal ejaculation (release of semen) and is timed on the stopwatch by 'start' (penetration) to 'stop' (ejaculation) and to record in the IELT diary. It will be made clear by the clinical site staff that either partner can be responsible for using the stopwatch as long as it's the same person each time. They will also be requested to note the date and time of the act in the IELT diary. An investigation stopwatch together with the training on stopwatch measures will be provided to ensure there is an understanding of when to 'click' the stopwatch and that the subjects or their female partner are capable of accurate measurements. Training (verbally and written format) in the correct use of the condoms will also be provided. Subjects and their female partners will be informed that should they experience a condom failure, including breakage and slippage, and believe that they are at risk of pregnancy, they should contact the clinical site where they will be provided with access to emergency contraception and the appropriate follow-up (if necessary). If either partner believes they may have contracted an STI they should contact the clinical site where appropriate measures, and follow-up will be taken.

Subjects will be trained by the clinical site staff on how to complete IELT diary, EMSEX pleasure scale, PGIC and SPQ.

Subjects and their female partners are required to confirm they are using an acceptable method of contraception as listed in inclusion criteria 9 and the contraception method will be entered into each subject's eCRF. Subjects and their female partners will return home to begin the baseline period.

Subjects will be instructed to complete an IELT diary within 2 hours after each coital act and to report a minimum of 4 IELT duration records over the 4-week baseline period. Each coital act must be at least 24 hours apart. During this 24-hour interval, subjects and their female partners will be instructed to refrain from any sexual activity including masturbation.

During the baseline period, subjects and their female partners will be protected from pregnancy by means of their second form of contraception. If the subject or his female partner feels there is at risk of a STI or there is any safety concern, they will be instructed to use commercial condom as well as commercial lubricant if desired for an intercourse. The commercial condom and commercial lubricant, which are not provided by the clinical site, should be non-medicated and should not have any performance enhancing functionality. The use of condom and lubricant will be reported by the subject in the IELT diary.

The female partners will be instructed that they can contact the clinical site to report an AE/ ADE or to discuss any concern during their participation in this clinical investigation.

All assessments conducted during the screening visit are detailed in Section 6 and summarised in Table 7-1. All clinical assessments and test results will be entered into each subject's eCRF.

7.3 Visit 2: Assessment Period 1

Subjects who fulfil all the eligibility criteria and have reported a minimum of 4 IELT duration records will return to the clinical site for assessment period 1. Clinical assessments consisting of a physical examination (if necessary in the opinion of the investigator) will be carried out.

Following confirmation of continued eligibility, subjects will be randomised as to which condom type they will receive first. Subjects will be assigned a randomisation number. Subjects will be given a carton containing their allocated condom type for use, with the second and third carton remaining in the kit at the clinical site. Lubricant will be made available to subjects who routinely use lubricant during intercourse or if requested.

The Investigator or delegate will examine the diaries for completeness. Training on stopwatch measure, the correct use of the condoms and the clinical investigation requirements will be provided if necessary in the opinion of the Investigator. Subjects will be reminded to complete an IELT diary and EMSEX pleasure scale with 2 hours after each coital act and to report a minimum of 4 IELT duration records within a maximum 4-week period (known as the condom assessment period). Each coital act must be at least 24 hours apart. During this 24hour interval subjects will be instructed to refrain from any sexual activity including masturbation. For all used condoms, subjects will be instructed to dispose them into a bin.

Subjects will also be instructed to complete a PGIC and a SPQ at the end of each condom assessment period. PGIC and SPQ can be completed at home or at next visit. Subjects will be reminded that should he and his female partner experience a condom failure and believe that they are at risk of pregnancy, they should contact the clinical site where they will be provided with access to emergency contraception and the appropriate follow-up (if necessary). If either partner believes they may have contracted an STI they should contact the clinical site where appropriate measures, and follow-up will be taken. If necessary, in the opinion of the investigator, the female partner will

attend the clinical site and a urine pregnancy test will be carried out. In between condom assessment periods, subjects and their female partners will be protected from pregnancy by means of their second form of contraception.

All assessments conducted during assessment period 1 are detailed in Section 6 and summarised in Table 7-1. All clinical assessments and test results will be entered into the subject's eCRF.

7.4 Visit 3 and 4: Assessment Period 2 and 3

Visits 3 and 4 will be conducted within 7 days after the completion of each condom assessment period weeks (or earlier if the subject has reported a minimum of 4 IELT duration records). A 3-day washout period, where no test condom will be used, is required before subjects attend the clinical site to return unused condoms and be supplied with their subsequent condom type. During the 3-day washout period, coital act is allowed with a 24 hour gap maintained between the last coital act or masturbation and the visit to the clinical site. Procedures and assessments will be the same as those performed in assessment period 1, except for randomisation, which is performed at Visit 2 only.

Subjects will be required to return all unused condoms of the first and second condom type (respectively). Following confirmation of continued eligibility, subjects will be provided with the alternative condom type from the kit to be used for the subsequent condom assessment period. Additional supply of lubricant will also be provided if required and the empty lubricant bottle/tube should be returned.

In the opinion of the Investigator, a subject who fails to remain eligible for the clinical investigation will be withdrawn.

The Investigator or delegate will examine diaries and questionnaires for completeness. Training and instruction on diary and questionnaire completion and safety reminder will be repeated as Visit 2.

All assessments conducted during assessment period 2 and 3 are detailed in Section 6 and summarised in Table 7-1. All clinical assessments and test results will be entered into the subject's eCRF.

7.5 Visit 5: Follow-up Visit

The follow-up visit will be conducted within 7 days after the completion of the third condom assessment period (or earlier if the subject has reported a minimum of 4 IELT duration records) or within 7 days in the event of a subject's withdrawal from the clinical investigation. Clinical assessments consisting of a physical examination (if necessary in the opinion of the investigator), vital signs recording, concomitant medication, AEs/ ADEs review will be carried out.

Subjects are to return all unused condoms, used/unused lubricant(s) (if supplied) and the investigation stopwatch. The Investigator or delegate will examine diaries and questionnaires for completeness. All assessments conducted during follow-up visit are detailed in Section 6 and summarised in Table 7-1. All clinical assessments and test results will be entered into each subject's eCRF.

7.6 Unscheduled Visits

If unscheduled visits occur, the Investigator must record the reason for unscheduled visit in the subject's eCRF, including any AEs/ ADEs that the subject and his female partner have experienced since the subject's last visit, concomitant therapy changes, withdrawal (if deemed appropriate) and any clinical assessments deemed appropriate for the clinical care of the subject and/or his female partner.

Unscheduled visits should not alter the timing of the routine investigation schedule.

8 SAFETY REPORTING

The assessment and reporting of AEs in the investigation are in compliance with the Regulation (EU) 2017/745, the guidance of MDCG 2020-10/1 and guidelines on medical devices, MEDDEV 2.7/3 revision 3, May 2015.

8.1 Adverse Event Definitions

Adverse Event

An Adverse Event (AE) is any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational medical device.

This definition includes events that are anticipated as well as unanticipated events.

This definition includes events occurring in the context of a clinical investigation related to the investigational device, the comparator or the procedures involved.

Adverse Device Effect

An Adverse Device Effect (ADE) is an AE related to the use of an investigational device.

This includes any AE resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, operation, or any malfunction of the investigational medical device. This includes any event that is a result of a use error or intentional misuse.

Device Deficiency

Any inadequacy in the identity, quality, durability, reliability, safety or performance of an investigational device, including malfunction, use errors or inadequacy in information supplied by the manufacturer.

Serious Adverse Event

A Serious Adverse Event (SAE) is an AE that led to any of the following:

a. Death,
b. Serious deterioration in health of the subject, that resulted in any of the following:
    - a life-threatening illness or injury,
    - a permanent impairment of a body structure or a body function,

- hospitalisation or prolongation of patient hospitalisation,
- medical or surgical intervention to prevent life threatening illness or injury of permanent impairment to a body structure or a body function,
- chronic disease,

c. foetal distress, foetal death or a congenital physical or mental impairment or birth defect.

A planned hospitalisation for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered to be an SAE.

This includes device deficiencies that might have led to a SAE if

a. suitable action had not been taken or

b. intervention had not been made or

c. if circumstances had been less fortunate.

Serious Adverse Device Effect

A Serious Adverse Device Effect (SADE) is an ADE that has resulted in any of the consequences characteristic of a SAE.

Unanticipated Serious Adverse Device Effect

An Unanticipated Serious Adverse Device Effect (USADE) is an effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment.

Anticipated Serious Adverse Device Effect

Anticipated SADE (ASADE): an effect which by its nature, incidence, severity or outcome has been previously identified in the current risk assessment.

8.2 Assessment of Adverse Events

All AEs that arise after the subject and his female partner have given informed consent will be recorded in the subject's source documents and CRF. AEs can be reported spontaneously by the subject/his female partner or in response to non-leading questioning, observation by the Investigator or be a significant laboratory abnormality.

All AEs, ADEs, SAEs, SADEs and USADEs are collected, fully investigated and documented.

SAE / SADE / USADEs should be followed until resolution or stabilisation. Subjects and their female partners with ongoing SAE / SADE / USADEs at investigation termination will be further followed up until recovery or until stabilisation of the disease after termination.

For each AE a causality assessment of the event to the investigational device, the comparator or the investigation procedure must be performed. The relationship to the investigational device, the comparator or the investigation procedure must be determined by the Investigator (if medically qualified) or by a medically qualified Co-Investigator.

Relationship	Description
Not related	Relationship to the investigational device, comparator or procedures can be excluded when: ▪ the event has no temporal relationship with the use of the investigational device or the procedures related to application of the investigational device. ▪ the serious adverse event does not follow a known response pattern to the investigational device (if the response pattern is previously known) and is biologically implausible. ▪ the discontinuation of investigational device application or the reduction of the level of activation / exposure - when clinically feasible - and reintroduction of its use (or increase of the level of activation / exposure), do not impact on the serious adverse event. ▪ the event involves a body-site or an organ that cannot be affected by the device or procedure. ▪ the serious adverse event can be attributed to another cause (e.g. an underlying or concurrent illness / clinical condition, an effect of another device, drug, treatment or other risk factors). ▪ the event does not depend on a false result given by the investigational device used for diagnosis, when applicable. In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device / procedures and the serious adverse event.
Possible	The relationship with the use of the investigational device or comparator or the relationship with procedures is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness / clinical condition or / and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.
Probable	The relationship with the use of the investigational device or comparator or the relationship with procedures seems relevant and / or the event cannot reasonably explained by another cause.
Causal Relationship	The serious adverse event is associated with the investigational device, comparator or with procedures beyond reasonable doubt when: ▪ the event is a known side effect of the product category the device belongs to or of similar devices and procedures.

	▪ the event has a temporal relationship with investigational device use / application or procedures. ▪ the event involves a body-site or organ that: o the investigational device or procedures are applied to o the investigational device or procedures have an effect on ▪ the serious adverse event follows a known response pattern to the medical device (if the response pattern is previously known). ▪ the discontinuation of medical device application (or reduction of the level of activation / exposure) and reintroduction of its use (or increase of the level of activation / exposure), impact on the serious adverse event (when clinically feasible). ▪ other possible causes (e.g. an underlying or concurrent illness / clinical condition or / and an effect of another device, drug or treatment) have been adequately ruled out. ▪ harm to the subject is due to error in use. ▪ the event depends on a false result given by the investigational device used for diagnosis, when applicable. In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device / procedures and the serious adverse event.

For each AE a severity description should be given.

Severity	Description
Mild	The event is easily tolerated and does not limit everyday activities; the subject may experience slight discomfort.
Moderate	The event is sufficiently discomforting to interfere with everyday activities.
Severe	The event prevents normal everyday activities; the subject may experience intolerable discomfort or pain.

Expectedness for each AE will be determined based on the information in section 6 of the Investigator's Brochure.

Coding of AEs and medical history will be done using Medical Dictionary for Regulatory Activities (MedDRA) 26.0, or the most recent version if this has changed. If there is an update to MedDRA during the course of the investigation the most recent version will be used by <insert vendor name>. Concomitant medications are coded by the CRO using the WHO dictionary (including ATC coding).

8.3 Reporting of Adverse Events

In the event of an SAE, SADE, USADE or device deficiency that could have led to an SAE, the Investigator must report the event using the appropriate form to the Sponsor Adverse Event Management Team (AEMT) by email: [redacted] including in the email vendor and Sponsor Study Managers within 24 hours of knowledge of the event.

The out of hours emergency phone number is [redacted] if consultation is required by the Investigator.

This emergency phone number will be confirmed to the Investigator at the Investigation Initiation Visit.

All forms of SAE / SADE / USADE and Device Deficiency that could have led to a SAE/ SADE/ USADE must be provided via email. Any inconsistencies in the information received from the Investigator will be clarified on an updated SAE / SADE form. The Investigator must retain a copy of all the forms in the Investigator Site File.

The Investigator, if required by regulations, must inform their local Independent Ethics Committee (IEC) / Research Ethics Committee (REC) / Institutional Review Board (IRB) of all SAE / SADE / USADEs and reportable Device Deficiencies occurring in the investigation as per Sponsor instructions as described in the Safety Management Plan.

SAE / SADE / USADEs, Device Deficiencies and non-serious AE / ADEs will be reported to the appropriate regulatory authorities by the Sponsor in accordance with the authorities' requirements. The Sponsor is responsible for expedited reporting of all SAE / SADE / USADEs and reportable Device Deficiencies to relevant authorities and IECs / IRBs as required by regulations. If the event requires expedited reporting, AEMT will take actions as per the investigation specific Safety Management Plan.

Reporting timelines for reporting USADEs / SAE / SADE / Device Deficiencies that could have led to a SAE/ SADE/ USADE to the Competent Authority (CA) is:

- immediately or within 2 calendar days from initial receipt for reportable events or of new information in relation with an already reported event which indicate imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/subjects, users or other persons or a new finding to it.
- Any other reportable events, reporting timeline is immediately, but not later than 7 calendar days following the date of awareness by the sponsor of the new reportable event or of new information in relation with an already reported event.

If a reportable USADE / SAE / SADE / Device Deficiency occurs, AEMT will use the USADE Reporting Contact List for details of who and where to send details to the country where this is the case is Germany. The AEMT will provide the completed Manufacturer Incident Report (MIR) form to the Drug Safety Officer (DSO) who will complete the German SAE Report form in English, based on the information provided in the MIR, and send to the Competent Authority via email.

Reporting timelines for reporting SADE / Device Deficiencies that could have led to a SAE/ SADE/ USADE to the Notified Body is immediately but no later than 1 working day of reporting to the

Competent Authority. (This is only required for CE marked products: Test Condom A and Control NRL Condom).

The CA expects a quarterly summary on all reportable SAE/SADE/Device Deficiencies and in addition SAE/SADE/Device Deficiencies that are included in the endpoints according to the CIP.

The Investigator must report all reportable events to the sponsor immediately but not later than 24 hours after investigational site investigation personnel's awareness of the event.

The Investigator should not break the randomisation code except when it is necessary to do so in order to ensure the subject receives appropriate medical care.

8.4 Follow-up of Adverse Events

All SAE / SADE / USADEs and all AE / ADEs that have not resolved by the end of the investigation will be followed up by the Investigator until resolution or until the Investigator believes there will be no further change, whichever is the earlier. This may involve the subject or the female partner making additional visits to the site.

In the case of loss to follow-up, at least two documented attempts to contact the subject must be made by the Investigator or designee before this is defined.

The end of the investigation is defined as the last visit of the last subject in the investigation.

All SAE/ SADE/ USADEs and all AE/ ADE that cause premature withdrawal of the subject and the female partner from the investigation and have not resolved by the end of the investigation will be followed up by the Investigator until resolution or until the Investigator believes there will be no further change.

This may involve the subject or the female partner making additional visits to the site. The minimum data required are the subject number, suspected investigational product, final outcome and date, which may be obtained by the Investigator in a documented telephone conversation with the subject/female partner or subject's/female partner's general practitioner (GP)/ Primary Care Physician (PCP).

Subjects/Female partners who experience the onset of an (S)AE after the last visit (end of the investigation) will not need to be recorded.

8.5 Misuse and Medical Device administration Errors

The Sponsor defines "misuse" as situations where the medical device is intentionally and inappropriately used not in accordance with the authorised product information.

All incidences of misuse are reportable to the Sponsor irrespective of the presence of an associated AE. The misuse and any associated untoward event will be captured on an AE / ADE CRF page or on a SAE / SADE / USADE form.

Medical device administration errors are any unintentional errors in administration which relates to:

- Using / being administered an incorrect medical device
- Using / being administered the medical device by the wrong route of administration / application

- The accidental administration of the medical device to a person who is not a subject within the investigation

Medical device administration errors are reportable to the Sponsor irrespective of the presence of an associated AE. Medical device administration errors with or without an associated untoward event will be captured on an AE / ADE eCRF page or on a SAE / SADE / USADE form.

In all cases of misuses and administration errors, in the judgement of the Investigator, the Investigator can withdraw the subject if the event effects the subject's/female partner's safety. Follow-up assessments should be conducted as described for the follow-up visit (Section 7.5).

8.6 Pregnancy

Pregnancy in the female partner of a male subject is considered a collectable event and will be recorded as an AE in all cases. It will be qualified as an SAE only if it fulfils SAE criteria.

The subject, whose female partner is pregnant, must immediately be withdrawn from the clinical investigation and the Sponsor must be promptly notified of the event. Any pregnancy during the investigation will be reported to the Sponsor within 24 hours of becoming aware of the pregnancy. The course and outcome of the pregnancy should be followed up carefully by the Sponsor Pharmacovigilance personnel, DSO, as part of their safety monitoring responsibilities and will not form part of the investigation dataset. The Sponsor Pharmacovigilance will liaise with the Investigator via the Sponsor's clinical study manager for follow up with the subject. Three documented follow up attempts should be made.

Any abnormal outcome regarding the mother or the child should be documented and reported.

9 STATISTICAL CONSIDERATIONS

This section presents a summary of the planned statistical analyses. A statistical analysis plan (SAP) that describes the details of the analyses to be conducted will be written prior to database lock.

Summary statistics for continuous variables will typically include the number of subjects (n), mean, standard deviation (SD), median, minimum and maximum. For categorical variables, summary statistics will typically include the number and percentage of patients in each category. All data will be presented in listings.

Baseline values are defined as the last measurements taken before administration of the randomised product.

9.1 Statistical Analysis Plan

Details of statistical methods and analysis will be documented in the SAP.

If there are any deviations to the proposed statistical analysis as described in this protocol these will either be documented in a protocol amendment and / or the final SAP prior to database lock with the rationale and impact of the changes addressed.

9.2 Interim Analysis

No interim analysis is planned.

9.3 Analysis Datasets

The analysis populations will be as follows:

- The safety population will include all randomised subjects who use at least one of the study condoms. The safety population will be used for all baseline summaries and summary of safety data. For the safety population, subjects will be analysed according to treatment received. The Full Analysis Set (FAS) will include all randomised subjects who use at least one of the study condoms and who have IELT recorded in at least one of the post-baseline study periods. The FAS will be used for the analysis of all efficacy endpoints. For the FAS, subjects will be analysed according to their randomised treatment.
- The Per Protocol (PP) population will consist of all patients in the FAS who do not deviate from the protocol in such a way as to impact the evaluation of the primary endpoint. Subjects who do not have an IELT recorded for at least 4 condom uses within a treatment period will be excluded from the PP population for that period. All decisions on exclusions from the PP population will be made prior to database lock. For the PP population, subjects will be analysed according to treatment received.

9.4 Subject Disposition and Characteristics

The number of subjects screened, randomised, completing, and withdrawing, along with reasons for withdrawal, will be tabulated. The number of subjects in each analysis population will be reported. Demographic and baseline characteristics (including age, gender, ethnicity, weight, height and BMI) will be summarised using descriptive statistics. No formal statistical analysis will be performed.

9.5 Statistical Analyses

All statistical analysis will be performed using SAS® version 9.4 or higher. For all endpoints, in the event that the assumptions underlying the parametric approach are violated, alternative non-parametric methods will be used.

9.5.1 Primary Endpoint(s)

9.5.1.1 Primary Analysis

The primary endpoint of the investigation is the change from baseline in IELT with the 5% Benzocaine condom versus the standard NRL condom, over a 4-week assessment period. For each subject, a mean IELT will be calculated across all intercourse episodes within a study period (baseline, assessment period 1, assessment period 2 and assessment period 3) and used for analysis. The change from baseline in IELT will be analysed using a linear mixed model using data from all three condom groups, with the primary comparison between the 5% benzocaine condom

with the standard NRL condom. The model will include fixed effects for treatment and period, a covariate for baseline IELT, and subject as a random effect. The differences between the 5% benzocaine condom with the standard NRL condom will be presented with a 95% CI and an associated p-value. Statistical significance will be assessed at the two-sided 5% level. No adjustment for multiplicity will be made since there is a single primary comparison (5% benzocaine condom versus standard NRL condom). No assumptions of normality will be checked based upon the utilization of the Generalized Linear Mixed Model (GLMM) to analyse the primary endpoint. If the model can't handle the violation, then worst case scenario a non-parametric model will be used, such as Wilcoxon signed ranks test with Hodges Lehmann estimator for treatment differences.

9.5.1.2 Secondary Analysis

In the event of any protocol deviations that warrant exclusion from the FAS, an analysis of the primary endpoint based on the PP population will be performed.

9.5.2 Secondary Endpoint(s)

All secondary endpoints will be evaluated based on comparing the 5% and 3% benzocaine condoms with the standard NRL condom. No adjustment for multiplicity is planned for the secondary endpoints, and so p-values will be interpreted with appropriate consideration of Type I error.

9.5.2.1 Secondary Endpoint Analyses

The secondary endpoints of the investigation are:

- Change from baseline in IELT with the 3% Benzocaine condom compared to the standard NRL Condom, over a 4-week assessment period.
- Proportion of subjects who achieve an increase of 2 mins from baseline in IELT in the 5% and 3% benzocaine condoms compared to the standard NRL Condom.
- Proportion of subjects who achieve an increase of 3 mins from baseline in IELT in the 5% and 3% benzocaine condoms compared to the standard NRL Condom.
- Proportion of subjects who achieve an increase of 4 mins from baseline in IELT in the 5% and 3% benzocaine condoms compared to the standard NRL Condom.
- A measure of Patient Global Impression of Change (PGIC) at the end of each 4-week assessment period, in subjects using the 5% and 3% benzocaine condoms compared to the standard NRL Condom.
- A measure of EMSEX pleasure scale at the end of each 4-week assessment period, in subjects using the 5% and 3% benzocaine condoms compared to the standard NRL Condom.
- User acceptability, experience and preference of each condom type will be evaluated through subject perceived questions , asked at the end of each 4-week assessment period.

- The in-use tolerability of each condom type will be evaluated through subject perceived questions, asked at the end of each 4-week assessment period.
- A measure of the total clinical failure rate of Test Condom A, Test Condom B and Control NRL condom.
- Overall proportion of subjects with Adverse Events/ Adverse Device Effects (AEs/ ADEs), i.e. the occurrence of one or more AEs/ ADEs per subject.

The change from baseline IELT with the 3% benzocaine condom compared to the standard NRL condom will be evaluated using the same linear mixed model as for the primary endpoint. The difference in least square means and associated 95% CI will be calculated, with a p-value to assess statistical significance.

The proportion of subjects who achieve an increase of 2, 3 or 4 mins from baseline in IELT (calculated from the mean across all intercourse episodes within a period) will be calculated for each condom type. The proportion achieving an increase of 2, 3 or 4 mins will be compared for the 5% and 3% benzocaine condoms versus the standard NRL condom using a GLMM with marginal means under the assumption that the mean of the outcome variable (1=success or 0=failure) follows a binomial distribution. Factors in the model will include fixed effects for treatment and period, and baseline IELT as a covariate. Subject will be included as a random effect. Comparison between the 5% and 3% Benzocaine condoms with the standard NRL condom will be expressed as an odds ratio, with an associated 95% CI and p-value.

The PGIC recorded at the end of each condom assessment period will be summarised by condom type, as the number and percentage in each category of the PGIC (Very much better, Better, Little better, No change, Little worse, Worse, Very much worse). A comparison of the PGIC in each of the 5% and 3% Benzocaine condoms versus the standard NRL condom will be performed using a GLMM, assuming a multinomial distribution for the response variable. Factors in the model will include fixed effects for treatment and period. Subject will be included as a random effect. Comparison between the 5% and 3% Benzocaine condoms with the standard NRL condom will be expressed as an odds ratio, with an associated 95% CI and p-value. In the event that some categories of the PGIC have too few subjects for the model to fit, the number of categories in the PGIC responses may be reduced (e.g. better, no change, worse) for purposes of analysis.

After each coital act, the mean of the responses on the EMSEX pleasure scale (0 to 100) will be calculated as the sum of responses divided by number of questions answered. For each condom assessment period, a subject-level mean EMSEX pleasure scale will then be derived using data from all coital acts. The EMSEX pleasure scale score will be analysed using a linear mixed model using data from all three condom groups, with comparisons between the 5% and 3% Benzocaine condoms with the standard NRL condom. The model will include fixed effects for treatment and period, and subject as a random effect. The between group differences will be presented with a 95% CI and an associated p-value.

Responses to SPQs will be summarised for each condom type using descriptive statistics.

9.5.3 Descriptive Statistics and Listings

All data (including vital signs, physical exam, number of intercourse episodes for each condom type and IELT) will be summarised using descriptive statistics where appropriate, and subject-level data will provided in data listings.

9.6 Adverse Events

Safety endpoints will include incidence of treatment-emergent AEs (TE AEs), ADEs (TE ADEs) and concomitant medications. An AE will be considered treatment emergent if it started after the first condom used. Data listings will be provided for CIP-specified safety data. MedDRA (Version 26.0 or the most recent version if this has changed during the course of the clinical investigation) will be used to code all AEs with respect to system organ class and preferred term. AE summaries will include only TE AEs and TE ADEs, which will be summarised (incidence and frequency) separately for males and females, by treatment group. Treatment-emergent AEs and ADEs will also be summarised by severity and relationship to randomised treatment (condom type) and by relationship to the investigational procedure.

Concomitant medication usage will be listed and summarised by coded term separately for males and females, by treatment group.

9.7 Handling of Missing Data and Drop-outs

There will be no imputation for missing data. By using a mixed model, subjects who provide data for only one or two of the three assessment periods will be included in the analysis. For the calculation of mean IELT within an assessment period, only intercourse episodes where IELT is recorded will be included in the analysis. For the calculation of the mean EMSEX pleasure score (using the 11-items), if more than 50% of the 11 items are missing for a particular coital act, the EMSEX pleasure score will be set to missing for that coital act. Subjects with a missing PGIC score will be omitted from the respected PGIC analysis.

10 DATA HANDLING AND RECORD KEEPING

10.1 Case Report Forms

For each enrolled subject an eCRF using fully validated software that conforms to 21 CFR Part 11 requirements, will be maintained. In the event of a screen failure, data will be recorded in the eCRF up until the point of screen failure. The Investigator is responsible for the quality of the data recorded in the eCRF. The data recorded should be a complete and accurate account of the subject's record collected during the clinical investigation. Subjects must not be identified in the eCRF by name or initials.

The Investigator and clinical site staff who have been delegated responsibility for entering data into the eCRF at each visit will be trained in the use of the eCRFs before they will be given access and before the first subject at the clinical site is screened. The Investigator must certify that the data entered into the eCRF are complete and correct.

The Investigator agrees to complete the eCRFs in a timely fashion after completion of each subject and make them available to the clinical investigation monitor for full inspection. In addition, any data queries raised should be answered promptly. Following monitoring and data management review of each subject's eCRF, the Investigator will electronically sign the eCRF. Re-signature by the Investigator may be required prior to database lock after resolution of data queries identified at the data review meeting.

Upon completion of monitoring and once Data Management has performed all edit checks, the eCRF will be declared clean and all access will be removed.

The subject reported outcomes (IELT, EMSEX pleasure scale, PGIC and SPQ) will be documented on pCRFs and transferred into the eCRF via double data entry.

10.2 Specification of Source Documents

Source data must be available at the clinical site to document the existence of the investigational subjects and the female partners. Source data must include the original documents relating to the clinical investigation, as well as the medical treatment and medical history of the subject and the female partner. The Investigator and monitor will identify the data that will be recorded directly on the eCRF and for this data the eCRF will be considered the source document (i.e. no prior written or electronic record of the data). The monitor will confirm this at the Initiation visit.

Source data (e.g. ICF, medical history, concomitant medication, diaries, questionnaires) contained in the subject records will be held in the ISF.

Where source data are in the form of a computer print-out (e.g. laboratory data) they will be signed and dated by the Investigator, confirming that the print-out is a true and faithful record of the data. These print-outs will be filed in the ISF.

The Investigator agrees to provide direct access to source data for investigation-related monitoring, audits, IEC / REC / IRB review, and regulatory inspection(s). Direct access to source data requires that the subject and his female partner give written, documented consent to this.

No investigation records should be destroyed without prior written agreement by the Sponsor.

10.3 Data Management

The data management group at the CRO will be responsible for eCRF development and data management activities.

Access to the eCRF will be by password and the eCRF will be backed up.

Further processes of the data management will be described in the data management plan.

Any changes made by the Investigator and clinical site staff who have been delegated responsibility for entering data into the eCRF will be captured via an audit trail in the system.

Coding will be done manually outside of the eCRF and checked.

Automatic validation programs check for data discrepancies and, by generating appropriate error messages, allow the data to be confirmed or corrected before transfer of the data to the Biometrics group. The monitor is also able to raise queries in the eCRF as required.

Coding of AEs/ ADEs and medical history will be done using the most recent version of MedDRA V26.0 (or the most recent version if this has changed during the course of the clinical investigation) by the CRO. Concomitant medications will be coded by the CRO using the WHO dictionary (including ATC coding). All coding will be checked by the Sponsor using the most up-to-date version of MedDRA and WHO dictionary.

10.4 Reporting of CIP Deviations

The clinical site staff should make the monitor aware of any deviation from the CIP as soon as possible after occurrence. Waivers for inclusion / exclusion criteria are not allowed.

10.5 Retention of Essential Documentation

The Investigator should retain all essential documents (as defined in ICH E6 or according to other national and international regulations) until at least 10 years after the completion of the clinical investigation (defined as last subject last visit in the clinical investigation). These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by an agreement with the Sponsor. It is the responsibility of the Sponsor to inform the Investigator when these documents no longer need to be retained.

Subject files and other source data must be kept for the maximum period of time permitted by the clinical site. The Investigator must notify the Sponsor of the retention period if this is shorter than described above.

11 QUALITY CONTROL AND QUALITY ASSURANCE

11.1 Monitoring

The Sponsor/CRO will organise regular monitoring visits to be performed at intervals agreed with the Investigator. The anticipated monitoring frequency will be stated in the Monitoring Plan. Monitoring will also involve, as appropriate, correspondence and telephone contacts.

Monitoring includes source data verification (SDV) which is the procedure whereby the data contained in the eCRFs are compared with the primary source data and thereby verified as accurate. It will be performed in such a way as to preserve subject/female partner confidentiality, taking into account all ethical and legislative requirements.

The Investigator or designated clinical site staff, must be available at some time during the monitoring visit to review the data and resolve any queries and to allow direct access to the subject's and his female partner's records for SDV.

SDV will include as a minimum verification for subject/female partner identity (age, sex and subject number), record of entry into the clinical investigation and signature of the informed consent by the subject and his female partner. In addition, details of SAEs/ SADEs in the subject's notes will be verified. Details included in the subject's notes as a minimum:

- Clinical investigation number
- Date that the subject and his female partner gave written consent

- All visit dates
- All SAEs/ SADEs, including device deficiencies that could have led to an SAE/ SADE
- All concomitant medications

At a clinical site visit the eCRFs should be complete and available in order that the accuracy of their completion may be checked. Each completed eCRF for each subject must be signed electronically by the Investigator, to verify the data and statements submitted. Similarly, all alterations on paper records must be initialled and dated by the Investigator or designated clinical site staff, explained as necessary, with the original mistake left legible.

11.2 Audits and Inspections

For the purpose of ensuring compliance with the CIP, ICH GCP, ISO 14155:2020 and applicable regulatory requirements, clinical investigations sponsored by Reckitt may be subject to an independent audit at the clinical site which will be conducted by personnel from an appropriate Quality Assurance (QA) Unit. Full consultation with the Investigator will be made prior to and during such audit, which will be conducted according to QA Unit SOPs. All involved parties must keep the subject data, including female partner's data, strictly confidential. Full consultation with the Investigator will be made prior to and during such audit.

As soon as the Investigator is notified of a planned inspection by a Regulatory Authority (RA), he / she must inform the Sponsor promptly and allow the Sponsor to participate in the inspection as permitted by applicable regulations and local laws.

11.3 Sponsor Policy on Fraud in Clinical Studies

In accordance with GCP, it is the Sponsor's policy to always follow-up suspected cases of fraud.

12 ETHICAL AND REGULATORY ASPECTS

12.1 Ethics Review and Regulatory Authority Approval

This investigation will only be undertaken when written approval from an independent and appropriately constituted IEC/ REC/ IRB has been obtained for the CIP, ICF and any other investigation specific documents, as applicable. Any additional requirements imposed by the IEC or regulatory authorities will be followed. Documented approval must be provided to the Sponsor before any CIP related procedures.

This clinical investigation will be submitted to the RA and to the IEC/ REC/ IRB by the investigator/ the CRO.

The Investigator or CRO must also provide the Sponsor with a list of constituted IEC/ REC/ IRB members that includes each member's name and profession.

Any amendments to the CIP must be submitted to the RA and the constituted IEC/ REC/ IRB for approval unless where necessary to eliminate apparent immediate hazards to subjects/male partners and any administrative changes must be notified.

The Investigator or designated clinical site staff or CRO will notify the constituted IEC/ REC/ IRB within 15 days of the end of the clinical investigation (or within 24 hours if the investigation is terminated prematurely due to safety reasons).

The CRO will notify the RA within 15 days of the end of the clinical investigation (or within 24 hours if the clinical investigation is terminated prematurely due to safety reasons).

12.2 Early / Premature Termination of the Investigation

Reasons for early termination of the clinical investigation may include, but are not limited to:

- Recall of investigational product when replacements are not available.
- Unacceptable data quality.
- Withdrawal of approval from the Regulatory Authority (RA) or IEC/ REC/ IRB.
- Unresolved non-compliance with GCP or with the CIP that compromises the subject's/the female partner's rights or safety or the clinical investigation data.
- Serious breach in GCP suspected or substantiated.

If the decision is made by the Sponsor to terminate the clinical investigation, the Investigator at the site will be notified as soon as possible.

It is the responsibility of the Investigator or CRO to ensure that the IEC/ REC/ IRB will be informed of the decision to terminate the clinical investigation. The Investigator will also inform participating subjects and their female partners that the clinical investigation has been terminated, discontinue use (if required), and arrange for appropriate follow-up appointments, where the assessments listed in Section 7.5 will be performed. The Investigator will agree with the Sponsor on the fate of all clinical investigation materials following clinical investigation termination.

Clinical investigation records must be retained as noted in Section 10.5.

The CRO will notify the RA of the clinical investigation termination.

13 COMPENSATION, INDEMNITY AND INSURANCE

13.1 Clinical Investigation Agreement

Before the clinical investigation commences, a contract between the Sponsor and the CRO, who employs the Investigator, will be signed in which financial aspects of the clinical investigation (including financial disclosure) as well as responsibilities and obligations are described.

13.2 Insurance

In accordance with applicable regulatory and legal requirements, the Sponsor will take out Clinical Trials Liability Insurance on behalf of the Investigator and staff who conduct part or all of this clinical investigation and/ or on behalf of the subject/partners participating in the clinical investigation.

14 REPORTING, PUBLICATION AND PRESENTATION

The clinical investigation will be registered in a publicly accessible database before the start of recruitment activities in accordance with national regulations.

A clinical investigation report will be prepared according to ISO 14155:2020 (Annex D) as part of the Sponsor's commitment to GCP. The report will be a record of the total investigation conduct and findings and will be subject to approval by the Investigator who will sign the final report.

This report, or parts of it, must be submitted to the relevant authorities or ECs if applicable. The results will be entered in a publicly accessible database after completion of the clinical investigation.

The investigation data will be owned by the Sponsor. The Sponsor retains the right to publish the data independently of the Investigator. The Sponsor agrees that before it publishes the results, it will provide the Investigator with at least 30 days for full review prior to submission of the manuscript to the publisher. The Investigator must submit any proposed manuscript to the Sponsor for approval prior to submission for publication.

15 REFERENCES

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Related Documents (Data held by Reckitt)

Investigator's Brochure: [redacted]

Clinical Studies (Data held by Reckitt)

[redacted]

16 APPENDICES

Not Applicable.

5078401_Clinical Investigation Plan_08Jun2023_V2.0

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