TARGET PRODUCT PROFILES FOR MALE CONTRACEPTIVE METHODS

20 February 2026

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The consultation process for developing the technical product profiles for male contraceptive (MC) methods was led by Igor Toskin, assisted by Nancy Kidula and James Kiarie from the contraception, fertility care and reproductive system infection research (CFI unit). The landscape analysis was conducted by Christina Wang. Technical guidance including design and analysis of the Delphi survey was provided by Sandra Ifeyinwa Nwokwoha from the Research for Health, Evidence to policy and impact in the WHO Science Division. The drafting of the full MC TPP document including incorporation of feedback was done by Igor Toskin, Nancy Kidula and Christina Wang with support from the TPP DG.

WHO sincerely thanks the members of the male contraceptives Technical product profiles development group (TPP DG) for their contributions throughout the development of this document. WHO convened monthly TPP DG meetings from January to November 2025 to determine the parameters, and their target profiles. All members of the TPP DG participated in at least one meeting and in the Delphi survey providing invaluable inputs until the finalisation of this document.

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Finaly WHO thanks the members of the public who commented on the MC TPPs through the online public consultation process.

Declarations of Interest:

As per the WHO guidelines for declaration of interests (DOI) for WHO experts, all members of the Male contraceptives TPPs development group completed the WHO Declaration of interest. All DOI forms were carefully reviewed and assessed in collaboration with colleagues from the CRE Team. The DG members were thus approved to participate in the TPP development.

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Table of Contents

Abbreviations / Acronyms – TBD

Glossary of terms – TBD

1.BACKGROUND

1.1 Introduction

The Target Product Profiles (TPP) for Male Contraceptive (MC) Methods provide important information on key parameters and values to be used for research and development of high quality, evidence-based, effective, safe, acceptable and affordable male contraceptives. Male contraceptives are intended to improve men's sexual and reproductive health(1). The TPP is a reference document that facilitates monitoring the potential impact of reversible male contraceptive use.

Globally, 48% of pregnancies are unplanned or unintended, and 60% of these unplanned pregnancies ended in an abortion (2). In the US, even with access to modern contraceptives, rates of unintended pregnancy are approximately 45% (3, 4). Most unintended pregnancies are due to non-use, inconsistent use of contraception or contraceptive failure (5) . The use of a highly effective contraceptive results in significant mortality reduction, improvements in women's health and wellbeing and dramatically reduces abortion rates (6-9). Therefore, there is a great need for improved access to contraceptives and more contraceptive options for people at risk for unintended pregnancy.

Men are significant users of contraception, with about 30% of couples relying on a male method of contraception. Globally, 21.8% of couples rely on condoms for contraception while only 1.8% of couples use vasectomy (10). Survey studies from early 2000s consistently indicate men's willingness to use male contraceptive methods and that women would trust their male partner to use male methods of contraception (11-14). The willingness to use novel male contraceptive methods (NMC) is corroborated by the WHO Global study on male contraceptives (unpublished) with results from 4 LMICs showing over 75% of respondents willing to use NMC and over 85% of women reported they would trust their male partners to consistently use NMC (14).

A recent study survey of 12000 men and >9000 women in six low to middle income countries indicated that overall, 61% of men would try novel male contraceptive method within a year of availability which was higher than 39% in the United States. The men preferred daily transdermal patches or gels or pills compare to injections and implants. Female partners had high trust and interest in their male partners using male contraceptive (15). These studies provided evidence that the demand for novel male contraception is high and lends support to the current development of reversible hormonal contraception, targeted approaches to suppress sperm output and function, and injection of hydrogels block for vas occlusion (16).

This first edition of the WHO Target Product Profile (TPP) for male contraceptives contributes to improving sexual and reproductive health (1), as well as enhancing access to family planning and contraception services. With its focus on contraceptive developments for men, the WHO TPP for Male Contraceptives supports the attainment of Sustainable Development Goal (SDG) targets 3.7 (By 2030, ensure universal access to sexual and reproductive healthcare services, including for

family planning, information and education, and the integration of reproductive health into national strategies and programs) and SDG indicator 3.7.1 (Proportion of women of reproductive age (aged 15-49 years) who have their need for family planning satisfied with modern methods). The product is also in line with global efforts to accomplish SDG target 3.8, which addresses achieving universal health coverage, including financial risk protection, and access to essential health care services. As a regulatory document this TPP supports SDG 5.6 Ensuring universal access to sexual and reproductive health and reproductive rights and specifically SDG indicator 5.6.2 Number of countries with laws and regulations that guarantee full and equal access to women and men aged 15 years and older to sexual and reproductive health care, information, and education.

1.2 WHO's work to support male contraceptive development

The World Health Organization has been involved in male contraceptive development for over 50 years - initially, providing technical leadership, supporting early research, building research capacity and standardizing semen analysis procedures (17, 18). The World Health Organization (WHO) contraceptive efficacy trial on hormonal male contraception (19), marked a significant milestone in MC development indicating good contraceptive effectiveness for the injectable combination hormonal contraceptive for men and paving the way for advances in combined hormonal male contraceptive development. Additionally, The WHO Manual for the Laboratory Examination and Processing of Human Semen, first published in 1980 and now in its 6th edition (20) is the global reference document for procedures and methods for the laboratory examination and processing of human semen, and is widely used by male contraceptive developers and other practitioners involved in male fertility care. WHO recognizes the criticality of novel MCs in expanding the contraceptive method mix, facilitating choice, alleviating the contraception burden disproportionately shouldered by females, and enhancing men's direct participation in family planning and preventive healthcare (21).

1.3 Spermatogenesis, Sperm Function. Blockage of Sperm Transport and Male Contraception development

The goal of male contraceptive development is to identify methods that are effective, reversible, safe, acceptable, affordable, and available. An understanding of the process of spermatogenesis is necessary as it is the basis of male contraception development and therefore the standards in the MC TPP. Unlike the female reproductive system where ovulation occurs cyclically with production of typically one egg per cycle, spermatogenesis is continuous from puberty, takes a longer period (mean 74 days, 95% CI -69 to 80 days) with numerous sperm produced per second (22). Male contraceptives are therefore designed to target either spermatogenesis, sperm function including sperm motility and morphology, fertilizing capacity or sperm transport. The production of sperm is controlled by testosterone produced under the stimulation of luteinizing hormone (LH) and supported by the follicle-stimulating hormone (FSH). This relationship is the main

target of hormonal male contraceptives that act to suppress the circulating levels of these hormones and thus their function in facilitating spermatogenesis (23).

Figure 1. below depicts elements of the spermatogenesis cycle and the targets of the three groups of MC for which this TPPs have been developed namely: suppression of spermatogenesis, inhibition of sperm function and vas deferens occlusion (24).

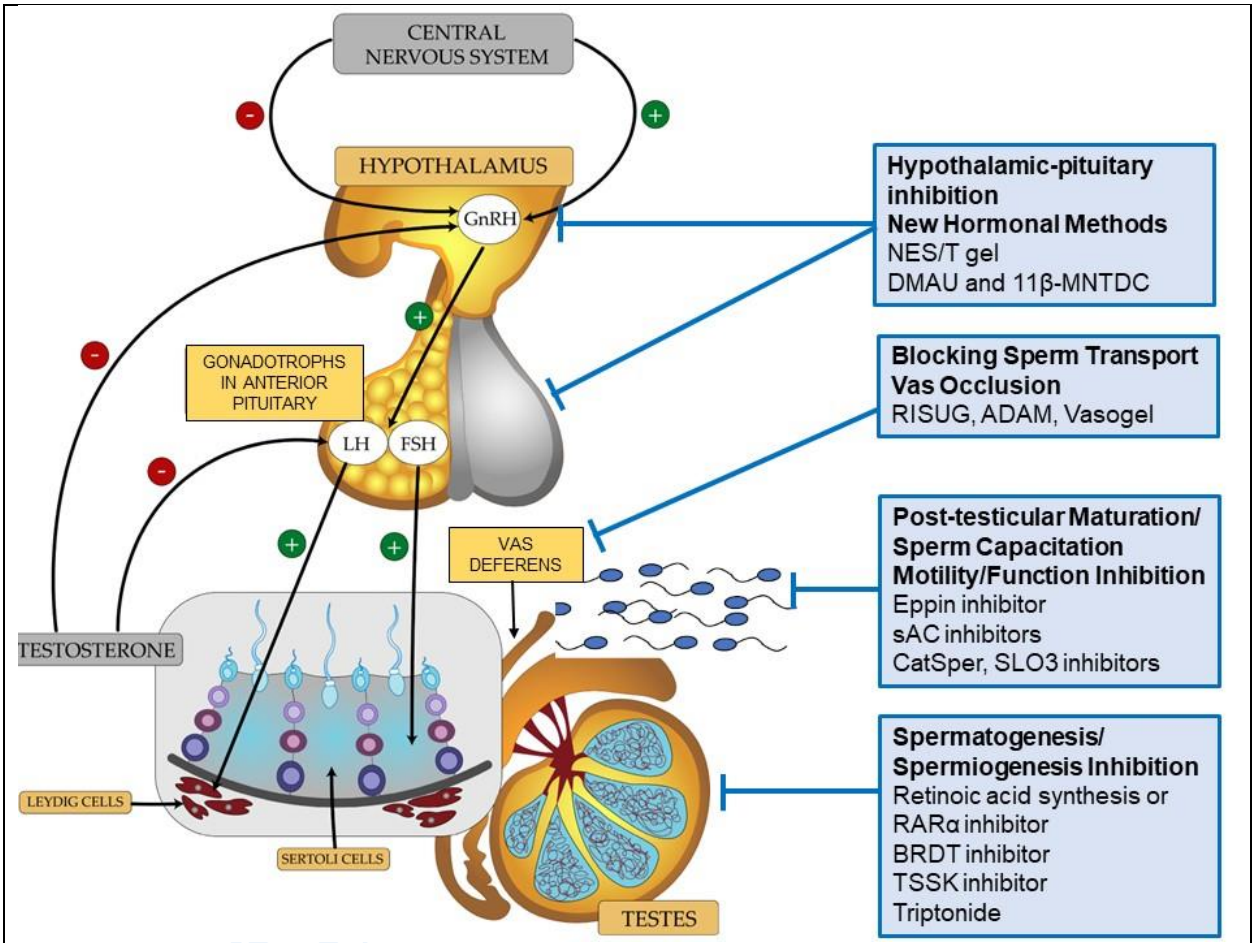

Figure 1. Overview of emerging targets of male contraception on the hypothalamic-pituitary-testis (HPT) axis. The HPT axis consists of the hypothalamus, pituitary gland, and testes. The hypothalamus releases gonadotropin-releasing hormone (GnRH) in a pulsatile fashion which signals for release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary. LH and FSH drive testosterone (T) production and spermatogenesis in the testes. T and the hormonal contraceptives (T ± a progestin) exert negative feedback on the hypothalamus to inhibit GnRH, LH, and FSH release, therefore suppressing spermatogenesis. Currently in clinical trials include nestorone/testosterone gel and androgens with progestogenic action dimethandrolone undecanoate (DMAU) and 11β-methyl-19-nortestosterone dodecylcarbonate (11β-MNTDC). Non-hormonal methods focus on distinct targets to inhibit spermatogenesis such as retinoic acid synthesis or retinoic acid receptor alpha (RARα), bromodomain testis-specific protein (BRDT) or spermiogenesis including testis-specific serine/threonine kinase (TSSK) and Triptonide. Other novel agents target sperm maturation or capacitation include epididymal protease inhibitor (Eppin), soluble adenylyl cyclase (sAC,); cation channel of sperm (CatSper); slowpoke homolog 3 (SLO3). Transport through the vas deferens can be blocked by cured-in-place hydrogel such as reversible inhibition of sperm under

guidance (RISUG), ADAM™, and Vasogel®. Arrows with + indicate activation; arrows with - indicate inhibition. Blue arrows ending with a bar indicates emerging male contraception methods and targets. *[Reproduced with permission. This figure was published in Encyclopedia of Human Reproduction 3e edition, ISBN: 9780443214783, Vol number 1, 2026, Author(s): Christina Wang, Ronald Swerdloff, Wei Yan, Title of article: Emerging Strategies for Developing Male Contraceptives, Page Nos 677-683, Copyright Elsevier]*

1.4 The assessment of contraceptive efficacy (pregnancy rate) -for the purpose of this TPP- should be based on months of exposure of the men to the new agent. Because the man receives the product, while the female partner has a variable duration of cycles, it is reasonable to consider the Kaplan-Meier for the primary endpoint (25, 26). The International Council on Harmonization (ICH) together with the FDA, the EMA, and other regulatory agencies have established guidelines for the safety requirements of drugs used for long-term treatment for non-life-threatening conditions (27, 28) that also will be applicable to the development of new molecular entities for male contraception.

1.5 The target audience for the TPPs is broad and includes clinicians, researchers working on male contraceptive methods, public health experts, epidemiologists, developers and representatives from manufactures (including biotech engineers), policy and decision makers, as well as representatives from regulatory bodies and agencies, donor agencies, and international organizations.

1.5 Rationale

The area of male contraceptive (MC) development is rapidly advancing with several candidates in advanced clinical trials. Concurrently, research scientists continue to look for novel male directed contraceptives that are efficacious, safe and acceptable in order to expand contraceptive options for men and promote shared responsibility for pregnancy prevention.

MC TPPs are crucial in guiding and aligning MC product developers, regulatory authorities, procurement agencies and other key stakeholders on the optimal characteristics of novel MCs including the minimal essential characteristics for their usability, while taking cognizance of end user preferences and public health priorities in SRH.

To date, WHO has not published a TPP for male contraceptives. Thus, this will be the first MC TPP from the organization in line with its core function to provide the global technical leadership for public health.

1.7 Scope:

This document includes the following male contraception TPPs.

- TPPs for male contraceptives that target spermatogenesis suppression
- TPPs for male contraceptives interfering with sperm function
- TPP for vas deferens occlusion

2. METHODOLOGY FOR DEVELOPMENT OF TPPs FOR MALE CONTRACEPTIVE

The WHO Department of sexual, reproductive maternal, child, adolescent health and ageing also referred to as Lifecourse Health and Reproduction (LHR) / Human Reproduction Program (HRP), plays a unique role in convening high standard multisite/country research as well as development of normative documents in the field of sexual and reproductive health (SRH) by assembling researchers, scientists, donors, policy makers and implementers. Its position, as well as its internationally recognized mandate and strong technical expertise in this field makes LHR/ HRP a unique international entity able to accelerate progress in development and further dissemination of Target Product Profiles (TPPs) for Male Contraceptives (MCs).

The Target Product Profile (TPP) for Male Contraceptives was developed in accordance with the 2nd Edition of "WHO target product profiles, preferred product characteristics, and target regimen profiles: standard procedure", https://worldhealthorg.sharepoint.com/sites/OneWHO_HQ_119/SitePages/WHO-Product-Profiles-.aspx. Recognizing the advances in male contraception development with several candidates in clinical trials, WHO LHR / HRP undertook the Global study on men and women's knowledge attitudes and behaviours around male contraception whose findings added to the body of evidence around men's willingness to use novel male contraception and their female partners acknowledging willingness to rely on male contraception as their sole contraceptive method.

In consultations with stakeholders involved in male contraceptive development e.g. Male Contraceptive Initiative (MCI), stakeholders working on male engagement in SRH (e.g. UNFPA) and discussions in conferences such as International Consortium for Male Contraception (ICMC), the need for initiating preparations for market introduction as well as instituting global regulatory standards for the development and implementation of novel male contraceptives was noted. This prompted WHO to initiate work on the first MC target product profile, earmarking it as a priority technical product and granting the requisite approvals for its development.

2.1 TPP Development group:

Consistent with the organizational requirements, a Target Product Profile (TPP) Development Group (DG) was established to oversee the TPP development process. International experts with significant experience in men's reproductive health, including male contraceptives, andrology, and biomedical sciences were identified to be part of this group. Once the list of potential members of the TPP DG was finalized, WHO explored their interest to become members of the TPP DG, with specified terms of reference. Their CVs, individual agreements, and statements of possible conflicts of interest (DOIs) were submitted to the secretariat. All DOI forms were carefully reviewed and assessed in collaboration with the WHO Office of Compliance, Risk Management and Ethics (CRE). A summary of the assessment and recommendations for mitigating potential risk is as follows:

- None of the candidates was receiving a remuneration for being employed/contracted by a private sector entity working on male contraception.
- The research grants declared predominantly 1) target the sperm function in the female tract or 2) were linked to basic research.
- The patents declared were either not considered as male contraception, have not been licensed yet, or are without personal benefit.

In light of the above discussions the secretariat in consultation with the CRE invited the proposed experts to be members of the TPP DG. However, whenever any topic related to the declared interests was discussed, the affected TPP members were recused from active discussion and decision making on the particular matter/approach/product in question. Additionally, the ethics unit noted the possible bias of some candidates who declared interests related to female contraception- these were monitored, and no incidences of concern occurred during the meeting or throughout the TPP development in this regard.

2.2 Decision making:

A landscape review of existing and novel male contraceptives was conducted to inform the development of TPPs. WHO-approved recommendations and guidance for implementing quality assurance were foundational for the TPP development. Under the supervision of WHO Steering Group, the TPP DG was tasked with drafting the TPP for Male Contraceptives. In recognition of the NMC already in clinical trials, the DG decided to focus on the following TPPs: MCs that suppress spermatogenesis, MCs that inhibit sperm function and TPPs for vas occlusive MCs. From the 30 January 2025 until 11 December 2025, the TPP DG met monthly on a virtual platform where the DG experts collectively discussed and proposed the parameters for each TPP and agreed on the content / value for each parameter. Appropriate literature including published systematic reviews on the topics informed the discussions.

After initial discussions and setting of the parameters, the DG was then divided into three smaller working groups to critically review each parameter and the related profile values with each team tackling one of the three TPPs based on their knowledge of the field and published literature. As this was the first TPP on male contraception developed by WHO, the focus was on providing guidance on minimal and optimal criteria for all defined product features. The draft content was reviewed by all members of the TPP DG and regular update and feedback rounds organized via email and tele/videoconferences. Decision-making on revisions was by consensus. Disagreements on the technical content were resolved through discussion and if necessary, through open voting. The profiles were then revised/ updated based on the discussions and any additional evidence.

2.3 Delphi survey

Following the drafting of the TPPs, a Delphi survey was undertaken to gain concurrence on specific parameters requiring full agreement. MC TPP 2 "Inhibition of Sperm Function " was

excluded from the Delphi survey due to full consensus among all members of the TPP DG. All 15 members of the TPP DG completed the Delphi surveys for MC TPP 1 “Suppression of Spermatogenesis” and MC TPP 3 “Vas Occlusion”. A 75% threshold was applied to assess the level of agreement. This threshold was reached for TPP1. Disagreements on the proposed value for "Effectiveness" in TTP3: “Vas Occlusion” were discussed further at the TPP DG meeting on 8 December 2025, and the adjustment of the value was approved by the majority of the TPP DG members through open voting. Analysis of two Delphi Surveys found no other disagreements between members of the TPP DG (results available upon request).

2.4 Public review

The draft TPP document was posted on the WHO LHR/ HRP website for public review for twenty-eight days where their feasibility and acceptability were assessed by TPP end users using a structured questionnaire. The targeted users included reproductive health experts, health care providers working in andrology, researchers in the field of sexual and reproductive health, including contraceptive product developers and manufactures. Their comments were used to revise the TPP before finalization and submission for requisite approvals by WHO.

3.TARGET PRODUCT PROFILE/S FOR MALE CONTRACEPTION

3.1 TPPs for male contraceptives that target spermatogenesis suppression

3.1.1 Preamble

3.1.1.1 Mechanisms of Action of agents that suppress spermatogenesis (see Figure 1)

Hormonal MC methods using testosterone alone or testosterone combined with a progestin (or another gonadotropin suppressing agent) suppress the hypothalamus-pituitary axis (like hormonal female contraception) by decreasing the intratesticular concentrations and suppression of follicle stimulating hormone, leading to profound suppression of spermatogenesis (29). The circulating testosterone is maintained by administration of testosterone at a physiological level. Spermatogonia (stem cells in the testis germinal epithelium) are not affected such that when the hormones are withdrawn full spermatogenesis occurs resulting in reversible MC (23). This MC method is most advanced in development with phase 2b trials proving efficacy and safety data. The next step would be a phase 3 clinical trial or trials for regulatory approval.

The strategy of novel MC targets genes is important for sperm production, maturation, or function; verifies the targets using gene knockout models; and screens for inhibitors of the target protein using high throughput screening of existing and new compounds. The identified drug targets undergo efficacy studies in vivo; toxicology and preclinical studies before first in human studies. New agents target directly the testis and agents such as retinoic acid synthesis inhibitor (30) and receptor antagonist (31) induces reversible infertility by arresting spermatogenesis at the spermatocyte and spermatids and induces apoptosis of the elongated spermatocytes (32). Withdrawal of retinoic acid receptor results in reversal of the spermatogenesis abnormalities and return to fertility in preclinical studies (31). Retinoic acid receptor inhibitors are in phase 1 safety and tolerability clinical trials. Other compounds that directly affect spermatogenesis include Bromodomain Testis specific protein (BRDT) inhibitors (33); Testis Specific Serine Kinase (TSSK) inhibitors acts on post-meiotic sperm and spermiogenesis and affects sperm morphology (34). Triptonide (35) induced abnormal sperm morphology and decreased fertilizing capacity in rodents but Triptonide in primate decreased sperm concentration.

3.1.1.2 Sperm concentration and output in the ejaculate as a biomarker of efficacy of spermatogenesis

Hormonal male contraceptive clinical trials initially used a threshold of suppression of spermatogenesis to a sperm concentration of ≤3 million sperm/mL ejaculate to enter efficacy phase where the couple used the MC as the sole method of contraception (36, 37). This was reduced by MC development experts to ≤1 million sperm/mL (38) and then verified in large multicenter clinical trials with testosterone alone (39, 40) or testosterone with a progestin (19)

that when the male's sperm concentration is suppressed to ≤1 million sperm/mL, the hormonal MC is as effective as hormonal female reversible contraceptive methods. Based on the results of the clinical studies, a reduction of sperm concentration to azoospermia in most men and/or severe oligozoospermia (≤1 million sperm/mL) has been used as a biomarker and a goal for agents that suppress spermatogenesis (41). This should be verified in agents not involving hormones.

3.1.1.3 Efficacy goal for agents that suppress spermatogenesis

The failure of rate for contraceptive development is expressed as the number of pregnancies in the female partner while the male is using MC. Using the Kaplan-Meier analyses (16, 26) that should be the same as effective female methods and for hormonal female contraception this is a 12 month cumulative pregnancy rate of seven (42).

3.1.2 TPPs

Parameter	Product profile
Goal of product	The goal of this product is the development of a safe, reversible method of male contraception that functions by inhibiting sperm production
Target population	Men over the age of 18 years (after attaining full puberty) at risk for fathering an unintended pregnancy in a female sexual partner. This value may vary based on local legislation/ regulations governing the use of contraceptive methods
Intended use	The intended use of a male contraceptive that suppresses spermatogenesis is to prevent an unintended pregnancy in the female sexual partner when the men/couple do not wish to have a child at a given time of their reproductive life.
Target use setting	Healthcare settings particularly at primary care level (level 1) or above (health care facilities level 2 and 3), in ambulatory clinics or doctors' offices, on-demand outside of healthcare facilities, and in pharmacies. They may also be prescribed in clinics or family planning centers or available via telehealth. A broad range of health care providers can prescribe these methods including primary care and family planning providers such as nurses and midwives, general doctors, and other specialist providers including urologists, endocrinologists, gynecologists.

<table>
<tr><td>Effectiveness</td><td>Assuming perfect use, the product results in prevention of pregnancy in the female partner to the same extent as current female reversible user-controlled contraceptive methods. [Typical use 12month cumulative contraceptive failure rates are about 7% for female daily patches, or pills (42)].

For agents that suppresses spermatogenesis, clinical efficacy studies conclusively showed that if sperm output is suppressed to ≤ 1 million sperm/mL ejaculate, the efficacy of preventing pregnancy is like female hormonal contraceptive methods (19, 40).

<table>
<tr><th>Minimal</th><th>Optimal</th></tr>
<tr><td>80% men with Sperm Suppression to < 1 million sperm/ml ejaculate</td><td>90% men with Sperm Suppression to < 1 million sperm/ml ejaculate</td></tr>
<tr><td>Time to suppression to < 1 million sperm/ml ejaculate within 12 weeks</td><td>Time to suppression to < 1 million sperm/ml ejaculate within 8 weeks</td></tr>
<tr><td>Failure to Prevent Pregnancy Kaplan-Meier 12month cumulative pregnancy rate < 7</td><td>Failure to Prevent Pregnancy Kaplan-Meier 12month cumulative pregnancy rate < 3</td></tr>
</table>
</td></tr>
<tr><td>Equipment</td><td>Equipment needs depend on the product and its formulation:
• Tablets need only a container evaluated for pharmaceutical use (sterility; protection from heat and humidity; safe opening top to prevent misuse by children).
• Injectables need disposable needles and preferably pre-filled syringes with fixed or adjustable volume delivery, painless delivery preferred.
• Gels need metered pumps or containers with controlled delivery volume, or in packets with fixed volumes of the gel.</td></tr>
<tr><td>Target use</td><td>Minimal and Optimal:
Suppression of Sperm production (< 1 million sperm/ml) in two consecutive samples about a week apart)</td></tr>
<tr><td>Mode of action</td><td>Suppression of sperm production to azoospermia or severe oligozoospermia ≤1 million sperm/mL ejaculate,

<table>
<tr><th>Minimal</th><th>Optimal</th></tr>
<tr><td>80% of men who use the product consistently achieve suppression in 12 weeks</td><td>90% of men compliant with the method achieve suppression ≤ 1 million/mL in 8 weeks</td></tr>
</table>
</td></tr>
</table>

Contraindications	1. Known hypersensitivity to any component of the investigational product (IP) 2. Abnormal serum chemistry values that may indicate clinically significant liver or kidney dysfunction. 3 Uncontrolled hypertension or severe heart failure 4. Known history of primary testicular disease or disorders of the hypothalamic-pituitary axis. 5. Known history of significant cardiac, renal, hepatic, or other chronic diseases. 6.. History of depression or other major psychiatric disorders. For products containing androgens (testosterone) and other hormones and in men >35yrs who smoke additional contraindications or specific warnings may apply including: 7. History of/or high-risk factors for thromboembolic disease. 8. PSA levels ≥ 4 ng/mL.- (should be in the reference range by age and populations) 9. History of prostate, testicular or breast carcinoma (only for products containing androgens). 10. Significant lower urinary tract obstruction symptoms (IPSS > 15).	
Efficacy: 1.Biomarkers as surrogates for efficacy before prevention of pregnancy studies 2. Prevention of pregnancy studies using Kaplan Meier assessment for cumulative pregnancy rates	**Minimal**	**Optimal**
	1. Perfect use: Suppression of sperm to ≤ 1 million/mL achieved in 80% of men 2. Kaplan Meier Twelve-Month Cumulative Pregnancy Percentage of not more than 7	1. Perfect Use: Suppression of sperm achieved in 90% of compliant men 2. Kaplan Meier Twelve-Month Cumulative Pregnancy Percentage of not more than 3
Time to result .	**Minimal**	**Optimal**
	Suppression of sperm production to ≤1 million/mL in 12 weeks	Suppression of sperm production reached to ≤ 1 million/mL in 8 weeks
Route of	**Minimal**	**Optimal**

Administration	• Self-administered daily administration (for oral tablets or gel dose) • Monthly or longer for injections. • Implants – once in 6 months or longer.	• Self-administered daily administration (for oral or other daily formulation). • Injections once in 3, or 6 monthly or yearly, • Implants for one year could/should be biodegradable.
Dosage schedule	**Minimal**	**Optimal**
	Used for several years depending on the uses' preference	Used indefinitely depending on the couples' preference
Return to normal range of semen parameters/characteristics	**Minimal**	**Optimal**
	Return to reference range of sperm concentration within 12 months	Return to reference range of sperm concentration within 6 months
Side effect profile	**Minimal**	**Optimal**
	• No more or less serious side-effects than approved products for similar indications (e.g. Female hormonal contraceptives, testosterone) • Less than 10% moderate adverse events such as depression, or changes in libido or erection • Any increased incidence of birth defects above the expected incidence in the general population in children born after use of a male contraceptive would be unacceptable. • Rare serious adverse events would be tracked in future post-marketing surveillance when products become available	• No serious side effects. Side effects would be mild or moderate (<10% incidence of most common side effects). • Less than 5% with moderate/severe effects adverse events including libido or erection, or depression. • Any increased incidence of birth defects above the expected incidence in the general population in children born after use of a male contraceptive would be unacceptable. • Rare serious adverse events would be tracked in future post-marketing surveillance when products become available.
Shelf life	**Minimal**	**Optimal**
	2 years without refrigeration	3 to 4 years without refrigeration

Infrastructure	Minimal	Optimal
	• Trained providers for counselling and screening for contraindications at least via telemedicine. • Efficacy and biomarker testing would be available via mailed samples. • Trained and qualified staff to administer any medications requiring implantation or injection. Providers must be trained for implant insertion or removal. • User-controlled methods (daily use of gel or oral pills require only trained health workers to provide and check for contraindications in the label	• Trained providers for counselling and screening for contraindications including using telehealth. • Methods to be self-administered and efficacy/biomarker testing would be available on site or at home (e.g., sperm at-home test kit) and available in real time or samples can be mailed in. • Injection provided as pre-filled syringes to be administered by user after training by provider. • User-controlled methods (daily use of gel or oral pills require only trained health workers to provide and check for contraindications in the label
Product kit	According to the specific product. All materials required for product use, including devices or other consumables (for example alcohol swabs) to use for one individual, included in packaged, self-contained kit (either packaged individually as one product per product kit or sufficient to perform the number of number of individuals in the product kit box – e.g. 30, 50 or 100 products Product kit should include detailed information e.g. **Oral** -Dosage, when and how to take, missed doses, what to avoid etc **Gel** application- areas of application shoulder and upper arms. Instructions of how to apply the gel. (Must wash hands after each application. Wait as long as possible before showering or washing. Wash application site or wear clothing to cover application site before close skin contact with another person to avoid skin to skin transfer of active product). **Injections**- how to use the prefilled syringes and body sites that can be used for injections, alcohol swabs	
Additional consumables required but not provided within the product kit	Potentially pre-filled syringes or canisters of gel, or bottles of tablets for dispensing medication. If pre-filled syringes are not available, vials, needles, and syringes for administration.	

Product kit stability and storage conditions .	**Minimal**	**Optimal**
	12 months stability stored at room temperature (20 °C/68 °F – 25°C/77 °F) at 70% humidity.	18 months stored at room temperature (20 °C/68 °F – 25°C/77 °F) 90% humidity.
Environmental tolerance of packaged product kit	The minimal or optimal characteristics may differ according to different products and excipients (example canister of gels with alcohol content is flammable.) To be discarded or recycled according to manufacturer recommended procedures Temperature variations would vary according to stability testing for each product.	
Operating conditions	**Minimal**	**Optimal**
	Between 15 °C and 40 °C at an altitude up to 2000 meters Extremely low relative humidity	Between 10 °C and 45 °C at an altitude up to 4500 meters Both low and high humidity
Training required	**Minimal**	**Optimal**
	Counseling should be available online and in person training should take no more than 30 minutes.	Counseling should be either in person or available online with the ability to ask questions of experts and take no more than 15 minutes.
Clean water	Minimal: clean water should be available for the administration of oral dosage forms and cleaning of any instruments used during administration (e.g., with implants). Sterilization of needles or trocars is required, or preferably single use / disposable material	
Waste/disposal requirements	**Minimal**	**Optimal**
	Minimally acceptable: Used containers should be discarded in household trash in a manner that prevents accidental application or ingestion by children or pets.	Ideal: Used containers are recyclable Biological products disposed in special biohazard containers and syringes in “Sharps” containers.

	Injection syringes and needles must be disposed according to the guidelines of each country	
Device control	**Minimal**	**Optimal**
	For all formulations, expiration dates based on stability testing should be included in the package. Contraceptive gels -2 year Pills -2 years Injectable -2 years Implants-1 year	Optimal: Expiration dates in addition to physical methods (e.g., chemical strips, visual inspection to exclude precipitation of injected solutions) are performed to ensure full potency of contraceptive. Contraceptive gels -3 years Pills -4 years Injectable -3 years Implants -3 years
Regulatory requirements, compliance with appropriate standard/regulations	FDA/EMA approval to be aligned with the required standards and regulatory processes of each country according to International Council of Harmonization guidelines WHO provides a list of WHO listed Authorities i.e. *regulatory authorities (RA) or regional regulatory systems (RRS) that comply with all the relevant indicators and requirements specified by WHO for regulatory capability as defined by an established benchmarking and performance evaluation process.* *https://www.who.int/news-room/questions-and-answers/item/who-listed-authorities*	
Health service user identification capability	Ideal: Providers should be qualified medical professionals with current, unexpired licenses. For implantation and retrieval of implants an additional training certification may be required.	
Target price per product kit	**Minimal**	**Optimal**
	Less than $30/month or $360 per year for effective contraception in low- and middle-income countries	Less than $5/month or $60 per year, very low cost to low- and middle-income countries, scalable global production

3.2 Target Product Profiles (TPPs) for Male Contraceptives interfering with Sperm function

3.2.1 Preamble:

This TPP describes several potential targets that interfere with sperm motility, development of normal morphology, capacitation, and sperm fertilizing capacity. The mechanisms of action differ widely. Male contraceptives (MCs) for this category -that are in development- may be used on-demand, as daily oral pills or gels, injectables, and implants. High-throughput screening identified potential drug targets, usually inhibitors of the target protein important in sperm function. Many of these targets have been verified in *in vitro* systems and then in preclinical studies. While clinical studies are imminent, they have not yet started. These agents are therefore less developed than those that suppress spermatogenesis or block sperm transport (24, 43, 44).

3.2.1.1 Mechanisms of Action

The target inhibitors have different mechanisms of action, and it should be noted that efficacy has been demonstrated only in pre-clinical studies (Table 1). Because the mechanisms of action are so different, the time to efficacy is very dependent on the method. E.g., soluble adenylate cyclase is being developed as a rapid onset and offset on-demand method. Others that inhibit sperm hyperactivation which usually occurs in the Fallopian duct could be developed as a male and female novel contraceptive method.

Table x. Potential Male Contraceptive Methods that Interfere with Sperm Function

Mechanism of action	Example (References)	Status
Blockade of semen liquefaction and impaired sperm motility	EPPIN (45-49)	Pre-clinical
Inhibition of sperm motility via inhibition of calcium influx and sperm hyperactivation	CatSper inhibitors (50-54)	Pre-clinical
Inhibition of sperm motility, acrosome reactivity and hyperactivation via inhibition of potassium efflux	SLO3 inhibitors (55-57)	Pre-clinical
Reduction in sperm motility and reduced ability of sperm to undergo capacitation via inhibition of cAMP formation in sperm	Soluble adenylate cyclase (sAC) inhibitors (58-59)	Pre-clinical
Reduction in sperm morphology and fertilizing capacity via inhibition of testis specific kinases	TSSK inhibitors (34,60)	Pre-clinical
Reduction in sperm morphology and fertilizing capacity and sperm production via other mechanisms	Triptonide (35)	Pre-clinical

3.2.1.2 Biomarkers for Effectiveness of Agents Interfering with Sperm Function

For novel compounds such as EPPIN (Epididymal Protease Inhibitor) that impairs sperm motility, the surrogate biomarker could be sperm motility. With the current data available for fertile and infertile men, it is not certain what is the lower threshold for sperm motility and morphology that will prevent pregnancy in women (61). Thus for agents that alter sperm motility and morphology, complete absence of motile or normal sperm may be required (41). For other compounds that affect sperm function, specific biomarkers need to be developed for each of the compounds in addition to sperm function tests such as acrosome reaction and hyperactivated motility. The validity of the biomarkers should be verified by the ability to prevent pregnancy in the female partner.

3.2.1.3 Efficacy Goals for Male Contraceptive Methods that Interfere with Sperm Function

This should be the same as for agents that suppress spermatogenesis, The failure rate for contraceptive development is expressed as the number of pregnancies in the female partner while the male is using the MC. Using the Kaplan-Meier analyses (16, 26) that should be the same as effective reversible female methods - that is a 12 month cumulative pregnancy rate of no more than seven (42).

3.2.2 TPPs

Parameter	Product Profile
Goal of product	The goal of this product is the development of a safe, reversible method of male contraception that functions by the interference of sperm function and reduction of the capability of sperm to reach and fertilize an egg. This could include agents that target sperm motility, capacitation, hyperactivation, the acrosome reaction, and/or binding to or fusing with the egg.
Target population	The target population is men over the age of 18 (post-puberty to ensure full development of spermatogenesis and functional sperm) at risk for fathering an unintended pregnancy in a female sexual partner. *(The target population depends on local/country legislation/regulations governing the use of contraceptive methods.)* Novel male contraceptives would be of interest to most men, allowing men to take a more active role in the prevention of unintended pregnancy.

Intended use	The intended use of a male contraceptive that impairs sperm function is to prevent an unintended pregnancy in the female sexual partner when the men/couple do not wish to have a child at a given time of their reproductive life.
Target use setting	Healthcare settings particularly at primary care level (level 1) or above (health care facilities level 2 and 3), in ambulatory clinics or doctors' offices, on demand outside of healthcare facilities, and in pharmacies. These could also be prescribed in clinics or family planning centers or available via Telehealth. A broad range of health care providers to provide these methods including primary care and family planning providers such as nurses and midwives, general doctors, and other specialist providers including urologists, endocrinologists, gynecologists.
Effectiveness	Product should result in the prevention of pregnancy in the female partner to the same extent as current reversible female contraceptive methods (COCs, Injectables -DMPA/ NET EN). The minimal acceptable 12-month cumulative pregnancies are 7 and optimal is 3 as in female reversible hormonal contraceptive methods
Equipment	Tablets need a container tested for pharmaceutical use to allow for protection from heat and humidity; as well as child-proof safe opening top. Injectables need disposable needles and preferably pre-filled syringes with fixed or adjustable volume delivery. Gels need metered pumps or containers with controlled delivery volume; or can be administered in packets with fixed volumes of the gel.
Target use Mode of action	Potential targets for male contraceptive that impair sperm function are shown in the table in the Preamble. The time to efficacy will depend on each method.
Contraindications	The contraindication depends on the mechanism of action of the compound and includes • Hypersensitivity to any component of the investigational product. • History of severe male factor infertility • For potassium or calcium channel blockers, potential for contraindications in settings of known ion channelopathies (e.g. Brugada syndrome, Long QT-syndrome), although speculative at this point. • For sAC inhibitors, history of nephrolithiasis

Efficacy:	**Minimal**	**Optimal**
	Should be superior to unintended pregnancy rate observed with the use of a condom as the sole method of contraception and on par with efficacy of female contraceptive methods (12-month cumulative pregnancies <7)	Better than the efficacy of female hormonal contraceptives (12-month cumulative pregnancies < 3).
Time to result:	**Minimal**	**Optimal**
	Depending on the method, sperm function should be impaired after one month of administration.	Depending on the method, sperm function should be impaired after first dose of contraceptive.
Route of Administration	**Minimal**	**Optimal**
	• Daily oral, transdermal or sublingual dosing are acceptable. • Weekly to monthly subcutaneous injection or intramuscular injection are acceptable. • Intravenous/intrathecal or other parenteral routes are unacceptable. • Drug should be safe to use for an extended period or indefinitely without concern related to long-term exposure.	
Dosage schedule	**Minimal**	**Optimal**
	Depending on the method - Minimum dose to achieve desired efficacy and safety standards	
Return to normal range of semen parameters/characteristics.	**Minimal**	**Optimal**
	Depending on the methods, sperm function and fertility should return to normal after one month of contraceptive cessation.	Depending somewhat on the method, sperm function and fertility should return to normal one day after contraceptive cessation. Any instance of failure to restore fertility is unacceptable.
Side effect profile	**Minimal**	**Optimal**

	Side effects would be present, but mild (<20% incidence). Any serious adverse events such as death, heart attack or stroke, would be unacceptable. Any increased incidence of birth defects in children born after use of a male contraceptive would be unacceptable.	Side effects would be minimal and mild (<5% incidence at most common).
Shelf life	**Minimal**	**Optimal**
	Product usable when stored at room temperature for 1 year without need for refrigeration. Refrigeration requirements should not exceed those of common childhood vaccines provided at primary level [2 to 8^0C *or 36 - 46 ^{0} F]*	3-4 years without refrigeration.
Infrastructure	**Minimal**	**Optimal**
	• Trained providers for counselling and screening for contraindications at least via telemedicine. • Efficacy and biomarker testing would be available via mailed-in samples. • Staff would be qualified to administer any medications requiring implantation or injection.	• Trained providers including community health workers for counselling and screening for contraindications. • Methods would ideally be self-administered-user-controlled without the need of trained providers. • Efficacy/biomarker testing would be available on site or at home (e.g. sperm-check kit) and available in real time. • Staff would be qualified to administer any medications requiring injections or insertion of implants.

Product kit	Product kit should include detailed information on proper use and administration of the male contraceptive. • For oral medications information on frequency of dosing (e.g. daily), time of day, whether to take with food or on an empty stomach and other instructions regarding what to do in case of a missed dose, etc. • For injections, information about safe administration and dose frequency and how to safety dispose of spent syringes. • For implants, ideal state is a single use/disposable sterile inserter and trocar.	
Additional consumables required but not provided within the product kit	Potentially pre-filled syringes or bottles of tablets for dispensing medication. If pre-filled syringes are not available, vials, needles and syringes for administration.	
Product kit stability and storage conditions	**Minimal**	**Optimal**
	Product stored in regular refrigerator (2 to 8^0C *or 36 - 46 ^{0} F*) prior to use for 12 months.	Product storable at room temperature (20-25ºC) without refrigeration for periods of up to one year.
Environmental tolerance of packaged product kit	This will depend on the different products and excipients in each formulation. For example, alcohol containing transdermal formulation has the potential for flammability and should be stored away from heat sources and open flames. Heat excursions greater than 25ºC can be harmful for many solid dosage forms and should be avoided.	
Training required	**Minimal**	**Optimal**
	Counseling to providers-in-training should be available online and training should take no more than 30 minutes.	Counseling should be either in person or available online with the ability to ask questions of experts and take no more than 15 minutes.
Clean water	Minimal: Clean water should be available for administration of oral dosage forms and cleaning of any instruments used during administration (e.g. with implants).	
	Minimal	**Optimal**

Waste/disposal requirements:	Used containers should be discarded in household trash in a manner that prevents accidental application or ingestion by children or pets. Injection syringes and needles must be disposed according to local guidelines.	Used containers are recyclable. Biological products disposed in special biohazard containers and syringes in "Sharps" containers.
Device control	**Minimal**	**Optimal**
	For all formulations, expiration dates based on stability testing should be included in the package.	Expiration dates in addition to physical methods (e.g. chemical strips, visual inspection to exclude precipitation of injected solutions) would be performed to ensure potency of contraceptive.
Regulatory requirements	• Any male contraceptive will require registration as a medicinal product or medical device in accordance with national legislation approval prior to clinical use. • Additional approvals may be required depending on jurisdiction of use. For example, FDA approval would be required for US use and EDA approval within the EU. • WHO provides a list of WHO listed Authorities i.e. *regulatory authorities (RA) or regional regulatory systems (RRS) that comply with all the relevant indicators and requirements specified by WHO for regulatory capability as defined by an established benchmarking and performance evaluation process.* *https://www.who.int/news-room/questions-and-answers/item/who-listed-authorities*	
Health service user identification capability	Ideal: Providers should be qualified medical professionals with current, unexpired licenses. For implantation additional training certification may be required.	
Target price per product kit	**Minimal**	**Optimal**
	Less than $30/month or $360 per year for effective contraception in low- and middle-income countries.	Less than $5/month or $60 per year in low- and middle-income countries, scalable global production

3.3 Target Product Profile (TPP) for Vas deferens occlusion

3.3.1: Preamble

Vasectomy is an established method of male contraception and is offered as a non-reversible method. The success of vasectomy is very high (over 99%), and 12-month cumulative contraceptive failure rate is less than 0.1 pregnancy (62). Acceptance varies widely among regions and countries with < 0.1% of men in middle to low income countries relying on vasectomy (63) and vasectomy rate decreasing in the past 20 years. The approach to vasectomy is universally the no-scalpel method (64) which has been shown to have less adverse events after surgery (65-67).

Reversal of vasectomy requires skilled surgeons and the success rate and return to fertility (68, 69) depends on the interval since vasectomy (70), age of patient and his partner. Recent studies indicate that the presence of anti-sperm antibodies may not affect pregnancy after vasectomy reversal (71-73).

In general vasectomy procedures, success rate and assessment of post-vasectomy semen analyses follow the American Urological Association Guidelines (62) to which other professional urology association also adhere (74).

3.3.1.1 Mechanism of Action

Recent progress has been made on injection of compounds into each vas to form a block (hydrogel, polymer) preventing sperm traversing the block. When fertility is desired, the hydrogel block can be flushed out with fluids or solvents without surgery. The early clinical studies in India utilized styrene maleic anhydride (SMA) in a solvent vehicle of dimethyl sulfoxide (DMSO). Phase 1 and 2 clinical trials of this method RISUG (Reversible Inhibition of Sperm Under Guidance) showed azoospermia in all men (75, 76). The product is now being developed as Vasalgel (Plan A™) and preclinical studies are complete and pending clinical studies (77), Other have used polymers and clinical studies showed success in vas occlusion but not in reversibility (78-80). A two component hydrogel ADAM ™ completed preclinical studies and is currently in Phase 1 clinical trial in man (81). The current development utilized disposable injection systems and required visual identification of the vas deferens through no-scalpel vasectomy technique.

3.3.1.2 Surrogate Biomarkers of Succes of Vas Occlusion

A single post-vasectomy semen analysis without centrifugation demonstrating azoospermia or less than 100,000 motile sperm/mL ejaculate is defined as a success for vasectomy and provides a 12-month cumulative pregnancy of < 0.1. The sample can be submitted as early as 8 weeks after vasectomy. If there is persistent motile sperm, counseling for repeat vasectomy should be offered 6 months after the initial surgery (62). Surrogate biomarkers for vas occlusion success

should follow the vasectomy guidelines that are accepted throughout the world. Success of reversibility is demonstration of motile sperm in the ejaculate after the block is dissolved and/or flushed out (68).

3.3.1.3 Goals of Efficacy and Reversibility of vas occlusion as a New Male Contraceptive Method

Vasectomy has been proven to be safe and has a very low contraceptive failure of 12 month-cumulative pregnancy rate of < 0.1. The no-scalpel vasectomy procedure after training can be performed by providers in low and medium income regions (82). Reversal of vasectomy required skilled surgeons. The goals of successful vas occlusion should be the same as that for vasectomy. The injection of occlusive agents into the vas offers the possibility of flushing or dissolving the occlusive agent when reversal is desired and skilled surgeons may not be required, or that the occlusive agent is biodegradable after certain period of several years. Developers of vas occlusion must first demonstrate efficacy of inducing azoospermia or near azoospermia with presence in immotile sperm and then reversibility whenever the use is desired (74).

3.3.2: TPPs

Goal of product	**The goal of this product is the development of a long-acting and reversible or a permanent method of contraception for males through occlusion of the vas deferens**	
Target population	**Minimal** Men seeking contraception who can give consent for the procedure. This depends on the local/ country legislation, regulations governing the use of contraceptive methods requiring minimally invasive surgery.	**Optimal** For permanent occlusion: Males or couples that have achieved their desired family size or number of children, and who have been informed of the effect of permanent contraceptive and the possibility of non-reversibility. For reversible occlusion: Males seeking a long-acting but reversible method of contraception.
Intended use	These methods prevent unintended pregnancy by blocking or occluding the vas deferens bilaterally, thereby preventing the passage of sperm into the ejaculate and the possibility of pregnancy. The intended use is to prevent conception in the female partner by preventing the passage of sperm cells	

	along the vas deferens during ejaculation in men who no longer want to have a child for permanent methods or long-term for reversible methods.
Target use setting	Healthcare settings particularly at primary care level (community-based facilities preferred for Universal Health Care) or above (health care facilities level 2 and 3), in ambulatory clinics or doctors' offices, on-demand outside of healthcare facilities, or outreach services setting. Health workers: primary care providers, family planning providers, other specialist providers (urologist-surgeons, health professionals trained to perform the procedure of vas deferens blocking).
Effectiveness **The effectiveness should be the same as that of female contraceptive methods**	Product results in prevention of pregnancy in the female partner with similar efficacy to highly effective female methods of contraception (female sterilization)— in typical or best use scenarios. Vas deferens occlusion is achieved with injection or instillation of occluding agents into the vas deferens, using a small incision like the no-scalpel technique for vasectomy or percutaneously under ultrasound guidance in injectable methods. Male vas deferens blocking/occlusion has the potential to be an effective method that would entail low cost and may result in minimal complications compared to female voluntary surgical contraception (Notably less bleeding and hematoma when using a minimally invasive techniques).
Quantitative assessment of effectiveness to be included for these methods	Azoospermia or a sperm concentration less than 100,000 non-motile sperm /ml of ejaculate.
Equipment and provider proficiency	• The WHO requires that the procedure be performed by a health or paramedical professional trained on performing no-scalpel vasectomy which includes competencies on how to access the vas deferens (82 - 84). This is important for vas occlusion methods where visual injection is required for inserting/injecting (Cure-in place) the occluding agent within the lumen of the vas deferens for methods intended to be reversible (74). • For vas blockage, minimally invasive procedures, like the no-scalpel technique is the preferred approach (62, 82). • Depending on the method of vas blocking.

	○ Using minimally invasive surgical access with small incisions to allow visual inspection of the vas deferens bilaterally, with minimal repair for closure after the procedure. ○ Usual no-scalpel vasectomy instruments— device kits provided by the manufacturer of an injection system designed for the vas occlusion product. ○ May use a syringe for injection of agents that block the vas deferens. ○ Percutaneous injections techniques may require the use of ultrasound or other modalities to visualize the lumen of the vas deferens • Generally, these procedures are to be done using direct visualization or using special instruments for better visualization, although percutaneous procedures may be possible • In practice, all procedures are to be done under ASEPTIC AND ANTISEPTIC CONDITIONS.
Target use	Minimal and optimal: Blocking the vas deferens bilaterally by injecting an occluding agent.
Mode of action	The vas deferens blocking methods prevent the passage of sperm cells along the vas deferens to the ejaculatory ducts thereby preventing the release of sperm during an ejaculation. Importantly, there may be residual sperm cells in the portion of the vas deferens distal to the site of occlusion until around 12-weeks after the vas occlusion.
Considerations following the Medical Eligibility Criteria (MEC) for male voluntary surgical contraception(24)	1. Caution for young males because this group is more likely to have the procedure reversed versus older age groups (86, 87). 2. Caution for those with scrotal tumors, cysts, or previous injury, which should be managed before any procedure. 3. Delay the use of this method for men with local infection, systemic infection or gastroenteritis, filariasis or elephantiasis, undiagnosed intra-scrotal mass. 4. Potential special considerations for coagulation disorders, cryptorchidism, inguinal hernia, severe or advanced HIV clinical disease.

Efficacy	Minimal Use Less than 1% failure rate (less than 1% chance of pregnancy during one year of use)	Optimal Use Less than 0.1% failure rate (less than one pregnancy in one thousand couples during one year of use).
Time to azoospermia	8 to 12 weeks after the occlusion of the vas deferens ( )	
Reversal of vas occlusion to restore fertility No data in humans on reversal after removal of vas deferens occlusive agents.	Minimal Demonstration of sperm in ejaculate after reversal **at least 1 year** after vas deferens blocking	Optimal Demonstration of sperm in ejaculate after reversal **at least 3-years** after vas deferens blocking
	The vas deferens occlusion material may be a hydrogel or other material that may be biodegradable after a certain time as defined by the manufacturer. Reversal may also be through an injection to dissolve any previous blocking agent or by flushing the prior block. Presence of motile, morphologically normal sperm after the reversal procedure shows evidence of reversal. (Waller; Matsumoto et al 2025)	The vas deferens occlusion material may be a hydrogel or other material that may be biodegradable after a certain time to be defined by the manufacturer. Reversal may be through injection of another substance to dissolve the block or flushing the blocking material. or through ultrasound, or by removal of the blocking agent by chemical or mechanical means. Presence of motile, morphologically normal sperm after the reversal procedure shows evidence of reversal but does not equate return to fertility.
Side effect profile	Minimal	Optimal
	Pain at operative site and other complications very uncommon **< 5 %** of men.	Pain, hematoma, infection uncommon **(< 1%** of men). Use of new blocking agents needs to be evaluated in preclinical trials and monitored in post marketing phase 4 studies for possibility of carcinogenesis.

Duration and volume of instrument use	Mechanical and electrical devices.	Other requirements like autoclave/sterilizer, soaking solutions and high-level disinfectants.
Required instruments	Minimal The sharp and pointed vas dissecting forceps are reported to dull after 40-uses	Optimal The instruments last longer, especially if well maintained
Infrastructure **Depends on method or preferred technique of vas occlusion.**	Minimal For office or clinic- based procedures with area for privacy and antisepsis.	Optimal Surgical suites especially for surgical procedures.
Health workforce	Minimal Trained providers for counselling and screening for contraindications, and training for the procedure.	Optimal Trained service providers and primary care or family planning providers in a clinic set-up, at best with on-call and partner specialists who may address complications.
Product kit	The product be delivered by a disposable syringe injection system or kit This will differ from each manufacturer. Equipment in the kit should preferably leave minimal environmental footprint e.g. use compostable plastics as appropriate Preferably, all materials required for product use, including devices or other consumables should be included in a packaged, self-contained kit to be used for one individual The kit for use on one side of the scrotal sac may require another set (or partial use) for the other side.	
Additional consumables required but not provided within the product kit	In addition to the vas deferens blocking instruments — the method requires anesthetics and injections, drapes and operating gowns, running water for washing, and sterilization equipment for the instruments.	

	For injectable methods, the product will likely be delivered by a disposable syringe injection system or kit.	
Operating conditions	While most surgeons and health workers performing minor surgery prefer cooler air-conditioned rooms — vas deferens occlusion or vas deferens blocking is best done where temperatures are high enough to not cause retraction of the scrotum thus enabling the vas deferens to be manipulated more easily. “The temperature of the operating room should be at least 70 to 80 degrees F (approximately 20 to 25 degrees C)” ( )	
Training required	Minimal	Optimal
	Counselling and Basic-Comprehensive Family Planning in particular that vas occlusion may not be reversible. Training on a preferred method of blocking the vas deferens.	In-house capacity to address complications or have referral arrangements. Capacity for reversal/removal of the vas deferens blockade. In some countries, placement of the vas blocking agent may require completion of a certification course or be a board-certified urologist.
Clean water	Minimal: clean running water should be available for cleaning, washing and for instrument processing	
Waste/disposal requirements	**Minimal**	**Optimal**
	Minimally acceptable: Used containers should be discarded in household trash in a manner that prevents accidental application or ingestion by children or pets. Injection syringes and needles must be disposed of as per national guidelines	Ideal: Used containers are recyclable. Biological products are segregated in special leak proof biohazards containers and disposed of as per national guidelines Syringes are placed in puncture resistant sharps disposal containers and disposed of as per national guidelines

Regulatory requirements	Vas deferens occlusion male contraceptive will require registration as a medical device in accordance with national legislation and appropriate standard regulations [e.g. by Health Ministries or Departments, Medical Device Regulatory agencies, Health Insurance agencies, Environmental Agencies and other National/Sub-national Offices.] prior to clinical use. Additional approvals may be required depending on jurisdiction. For example, FDA approval would be required for US use and EU MDA approval within the EU. WHO provides a list of WHO listed Authorities i.e. *regulatory authorities (RA) or regional regulatory systems (RRS) that comply with all the relevant indicators and requirements specified by WHO for regulatory capability as defined by an established benchmarking and performance evaluation process.* *https://www.who.int/news-room/questions-and-answers/item/who-listed-authorities*
Cost per Acceptor, Couple-Year Protection	The range of costs of a surgical procedure for permanent male sterilization is from USD 150 and above. The range of costs of a surgical injectable kit for long-acting contraception is around USD 30 to 40, but the possible need to use one kit for each side may bring the costs to USD 50 to 75. Since these are highly effective permanent or long-acting methods, the couple-year protection would be at the highest level.

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