

SEXUAL AND REPRODUCTIVE HEALTH R&D SCOPE

This document sets out the sexual and reproductive health (SRH) research and development (R&D) activities that are included within the scope of the G-FINDER survey, as well as research activities that are excluded or partially excluded (restricted).

The intention of the G-FINDER SRH survey is to capture investment in SRH R&D that is relevant to and appropriate for the SRH needs of people and populations in low- and middle-income countries (LMICs), regardless of whether or not this investment explicitly targets LMICs.*

Accordingly, and in consultation with an international Expert Advisory Group, the G-FINDER SRH scope has been defined in line with the following overarching criteria:

1. The SRH area is a significant health issue affecting people in LMICs
2. There is a need for new products (i.e. there is no existing product, or improved or additional products are needed to meet the needs of people in LMICs)

The G-FINDER SRH survey only captures investments that support R&D for products that are suitable for addressing SRH issues amongst populations in LMICs that either do not already exist, or are inappropriate for resource-limited settings. As such, each SRH issue included in the survey may have further restrictions based on the specific R&D gaps identified. Restrictions that apply to each SRH issue and product category are set out in survey scope restrictions.

A quick overview of the SRH areas, products and technologies included in the G-FINDER survey is presented in the SRH R&D matrix.

A description of the G-FINDER survey scope restrictions by health issue, including product area inclusions and exclusions, are set out in the Scope restrictions by health issue section.

The R&D activities for each product area included within the scope of the survey are set out in the Scope by product section.

** For the purpose of the G-FINDER survey, the World Bank’s definitions of low- and middle-income countries are used*

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SRH R&D MATRIX

		Basic research	Drugs	Vaccines (preventive)	Vaccines (therapeutic)	Diagnostics	Devices & combinations
Contraception	On-demand*	-	✓	-	-	-	✓
	Short-acting†	-	✓	-	-	-	✓
	LARC‡	-	✓	-	-	-	✓
	Permanent§	-	✓	-	-	-	✓
HPV-related cervical cancer		<u>Restricted</u>	<u>Restricted</u>	<u>Restricted</u>	<u>Restricted</u>	✓**	-
Non-HIV sexually transmitted infections (STIs)	Syphilis	<u>Restricted</u>	<u>Restricted</u>	✓	✓	-	-
	Gonorrhoea	<u>Restricted</u>	<u>Restricted</u>	✓	✓	✓	-
	Chlamydia	<u>Restricted</u>	-	✓	✓	✓	-
	HSV-2	<u>Restricted</u>	✓	✓	✓	✓	-
	HTLV-1	✓	✓	✓	✓	✓	-
	Multiple STIs††	<u>Restricted</u>	<u>Restricted</u> ‡‡	✓	✓	✓	-
	Other STIs§§	<u>Restricted</u>	✓	✓	✓	✓	-
Post-partum haemorrhage (PPH)		-	✓	-	-	-	<u>Restricted</u>
Pre-eclampsia		<u>Restricted</u>	<u>Restricted</u>	-	-	✓	-
Other investment applicable to more than one sexual / reproductive health issue							
Multipurpose prevention technologies (MPTs)***		Platform technologies				Core funding of an SRH R&D organisation	
Drugs	Devices & combinations	Adjuvants & immunomodulators		Delivery technologies			
✓	✓	✓		✓			

✓ denotes a category where a disease or product is included in the survey

Restricted denotes a category where only some investments are eligible

* On-demand: methods that require action at the time of intercourse or pericoitally for efficacy (e.g. emergency contraception)

† Short-acting: methods that work for < 1 year but do not require action at the time of intercourse (e.g. injectable hormones)

‡ LARC: long-acting reversible contraceptives that work for ≥ 1 year (e.g. implants; IUDs)

§ Permanent: irreversible methods

** Includes both diagnostics for HPV infection and diagnostics for cervical lesions

†† Multiple STIs: two or more STIs, including but not limited to chlamydia, gonorrhoea, syphilis, and HIV

‡‡ Includes therapeutic drugs for the treatment of two or more STIs. For preventive drugs that address two or more STIs, please enter data under MPTs

§§ Other STIs: STIs that disproportionately affect populations in LMICs, including but not limited to trichomoniasis, chancroid, mycoplasma genitalium, lymphogranuloma venereum, and granuloma inguinale (donovanosis)

*** MPTs: preventive drugs (including microbicides) and devices & combinations that address two or more SRH indications in the following combinations: Contraceptive + HIV; Contraceptive + STI; Contraceptive + STI + HIV; STI + HIV; and more than one STI. If a product has action on two or more SRH issues not covered in the combinations listed previously, please enter data under MPTs > other.

SCOPE RESTRICTIONS BY HEALTH ISSUE

HPV-related cervical cancer

The scope of the inclusion of funding for HPV-related cervical cancer R&D is currently restricted in the following areas:

- **Basic research:** only includes basic research that is related to:
 - preventive vaccines, therapeutic vaccines, diagnostics or drugs
 - or basic research that is explicitly targeted at LMIC needs
- **Drugs:** only includes R&D for drugs to clear or prevent HPV infection. Anti-neoplastic drugs for cervical cancer are excluded
- **Preventive vaccines:** only includes R&D for vaccines that represent an improvement over existing products (e.g. single dose, expanded oncogenic HPV strain protection)
- **Therapeutic vaccines:** only includes R&D for vaccines to clear HPV infection.

Non-HIV sexually transmitted infections

Syphilis

The scope of the inclusion of funding for syphilis R&D is currently restricted in the following areas:

- **Basic research:** only includes basic research that is related to:
 - preventive vaccines, therapeutic vaccines, diagnostics or drugs
 - or basic research that is explicitly targeted at LMIC needs
- **Drugs:** only includes R&D for drugs to prevent or treat late latent, tertiary, maternal or congenital syphilis

Gonorrhoea

The scope of the inclusion of funding for gonorrhoea R&D is currently restricted in the following areas:

- **Basic research:** only includes basic research that is related to:
 - preventive vaccines, therapeutic vaccines, diagnostics or drugs
 - or basic research that is explicitly targeted at LMIC needs
- **Drugs:** only includes R&D for drugs to prevent or treat AMR gonorrhoea

Chlamydia

The scope of the inclusion of funding for chlamydia R&D is currently restricted in the following area:

- **Basic research:** only includes basic research that is related to:
 - preventive vaccines, therapeutic vaccines, diagnostics or drugs
 - or basic research that is explicitly targeted at LMIC needs

HSV-2

The scope of the inclusion of funding for HSV-2 R&D is currently restricted in the following area:

- **Basic research:** only includes basic research that is related to:
 - preventive vaccines, therapeutic vaccines, diagnostics or drugs
 - or basic research that is explicitly targeted at LMIC needs

Multiple STIs

The scope of the inclusion of funding for R&D for multiple STIs is currently restricted in the following areas:

- **Basic research:** only includes basic research that is related to:
 - preventive vaccines, therapeutic vaccines, diagnostics or drugs
 - or basic research that is explicitly targeted at LMIC needs
- **Drugs:** only includes R&D for therapeutic drugs for multiple STIs. Preventive drugs for two or more STIs are included in the MPTs section of the survey

Other STIs

The scope of the inclusion of funding for R&D for other STIs is currently restricted in the following area:

- **Basic research:** only includes basic research related to preventive vaccines, therapeutic vaccines, diagnostics or drugs to address other STIs that disproportionately affect populations in LMICs, such as trichomoniasis, chancroid, mycoplasma genitalium, lymphogranuloma venereum, granuloma inguinale (donovanosis)

Post-partum haemorrhage

The scope of the inclusion of funding for pre-eclampsia R&D is currently restricted in the following area:

- **Devices and combinations:** only includes devices to treat PPH by targeting the underlying pathophysiology (e.g. uterine atony). Devices for use during PPH to treat shock alone (e.g. non-pneumatic anti-shock garments) have potential applications beyond PPH and so funding towards these devices cannot be considered purely SRH targeted funding. These devices are excluded

Pre-eclampsia

The scope of the inclusion of funding for pre-eclampsia R&D is currently restricted in the following areas:

- **Basic research:** only includes basic research that is related to:
 - preventive drugs or diagnostics,
 - or disease pathogenesis
 - or natural history and epidemiology, clinical diagnosis, and disease presentation in LMIC populations. Research that is related to epidemiology, clinical diagnosis, and disease presentation in HIC settings is excluded
- **Drugs:** only includes R&D for drugs to prevent pre-eclampsia. Drugs to treat pre-eclampsia are excluded

SRH R&D SCOPE DOCUMENT

I. BASIC RESEARCH

Studies that increase scientific knowledge and understanding about the disease, disease processes, or pathogen, but which are not yet directed towards a specific product.

1. NATURAL HISTORY AND EPIDEMIOLOGY

- 1.1 Basic mechanisms of disease transmission
- 1.2 Disease prevalence in relation to human genotype, strain variation, and inoculation rates
- 1.3 Genetic diversity and phylogeny
- 1.4 Epidemiological research on the roles of human behaviour and effects of specific host genotypes on disease transmission
- 1.5 Epidemiological research on host genetic factors influencing the prevalence of disease (e.g. sickle cell, HLA type, Rh factor) or the impact of disease in select host genotypes
- 1.6 Epidemiological research on the distribution of pathogen that is NOT related to the development of a specific product
- 1.7 Epidemiological research on the prevalence of morbidity and mortality due to the disease that is NOT related to specific product development
- 1.8 Epidemiological research on antigenic variability; population studies of human immunity to the disease
- 1.9 Epidemiology for drug resistance or evolutionary studies on resistance development for established, existing drugs

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2. IMMUNOLOGY OF DISEASE

- 2.1 Defining signalling pathways of immune function (mechanisms of systemic and/or mucosal immunity)
- 2.2 Interaction and impact of the signalling pathways with the pathogen
- 2.3 Development of assays or tools potentially useful for drug, vaccine, or microbicide research and development
- 2.4 Identification of immune correlates of protection, including in vivo and in vitro studies on the protective immune response (cellular, humoral and/or mucosal)
- 2.5 Investigating the immune response to particular antigens; studies of specific antigens or immunogens proposed as vaccine candidates
- 2.6 Development of animal models to determine immune correlates of protection
- 2.7 Genetics of the immune response to the disease and effects of antigen polymorphism or genetic diversity on specific vaccine candidates (as recognised from field studies)

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3. BIOLOGY OF DISEASE

- 3.1 Structure and morphology of different developmental stages of the pathogen
- 3.2 Host-parasite interactions and biology
- 3.3 Biology of invasion of host cells (entry mechanisms)
- 3.4 Localisation of pathogen proteins or antigens

- 3.5 Development of culture and purification tools to assist in the study of the pathogen
- 3.6 Descriptions of pathogenic species and characterisation of strains or subtypes in animal models (course of infection, susceptibility of different hosts)
- 3.7 *In vitro* studies of interactions between the pathogen and other infectious agents

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4. BIOCHEMISTRY OF THE PATHOGEN

- 4.1 Metabolism and nutrition
- 4.2 Protein sequencing, enzymology, and protein and enzyme characterisation (including antigen analysis)
- 4.3 Signal transduction; translation, processing and export of proteins
- 4.4 Glycosylation, Glycosylphosphatidylinositol (GPI) anchors, transporters, ion channels, mitochondrial metabolism, and electrophysiology studies
- 4.5 Influence of the pathogen on host-cell biochemistry
- 4.6 Characterisation of antigen/protein diversity of pathogenic strains and subtypes
- 4.7 Characterisation of proteins and molecular basis for host-cell invasion
- 4.8 Analysis & characterisation of drug-resistant strains and studies probing drug resistance mechanism/s or pathways
- 4.9 Non-specific research on the pathogen or host targets to identify potential drug, vaccine, or diagnostic targets (i.e. target identification)

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5. GENETICS OF THE PATHOGEN

- 5.1 Studies on chromosomes; genomic maps; genetic crosses
- 5.2 Cloning and sequencing of genes; cDNAs for functional proteins (including drug targets and vaccine candidates)
- 5.3 Expression of proteins from cloned genes; RNA analyses
- 5.4 Control and timing of gene expression; post-transcriptional processing
- 5.5 Analysis and characterisation of genes involved in drug resistance
- 5.6 Genetics of antigenic variability
- 5.7 Techniques for the genetic transformation of the pathogen
- 5.8 Tests for genotyping the pathogen for laboratory use

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6. BIOINFORMATICS AND PROTEOMICS

- 6.1 Microarray analysis
- 6.2 Genome annotation - gene predictions
- 6.3 Comparative genomics, sequence alignment, genome assembly
- 6.4 Variation, single nucleotide polymorphisms (SNPs)
- 6.5 Database applications, data mining tools
- 6.6 Structural and functional genomics
- 6.7 Structural and functional proteomics
- 6.8 Proteome analysis, protein structure alignment

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7. PATHOPHYSIOLOGY AND DISEASE SYMPTOMS

- 7.1 Clinical diagnosis and clinical observations of the disease presentation and pathophysiology
- 7.2 The role of nutritional status in determining disease severity and treatment effectiveness
- 7.3 Histopathology of the disease
- 7.4 The mechanisms of pathology of the disease; including, the role of the host immune system, and expression of adhesion molecules
- 7.5 Development of improved animal models to study disease pathophysiology, to evaluate the biological properties of drugs and microbicides
- 7.6 Identification of biomarkers for diagnostics or therapeutic monitoring
- 7.7 Studies of the mechanisms by which particular susceptible/resistant mammalian host genotypes exert their effect
- 7.8 Research on the effects of host co-morbidities and secondary effects of pathogen invasion
- 7.9 Interactions between the disease and other relevant concurrent infections, including determining timing and establishment of infection

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II. DRUGS

Research activities and processes necessary to develop and improve new small molecule compounds specifically intended to address SRH issues; including drug design, preclinical and clinical development, and other activities essential for successful drug development and uptake. This category includes preventive and therapeutic drugs, including microbicides.

Only includes R&D for drugs being developed that will be suitable for use in LMICs (e.g. heat stable, easy to use).

NOTE: *R&D for drugs (including microbicides) designed to prevent two or more STIs are considered by G-FINDER to be multi-purpose preventive technologies*

8. DISCOVERY AND PRECLINICAL

Research activities targeted at discovering and optimising investigational small molecule compounds, including the processes needed to allow new chemical entities to proceed to human trials; including:

- 8.1 Specific research aimed at discovery of topical applications for microbicide use (e.g. vaginal defence enhancers, surfactants, entry/fusion inhibitors and replication inhibitors)
- 8.2 Target validation, characterisation, and selection
- 8.3 High throughput screening, lead optimisation
- 8.4 Preclinical evaluation of microbicide candidates including determination of acceptable formulation and delivery modes
- 8.5 Studies supporting safety & immunogenicity testing in animal models and looking at *in vitro* correlates of *in vivo* protective response
- 8.6 Development of analytical tests for assaying drugs, including the development of animal models
- 8.7 Developing reagents and standardised methods to assess microbicide-induced immune response in animals and humans

- 8.8** Research on drugs from natural products; identification and characterisation of active ingredient
- 8.9** Measurement of the activity of potential drugs *in vitro* and in animal models; including safety and efficacy studies necessary to satisfy Investigational New Drug (IND) requirements
- 8.10** Studies evaluating the activity of new drugs on drug-resistant strains, their effect on genes involved in drug resistance, or their effect on resistance pathways
- 8.11** Development of tests for drug susceptibility of the pathogen for research purposes
- 8.12** Drug pharmacokinetic, toxicity and metabolism studies *in vitro* and in animal models, including bioavailability, adsorption, metabolism, and excretion (ADME) studies
- 8.13** Chemistry and synthesis of drugs, including process and scale-up manufacture, production of Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) batch for toxicology studies; and other Chemistry and Manufacture Control (CMC) activities required to allow new chemical entities to proceed to human trials
- 8.14** Optimisation of microbicide candidates, bioprocess development, formulation and mode of delivery of novel prevention tools for broad international use including production of Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP)-grade product for regulatory toxicology studies
- 8.15** Preparation of Investigational New Drug (IND) application for regulatory submission
- 8.16** Optimisation and manufacturing of new formulations to support label-expansion^{†††} for new patient sub-populations (e.g. infants, pregnant women)

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9. CLINICAL DEVELOPMENT - PHASE I

First-in-human clinical trials to determine safety and tolerability of investigational new drugs in a small group of patients or healthy volunteers; including:

- 9.1** Phase Ia single ascending dose studies to determine pharmacokinetics, pharmacodynamics and maximum tolerated dose
- 9.2** Phase Ib multiple ascending dose studies to determine the pharmacokinetics, pharmacodynamics, safety and tolerability of multiple doses
- 9.3** Trials of food effect or drug-drug interactions

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10. CLINICAL DEVELOPMENT - PHASE II

Clinical trials to determine the efficacy, safety and therapeutic dose of investigational new drugs in a small set of human subjects (up to several hundred); including:

- 10.1** Phase IIa proof of concept studies to demonstrate clinical efficacy or biological activity
- 10.2** Phase IIb dose-finding studies to determine dose with optimum biological activity with minimal adverse effects

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^{†††} Label-expansions refer to changes to drugs or their labels after they have been approved. This includes changes in manufacturing, recommended patient population and/or formulation. To change a label, market a new dosage or strength of a drug, or change the way a drug is manufactured, the company must submit a supplemental new drug application (sNDA) to regulatory authorities to obtain marketing approval

11. CLINICAL DEVELOPMENT - PHASE III

Clinical trials to support the registration of investigational new drugs or label-expansion of already registered drugs in a trial population large enough to provide statistical significance (from several hundred to several thousand); including:

- 11.1** Regulatory standard clinical trials to assess effectiveness of a new drug against current 'gold standard'
- 11.2** Regulatory standard clinical trials that support a formal registration for label-expansion* of an existing drug to a new disease or patient group (e.g. pregnant women or HIV-positive patients)
- 11.3** Regulatory standard clinical trials that support formal registration for label-expansion* of an existing drug to a new use, such as intermittent preventative therapy and pre-exposure prophylaxis

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12. CLINICAL DEVELOPMENT - BASELINE EPIDEMIOLOGY

Studies evaluating potential trial site populations to serve as the foundation for determining the optimal collection, analysis, interpretation and presentation of clinical trial data; including:

- 12.1** Epidemiological studies directly linked to the conduct or support of clinical trials of products in development, in order to assess or validate the epidemiology or incidence of SRH issues, or the health of target populations at trial sites
- 12.2** Preliminary studies of morbidity and mortality at potential clinical trial sites, where these studies are directly linked to planned product trials
- 12.3** Pre-trial activities designed to understand trial site conditions before the commencement of trials and to facilitate engagement

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13. CLINICAL DEVELOPMENT - UNSPECIFIED

Other costs required to support clinical testing of investigational new drugs as needed for regulatory approval; including:

- 13.1** Infrastructure and site development costs directly associated with the conduct of clinical trials for drug development in LMICs (e.g. refurbishment of hospital wing, vehicle purchase, generators, training and community relationship building)
- 13.2** Further pharmaceutical development to generate the final clinical formulation, dosage form and other Chemistry and Manufacture Control (CMC) activities required for regulatory submission
- 13.3** Compiling of all non-clinical and clinical data for submission of a New Drug Application (NDA) to regulatory authorities
- 13.4** Behavioural research prior to registration relating to risk assessment, factors affecting adherence to protocol, and product acceptability
- 13.5** Protocol development, investigator meetings, Good Clinical Practice (GCP)-monitoring, quality control, data management, analysis and reporting, establishing a Data Safety Monitoring Board (DSMB), and trial audits

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14. POST-REGISTRATION STUDIES

Studies relating to the detection, monitoring, evaluation, and prevention of adverse events associated with newly approved drugs so as to bridge the gap between highly controlled clinical trials intended for regulatory approval and the largely uncontrolled use of new drugs by patients. Also includes studies conducted after regulatory approval that assess drug effectiveness in the wider population or which are necessary to support product use in LMICs.

- 14.1** Pharmacovigilance and post-registration studies of newly registered drugs to assess adverse reactions, toxicology and safety
- 14.2** Effectiveness studies and head-to-head comparator studies of newly registered drugs (with other therapies or interventions)
- 14.3** Cost-effectiveness studies of newly registered drugs
- 14.4** Treatment interactions and population level studies (of newly registered products e.g., pharmaco-epidemiological and resistance studies)
- 14.5** Behavioural research post-registration of new drugs relating to risk assessment, factors affecting adherence to protocol, provider compliance, and product acceptability
- 14.6** Case history reports and assessment of long-term prophylaxis using newly registered drugs in communities in LMICs

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III. VACCINES (PREVENTIVE)

Research activities and processes necessary to develop and improve investigational vaccines specifically intended to prevent infection or disease; including vaccine design, preclinical and clinical development and other activities essential for successful vaccine development and uptake.

Only includes R&D for preventive vaccines being developed that will be suitable for use in LMICs.

15. DISCOVERY AND PRECLINICAL

Research activities targeted at discovering and optimising investigational vaccines, including the processes needed to allow new chemical entities to proceed to human trials; including:

- 15.1** Studies supporting novel vaccine design, including target validation & candidate optimisation
- 15.2** Development of animal models to assist in vaccine design and testing
- 15.3** Evaluation of vaccine technologies (e.g. adjuvants, delivery systems) to improve the immunogenicity of an identified candidate
- 15.4** Preclinical safety and immunogenicity studies with candidate vaccines, including use or development of functional assays
- 15.5** Preclinical animal studies, challenge models and addressing the correlation between *in vitro* models, animal models and field results
- 15.6** Studies on the genetics of the immune response to selected antigens as vaccine candidates, optimisation of animal models and correlates to clinical results
- 15.7** Manufacturing scale-up and consistency of manufacture, including production of Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) batches for regulatory toxicology studies and other Chemistry and Manufacture Control (CMC) activities required to allow a candidate vaccine to proceed to human trials
- 15.8** Research on safety and regulatory considerations (e.g. validation of preclinical assays to permit registration)
- 15.9** Preparation of an Investigational New Drug (IND) application for regulatory submission

- 15.10** Optimisation of vaccine candidates for global use (cheaper, more stable, improving ease of administration, addition of LMIC-specific strains)

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16. CLINICAL DEVELOPMENT - PHASE I

First-in-human clinical trials to determine the safety of investigational new vaccines for the first time in human subjects (up to one hundred); including:

- 16.1** Phase Ia studies assessing safety, dosing, and immunogenicity in human volunteers
- 16.2** Phase Ib studies assessing safety, dosing, and immunogenicity in clinically exposed or high-risk populations

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17. CLINICAL DEVELOPMENT - PHASE II

Clinical trials to continue to determine the efficacy and safety of investigational new vaccines in a small set of human subjects (typically several hundred); including:

- 17.1** Phase IIa challenge studies
- 17.2** Phase IIb safety and preliminary efficacy studies in exposed populations or those at high-risk of infection

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18. CLINICAL DEVELOPMENT - PHASE III

Clinical trials to demonstrate the safety and efficacy in a larger human subject population (from several hundred to several thousand) and support the registration of investigational new vaccines; including:

- 18.1** Expanded efficacy, effectiveness and safety studies required for registration purposes, including implementation, retention and follow-up of volunteers

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19. CLINICAL DEVELOPMENT - BASELINE EPIDEMIOLOGY

Studies evaluating potential trial site populations to serve as the foundation for determining the optimal collection, analysis, interpretation and presentation of clinical trial data; including:

- 19.1** Epidemiological studies directly linked to the conduct or support of clinical trials of preventive vaccines in development, in order to assess or validate the epidemiology of disease, disease incidence, or health of target populations at trial sites
- 19.2** Preliminary studies of morbidity and mortality at potential clinical trial sites, where these studies are directly linked to planned preventive vaccines trials
- 19.3** Pre-trial activities designed to understand trial site conditions before the commencement of trials and to facilitate engagement

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20. CLINICAL DEVELOPMENT - UNSPECIFIED

Other costs required to support clinical testing of investigational new vaccines as needed for regulatory approval; including:

- 20.1** Infrastructure and site development costs associated with the conduct of clinical trials for vaccine development in LMICs (e.g. refurbishment of hospital wing, vehicle purchase, generators, training and community relationship building)

- 20.2** Further biological/product development to generate the optimal clinical formulation and dosage form, and other Chemistry and Manufacture Control (CMC) activities required for regulatory submission
- 20.3** Compiling all non-clinical and clinical data to obtain a Biologics License from regulatory authorities
- 20.4** Behavioural research during clinical trials relating to risk assessment, factors affecting adherence to protocol, and product acceptability
- 20.5** Protocol development, investigator meetings, Good Clinical Practice (GCP) monitoring, quality control, data management, analysis and reporting, establishing a Data Safety Monitoring Board (DSMB) and trial audits

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21. POST-REGISTRATION STUDIES

Studies relating to the detection, monitoring, evaluation, and prevention of adverse events associated with newly approved vaccines so as to bridge the gap between highly controlled clinical trials intended for regulatory approval and the largely uncontrolled delivery of new vaccines. Also includes studies conducted after regulatory approval that assess vaccine effectiveness in the wider population or which are necessary to support product use in LMICs.

- 21.1** Pharmacovigilance and post-registration studies of newly registered preventive vaccines to assess adverse reactions, toxicology and safety
- 21.2** Effectiveness studies and head-to-head comparator studies of newly registered preventive vaccines (with other therapies or interventions)
- 21.3** Cost-effectiveness studies of newly registered preventive vaccines
- 21.4** Treatment interactions and population level studies (of newly registered preventive vaccines e.g., pharmaco-epidemiological and resistance studies)
- 21.5** Behavioural research post-registration of new preventive vaccines relating to risk assessment, factors affecting adherence to protocol, provider compliance, and product acceptability
- 21.6** Case history reports and assessment of long-term prophylaxis using newly registered preventive vaccines in communities in LMICs

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IV. VACCINES (THERAPEUTIC)

Research activities and processes necessary to develop and improve investigational vaccines specifically intended to treat infection; including vaccine design, preclinical and clinical development, and other activities essential for successful vaccine development and uptake.

Only includes R&D for therapeutic vaccines being developed that will be suitable for use in LMICs.

22. DISCOVERY AND PRECLINICAL

Research activities targeted at discovering and optimising investigational vaccines and including the processes needed to allow new chemical entities to proceed to human trials; including:

- 22.1** Studies supporting novel vaccine design including target validation and candidate optimisation
- 22.2** Evaluation of vaccine technologies (e.g. adjuvants, delivery systems) to improve the immunogenicity of an identified candidate
- 22.3** Preclinical safety and immunogenicity studies with candidate vaccines, including use or development of functional assays

- 22.4** Preclinical animal studies, challenge models, and studies addressing the correlation between *in vitro* models, animal models and field results
- 22.5** Studies on the genetics of the immune response to selected antigens as vaccine candidates, optimisation of animal models and correlates to clinical results
- 22.6** Manufacturing scale-up and consistency of manufacture, including production of Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) batches for regulatory toxicology studies and other Chemistry and Manufacture Control (CMC) activities required to allow a candidate vaccine to proceed to human trials
- 22.7** Research on safety and regulatory considerations (e.g. validation of preclinical assays to permit registration)
- 22.8** Preparation of an Investigational New Drug (IND) application for regulatory submission
- 22.9** Optimisation of vaccine candidates for global use (cheaper, more stable, ease of administration, addition of LMIC-specific targets)

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23. CLINICAL DEVELOPMENT - PHASE I

Clinical trials to determine the safety of investigational new vaccines for the first time in human subjects (up to a hundred); including:

- 23.1** Phase Ia studies assessing safety, dosing, and immunogenicity in human volunteers
- 23.2** Phase Ib studies assessing safety, dosing, and immunogenicity in clinically exposed or high-risk populations

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24. CLINICAL DEVELOPMENT - PHASE II

Clinical trials to continue to determine the efficacy and safety of investigational new vaccines in a small set of human subjects (typically several hundred); including:

- 24.1** Phase IIa challenge studies
- 24.2** Phase IIb safety and preliminary efficacy studies in exposed populations or those at high-risk of infection

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25. CLINICAL DEVELOPMENT - PHASE III

Clinical trials to demonstrate the safety and efficacy in a larger human subject population (from several hundred to several thousand) and support the registration of investigational new vaccines; including:

- 25.1** Expanded efficacy, effectiveness and safety studies required for registration purposes, including implementation, retention and follow-up of volunteers

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26. CLINICAL DEVELOPMENT - BASELINE EPIDEMIOLOGY

Studies evaluating potential trial site populations to serve as the foundation for determining the optimal collection, analysis, interpretation and presentation of clinical trial data; including:

- 26.1** Epidemiological studies directly linked to the conduct or support of clinical trials of therapeutic vaccines in development, in order to assess or validate the epidemiology of disease, disease incidence, or health of target populations at trial sites
- 26.2** Preliminary studies of morbidity and mortality at potential clinical trial sites, where these studies are directly linked to planned therapeutic vaccines trials

- 26.3** Pre-trial activities designed to understand trial site conditions before the commencement of trials and to facilitate engagement

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27. CLINICAL DEVELOPMENT - UNSPECIFIED

Other costs required to support clinical testing of investigational new vaccines as needed for regulatory approval; including:

- 27.1** Infrastructure and site development costs associated with the conduct of clinical trials for vaccine development in LMICs (e.g. refurbishment of hospital wing, vehicle purchase, generators, training and community relationship building)
- 27.2** Further biological/product development to generate the optimal clinical formulation and dosage form, and other Chemistry and Manufacture Control (CMC) activities required for regulatory submission
- 27.3** Compiling all non-clinical and clinical data to obtain a Biologics License from regulatory authorities
- 27.4** Behavioural research during clinical trials relating to risk assessment, factors affecting adherence to protocol, and product acceptability
- 27.5** Protocol development, investigator meetings, Good Clinical Practice (GCP) monitoring, quality control, data management, analysis and reporting, establishing a Data Safety Monitoring Board (DSMB) and trial audits

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28. POST-REGISTRATION STUDIES

Studies relating to the detection, monitoring, evaluation, and prevention of adverse events associated with newly approved vaccines so as to bridge the gap between highly controlled clinical trials intended for regulatory approval and the largely uncontrolled delivery of new vaccines. Also includes studies conducted after regulatory approval that assess vaccine effectiveness in the wider population or which are necessary to support product use in LMICs.

- 28.1** Pharmacovigilance and post-registration studies of newly registered therapeutic vaccines to assess adverse reactions, toxicology and safety
- 28.2** Effectiveness studies and head-to-head comparator studies of newly registered therapeutic vaccines (with other therapies or interventions)
- 28.3** Cost-effectiveness studies of newly registered therapeutic vaccines
- 28.4** Treatment interactions and population level studies (of newly registered therapeutic vaccines e.g., pharmaco-epidemiological and resistance studies)
- 28.5** Behavioural research post-registration of new therapeutic vaccines relating to risk assessment, factors affecting adherence to protocol, provider compliance, and product acceptability
- 28.6** Case history reports using newly registered therapeutic vaccines in communities in LMICs

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V. DIAGNOSTICS

Research activities and processes necessary to develop, optimise, and validate diagnostic tests; including discovery and design, preclinical and clinical evaluation, and other activities for successful deployment for public health use.

Only includes R&D for diagnostics being developed that will be suitable for use in resource-limited settings, or in support of registration of suitable diagnostics in LMICs (e.g. heat stable, easy to use).

29. DISCOVERY AND PRECLINICAL

Research activities targeted at discovering and optimising heat stable, reliable, easy-to-use diagnostics, including the processes necessary to allow a potential product to proceed to clinical evaluation including:

- 29.1** Validation, characterisation, and selection of targets suitable for diagnostic use
- 29.2** Validation of new diagnostic markers or biomarkers
- 29.3** Development and testing of stable, easy-to-use diagnostic tests (e.g. improved sample collection/preparation, cheaper ELISA assays), including manufacturing design
- 29.4** New or improved diagnostics for disease staging and therapy decisions
- 29.5** New or improved diagnostics to identify specific target populations
- 29.6** Tailoring diagnostic tools for LMIC-specific use, including improved point-of-care tests (rapid test), local laboratory test, reference laboratory tests and central laboratory tests
- 29.7** Creation of reference material banks

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30. CLINICAL EVALUATION

Activities and processes associated with clinical evaluation of investigational diagnostic tools so as to demonstrate sensitivity and specificity in human subjects, together with other costs required to support such clinical trials; including:

- 30.1** Clinical efficacy trials
- 30.2** Small-scale testing in humans to establish sensitivity and specificity and utility
- 30.3** Technical evaluation of tests and studies evaluating product performance
- 30.4** Establishment of product specifications, kit development and quality assurance
- 30.5** Submission of relevant data to regulatory authorities for approval
- 30.6** Assessment & validation of trial sites to carry out product trials
- 30.7** Infrastructure and site development costs directly associated with the conduct of clinical trials for diagnostic development (e.g. refurbishment of hospital wing, vehicle purchase, generators, training and community relationship building)

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31. OPERATIONAL RESEARCH FOR DIAGNOSTICS

Operational procedures and implementation activities associated with novel diagnostic tools, which are necessary to support World Health Organization recommendations for global public health use; including:

- 31.1** Larger-scale demonstration studies (assessing specificity, sensitivity and utility of the diagnostic test)
- 31.2** Cost-effectiveness studies assessing the diagnostic test

- 31.3 Identification of pitfalls of the technology and studies of safety measures needed to support the technology
- 31.4 Studies to determine at what level of the health care system the technology is applicable (e.g. reference labs, regional labs)
- 31.5 Identification of training needs
- 31.6 Collecting evidence for expanding the use of a diagnostic tool in different countries
- 31.7 Development of equipment and customer support documents
- 31.8 Head-to-head comparator studies (with current gold standard) and in the context of existing diagnostic algorithms
- 31.9 Behavioural research relating to risk assessment, factors affecting diagnostics use, and user acceptability (patient and provider)
- 31.10 Epidemiological studies to assess or validate the epidemiology of disease, disease incidence or health of target populations at potential trial sites, and which are directly linked to clinical trials of a new diagnostic

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VI. DEVICES AND COMBINATION PRODUCTS

Definitions:

A **device** is defined as an instrument, appliance, or other similar article intended to be used either to prevent pregnancy directly (e.g. copper intrauterine device) or facilitate the delivery of a contraceptive (e.g. intrauterine inserter), or to control post-partum haemorrhage (e.g. tools to assist bimanual compression). To be classified as a “device” in the G-FINDER survey, the technology must not contain a pharmaceutical element.

A **combination product** is defined as the combination of an instrument, appliance, or other similar article with a **pharmaceutical element** which are intended to prevent pregnancy, or the transmission of HIV or other STIs. To be classified as a “combination product”, the therapeutic properties of the product must only be achieved when the device would not provide protection independently, and/or is involved in the delivery of the drug (e.g. hormone- or antiviral-releasing vaginal ring, contraceptive implant).

Inclusions:

This section includes research activities and processes to develop or improve investigational devices and combination products; including device and combination product design, preclinical and clinical development, and other activities essential for successful device and combination product development and uptake.

Only includes R&D to develop devices and combination products that are suitable for use in LMICs (e.g. heat stable, easy to use).

32. DISCOVERY AND PRECLINICAL

Research activities targeted at discovering and optimising investigational compounds and including the processes needed to allow new devices and combination products to proceed to human trials; including:

- 32.1 Engineering analysis and testing, computational simulation, or biocompatibility testing including immunogenicity and carcinogenicity testing
- 32.2 Animal model testing of devices and combination products
- 32.3 Development and testing of heat stable, easy to use devices and combination products, including manufacturing design
- 32.4 New or improved devices and combination products for specific target populations
- 32.5 Creation of reference material banks

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33. CLINICAL DEVELOPMENT - PHASE I

Clinical trials to determine the safety of investigational new device and combination products for the first time in human subjects (up to a hundred); including:

- 33.1** Studies to determine the safety and tolerability of a device or combination product
- 33.2** Studies to determine the PK/PD of a combination product

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34. CLINICAL DEVELOPMENT - PHASE II

Clinical trials to continue to determine the efficacy and safety of investigational new drugs in a small set of human subjects (typically several hundred); including:

- 34.1** Phase IIa or proof of concept studies to demonstrate clinical efficacy or biological activity
- 34.2** Phase IIb or dose-finding studies to determine dose with optimum biological activity with minimal adverse effects

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35. CLINICAL DEVELOPMENT - PHASE III

Clinical trials to support the registration of investigational new devices and combination products and label-expansion of already registered devices and combination products in a larger group of people (from several hundred to several thousand); including:

- 35.1** Regulatory standard clinical trials to assess effectiveness of a new device or combination product against current 'gold standard'
- 35.2** Regulatory standard clinical trials that support formal registration for label-expansion* of an existing device or combination product to a new use, such as intermittent preventative therapy and pre-exposure prophylaxis

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36. CLINICAL DEVELOPMENT - UNSPECIFIED

Other costs required to support clinical testing of investigational new drugs as needed for regulatory approval; including:

- 36.1** Early and traditional feasibility studies to evaluate device design with respect to clinical safety, functionality, and efficacy
- 36.2** Pivotal studies to provide definitive evidence of the safety and efficacy of a device
- 36.3** Infrastructure and site development costs directly associated with the conduct of clinical trials for drug development in LMICs (e.g. refurbishment of hospital wing, vehicle purchase, generators, training and community relationship building)
- 36.4** Further pharmaceutical development to generate the final clinical formulation, dosage form and other Chemistry and Manufacture Control (CMC) activities required for regulatory submission
- 36.5** Compiling of all non-clinical and clinical data for submission of a New Drug Application (NDA) to regulatory authorities
- 36.6** Behavioural research **prior to registration** relating to risk assessment, factors affecting adherence to protocol, and product acceptability

- 36.7** Protocol development, investigator meetings, Good Clinical Practice (GCP)-monitoring, quality control, data management, analysis and reporting, establishing a Data Safety Monitoring Board (DSMB), and trial audits

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37. OPERATIONAL RESEARCH

Operational procedures and implementation activities associated with novel devices and contraceptive combination products, which are necessary to support global public health use; including:

- 37.1** Larger-scale demonstration studies (assessing utility of devices and combination products in LMICs)
- 37.2** Cost-effectiveness studies
- 37.3** Identification of pitfalls of the device or combination product and studies of safety measures needed to support the product
- 37.4** Identification of training needs
- 37.5** Collecting evidence for expanding the use of a device or combination product in different countries
- 37.6** Development of equipment and customer support documents
- 37.7** Head-to-head comparator studies and in the context of existing treatment algorithms
- 37.8** Behavioural research relating to risk assessment, factors affecting device and combination product use, and user acceptability (patient and provider)
- 37.9** Epidemiological studies to assess or validate the epidemiology of target populations at potential trial sites, and which are directly linked to clinical trials of a new device or combination product

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38. POST-REGISTRATION STUDIES

Studies relating to the detection, monitoring, evaluation, and prevention of adverse events associated with newly approved devices and combination products so as to bridge the gap between highly controlled clinical trials intended for regulatory approval and the largely uncontrolled use of new devices and combination products by patients. Also includes studies conducted after regulatory approval that assess device and combination product effectiveness in the wider population or which are necessary to support product use in LMICs.

- 38.1** Pharmacovigilance and post-registration studies of newly registered devices and combination products to assess adverse reactions, toxicology and safety
- 38.2** Effectiveness studies and head-to-head comparator studies of newly registered devices and combination products (with other therapies or interventions)
- 38.3** Cost-effectiveness studies of newly registered devices and combination products
- 38.4** Treatment interactions and population level studies (of newly registered products e.g., pharmaco-epidemiological and resistance studies)
- 38.5** Behavioural research post-registration of new devices and combination products relating to risk assessment, factors affecting adherence to protocol, provider compliance, and product acceptability
- 38.6** Case history reports and assessment of long-term prophylaxis using newly registered devices and combination products in communities in LMICs

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VII. CANNOT BE ALLOCATED TO ONE SRH ISSUE

39. MULTIPURPOSE PREVENTION TECHNOLOGIES (MPTS)

Definition:

To be an MPT, a product must have at least two of the following SRH indications: protection from HIV, protection from non-HIV STIs, and protection from unintended pregnancy. Acceptable combinations include Contraceptive + HIV; Contraceptive + STI; Contraceptive + STI + HIV; STI + HIV; two or more STIs. If a product has two or more SRH indications not covered in these combinations, enter data under MPT > other; multipurpose products with actions other than prevention are also included in this category (e.g. a combined menstrual cup and contraceptive device).

Inclusions:

Research activities and processes to develop or improve an MPT. MPTs include drugs (including microbicides), devices and combination products. Eligible investments include product discovery or design, pre-clinical and clinical development and other activities essential for successful product development and update.

If an MPT is in development for more than one indication, the earliest phase of clinical development for any individual indication listed for that product is considered the overarching development stage of that MPT. For example, a product in a phase III trial for STI prevention and in a phase II proof of concept trial for HIV prevention would be categorised as a phase II an MPT.

Only includes R&D to develop MPTs suitable for use in LMICs.

39.1 Drugs (including microbicides)

See section II for a full outline of the R&D activities included under this product category
ONLY includes R&D to develop drugs and microbicides that are a) heat stable, and b) easy to use.

39.2 Devices and combination products

See section VI for a full outline of the R&D activities included under this product category
ONLY includes R&D to develop devices and combination products that are a) heat stable, and b) easy to use.

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40. PLATFORM TECHNOLOGIES

Platform technologies are tools that can be applied to a range of areas, but which are not yet focused on a particular disease, health issue or product. The platform technology category includes adjuvants and immunomodulators, and delivery technologies.

40.1 ADJUVANTS AND IMMUNOMODULATORS

Adjuvants and immunomodulators are compounds or structures that aim to improve, modulate or potentiate the immune response. These include compounds such as CpG oligonucleotides, lipopolysaccharide derivatives, Toll-like receptor agonists, chemokines, and cytokines.

Only includes funding for R&D which meets the following conditions:

- a) It is research that is not directed towards a specific disease, health issue or product
- b) It is aimed at developing safer, cheaper, more immunogenic adjuvants and immunomodulators suitable for use in developing country products
- c) The resulting research findings or leads must be accessible to organisations developing pharmaceutical or biological products for SRH issues

40.2 DELIVERY TECHNOLOGIES

Delivery technologies comprise mucosal delivery tools, vaccine carrier systems, and alternative delivery technologies that facilitate the successful delivery of pharmaceutical or biological products in a resource-limited setting.

Only includes funding for R&D which meets the following conditions:

- a) It is research that is not directed towards a specific disease, issue or product
- b) It is research aimed at developing cheaper, faster, more user friendly delivery technologies and devices, suitable for use in resource-limited settings

Examples of R&D for delivery technologies included in the survey scope include micro-array patch, vaginal ring, or implant technologies as standalone products.

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41. CORE FUNDING OF AN SRH R&D ORGANISATION

This category may be used by organisations that disburse core funding or non-earmarked funding to an organisation that researches and develops products for multiple SRH areas, and where it is unknown how the funding has been allocated within the recipient organisation.

For example: Core funding has been allocated to an organisation that researches contraceptives and multiple non-HIV STIs, but the donor does not know how much has been allocated to each disease or issue.

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42. UNSPECIFIED SRH R&D

Only use this category when you have funding to report that meets the R&D scope criteria set out in this document, but you don't have enough information to allocate the funding to one of the specific SRH areas above.

If funding can be assigned to a specific SRH area, please do so.

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VIII. OUT OF SCOPE (EXCLUDED FROM THE SURVEY)

43. GENERAL EXCLUSIONS

The G-FINDER SRH survey only captures investments that support R&D for products that are suitable for addressing SRH issues amongst populations in LMICs that either do not already exist, or are inappropriate for resource-limited settings. Any product that would require highly skilled personnel or advanced infrastructure is excluded from the survey.

The following categories are also excluded from the survey:

43.1 General supportive, nutritional and symptomatic therapies

- 43.1.1 Micronutrient supplementation, vitamins
- 43.1.2 Anti-pyretics, painkillers

43.2 In-kind contributions

- 43.2.1 In-kind R&D contributions are excluded from the survey due to the difficulty in quantifying their value; however a sample of these contributions is highlighted in G- FINDER reporting. Typical in-kind contributions would include training of LMIC scientists, sharing of expertise or access to compounds

43.3 Additional exclusions for private sector involvement

- 43.3.1 Industry overhead costs, capital costs and opportunity costs are excluded, due to the difficulty of quantifying these and allocating them to the SRH investment. However, the published report will acknowledge the role of these in contributing to costs

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44. NON-PRODUCT R&D EXCLUSIONS**44.1 Clinical studies not linked to development of a new product**

- 44.1.1 Protocol studies, clinical trials, behavioural research, and post-registration evaluation using established, available products (not linked to formal label-expansion trials of new products)
- 44.1.2 Epidemiological surveillance and monitoring studies that are not directly linked to product development. For example, routine DSS (Demographic Surveillance System) activities

44.2 Health services and access research

- 44.2.1 Any clinical study not linked to development of a product
- 44.2.2 Disease management studies, studies of community attitudes, knowledge and practice in relation to SRH issues, and STI control programs
- 44.2.3 Health care service studies in relation to delivery of SRH care
- 44.2.4 Design of treatment and control programs appropriate to local prevailing conditions
- 44.2.5 Implementation and evaluation of large-scale SRH programs operated through health care services, government ministries, non-governmental organizations (NGOs), etc.
- 44.2.6 Advocacy, community education and policy activities related to use, access, or roll-out of new products

44.3 Operational programme assessment

- 44.3.1 Reviews on the status of SRH product development
- 44.3.2 Studies on the economic impact of SRH issue morbidity and mortality on communities
- 44.3.3 Studies on the economics of SRH issue primary prevention
- 44.3.4 Mathematical modelling of the disease (e.g. transmission, immune response)
- 44.3.5 Fostering collaboration between academia, industry, government agencies, and NGOs.

44.4 General capacity building (human infrastructure)

Capacity building activities are excluded unless they are DIRECTLY linked to development of a new SRH product.

The following capacity building activities are therefore excluded:

- 44.4.1 Building academic research capacity; improving existing academic capacity (except where directly linked to development of a specific product)
- 44.4.2 Providing training opportunities; strengthening R&D institutional capacity; developing and maintaining personnel (except where directly linked to development of a specific product).
- 44.4.3 Major infrastructure development (e.g. design, construction and validation of large-scale manufacturing facilities)

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