WOMEN'S HEALTH R&D SCOPE

This document sets out the women's health (WH) 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 WH survey is to capture investment in WH R&D that is relevant to and appropriate for the WH needs of people and populations in low- and middle-income countries (LMICs), regardless of whether or not this investment explicitly targets LMICs.

The WH scope has been reviewed and extended in 2024 in consultation with an international Expert Advisory Group (EAG) with the following criteria:

1. The condition or WH area must exclusively or disproportionately impact women.
   This includes conditions impacting mental health and well-being, as well as maternal health conditions primarily affecting the foetus as they can also impact the mother's mental and physical health.
1. The condition or WH area must be a significant health issue affecting mortality or morbidity in LMICs.
2. The condition or WH area must be characterized by a product gap (i.e. there is no existing product, or improved or additional products are needed to meet the needs of women in LMICs).
3. The condition or WH area must be characterized by a poverty-, gender-, and/or sex-driven market failure.

The conditions and health areas currently included in the WH scope were selected after a prioritisation exercise conducted with the EAG, alongside consideration of resourcing and feasibility of inclusion. The scope will be reviewed on an annual basis.

The G-FINDER WH survey captures R&D investments that support development of products that are suitable for LMIC populations or address an unmet need such as there is no existing product or existing products are unsuitable for resource-limited settings. As such, each WH issue included in the survey may have further restrictions based on the specific R&D gaps identified.

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

A description of the G-FINDER survey scope restrictions by a health issue, including product area inclusions and exclusions, is 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.

The G-FINDER project also tracks R&D for neglected diseases (NDs) and emerging infectious diseases (EIDs). Some women's health issues, products and technologies may overlap with the scope of these other global health areas.

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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WH R&D MATRIX

		Basic research	Drugs	Microbicides	Vaccines	Biologics	Diagnostics	Dietary supplements	Devices & combinations
Fertility regulation									
Abortion		-	✓	-	-	-	Restricted	-	✓
Contraception	On-demand[1]	-	✓	-	-	✓	-	-	✓
	Short-acting[2]	-	✓	-	✓	✓	-	-	✓
	Long-acting reversible (LARC)[3]	-	✓	-	✓	✓	-	-	✓
	Permanent[4]	-	✓	-	-	-	-	-	✓
	Multiple or unspecified duration	-	✓	-	✓	✓	-	-	✓
Gynaecological conditions									
Endometriosis		✓	✓	-	-	✓	✓	-	✓
Menopause		Restricted	✓	-	-	✓	✓	-	✓
Polycystic ovary syndrome		✓	✓	-	-	✓	✓	-	✓
Uterine fibroids		✓	✓	-	-	✓	✓	-	✓
STIs									
HIV/AIDS		Restricted	Restricted	✓	✓	Restricted	✓	-	-
Human papillomavirus (HPV) and HPV-related cervical cancer		Restricted	Restricted	✓	Restricted	✓	✓[5]	-	✓[6]
Multipurpose prevention technologies (MPTs)		-	✓	✓	-	✓	-	-	✓
Sexually transmitted infections (STIs)	Syphilis	Restricted	Restricted	✓	✓	✓	Restricted	-	-
	Gonorrhoea	Restricted	Restricted	✓	✓	✓	✓	-	-
	Chlamydia	Restricted	-	✓	✓	✓	✓	-	-
	Herpes simplex virus 2 (HSV-2)	Restricted	✓	✓	✓	✓	✓	-	-
	Human T-lymphotropic virus 1 (HTLV-1)	✓	✓	✓	✓	✓	✓	-	-
	Hepatitis B	Restricted	Restricted	-	-	Restricted	✓	-	-
	Multiple STIs[7]	Restricted	Restricted[8]	-[9]	✓	✓	✓	-	-
	Other STIs[10]	Restricted	✓	✓	✓	✓	✓	-	-
Maternal health conditions									
Maternal iron-deficiency anaemia		✓	✓	-	-	✓	Restricted	✓	-
Post-partum haemorrhage (PPH)		-	✓	-	-	✓	-	✓	Restricted
Pre-eclampsia and eclampsia		Restricted	Restricted	-	-	✓	✓	✓	-
Preterm labour		✓	✓	-	-	✓	✓	✓	-

Investment applicable to more than one WH issue, or to more than one global health area[11]

Platform technologies					Core funding of a multi-disease R&D organisation
Adjuvants & immunomodulators	Biologics-related platform technologies	Drug-related platform technologies	General diagnostic platform & multi-disease diagnostics	Vaccine-related platform technologies	
✓	✓	✓	✓	✓	✓

✓ denotes a category where a disease or product is included in the survey.
Restricted denotes a category where only some investments are eligible.

[1] On-demand: methods that require action at the time of intercourse or pericoitally for efficacy (e.g. emergency contraception)
[2] Short-acting: methods that work for < 1 year but do not require action at the time of intercourse (e.g. injectable hormones)
[3] LARC: long-acting reversible contraceptives that work for ≥ 1 year (e.g. implants; IUDs)
[4] Permanent: irreversible methods
[5] Includes both diagnostics for HPV infection and diagnostics for cervical lesions
[6] Includes devices that either clear HPV infection or treat cervical lesions
[7] Multiple STIs: two or more STIs, including but not limited to chlamydia, gonorrhoea, syphilis, and HIV
[8] Includes therapeutic drugs for the treatment of two or more STIs. Preventive drugs that address two or more STIs are captured under the MPT section (MPTs > drugs)
[9] Microbicides for the treatment of two or more STIs are in scope, but are captured under the MPT section as microbicides
[10] Other STIs: STIs that disproportionately affect populations in LMICs, including but not limited to trichomoniasis, chancroid, *Mycoplasma genitalium*, lymphogranuloma venereum, and granuloma inguinale (donovanosis)
[11] The G-FINDER project covers three global health areas: neglected diseases, emerging infectious diseases, and women's health issues. Please note **HIV, Hepatitis B, and general diagnostic platforms & multi-disease diagnostics *(except for multiple STIs)*** are captured through the G-FINDER neglected disease survey.

SCOPE RESTRICTIONS BY HEALTH ISSUE & CHANGES

Fertility regulation

Abortion

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

- **Diagnostics:** only includes early pregnancy tests (<21 days after ovulation or 4 weeks amenorrhea)

Gynaecological conditions

Menopause

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

- **Basic research:** only includes basic research where menopause is the outcome of interest, and not an exposure factor. For example, research on cardiovascular conditions, where menopause or aging is a risk or contributing factor is considered out of scope, while research focusing on vasomotor symptoms of menopause or genitourinary syndrome is in scope.

Sexually transmitted infections (STIs)

HIV/AIDS

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

- **Basic research:** only includes basic research related to vaccines (e.g. immunological responses to potential antigens), biologics and microbicides (e.g. mechanism of mucosal transmission), or basic research explicitly targeted at LMIC needs.
- **Drugs:** only includes LMIC-specific costs for label-expansion clinical trials of new drugs and reformulations for LMIC use (e.g. paediatric or slow-release formulations; fixed dose combinations; low-dose drug formulations for prophylaxis; long-acting injectables for treatment or prophylaxis), or preclinical research targeted at developing such products.
- **Biologics:** only includes R&D for biologics being developed specifically for LMIC needs or in support of registration of biologics in LMICs.

NB HIV/AIDS data is collected via the G-FINDER neglected disease survey.

Human papillomavirus (HPV) and HPV-related cervical cancer

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

- **Basic research:** only includes basic research that is related to:
  - Drugs (to clear HPV infection), microbicides, vaccines (that are improvements over currently available products), biologics, diagnostics, or devices & combinations.
  - 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.
- **Vaccines:** only includes R&D for vaccines that represent an improvement over existing products (e.g. single dose, expanded oncogenic HPV strain protection).

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:
  - drugs (for late latent, tertiary, maternal or congenital syphilis), microbicides, vaccines, biologics, or diagnostics (for neonatal syphilis)
  - 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.
- **Diagnostics:** only includes R&D for diagnostics for neonatal 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:
  - drugs (for AMR gonorrhoea), microbicides, vaccines, biologics, or diagnostics
  - 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:
  - microbicides, vaccines, biologics, or diagnostics
  - or basic research that is explicitly targeted at LMIC needs.

Herpes simplex virus 2 (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:
  - drugs, microbicides, vaccines, biologics, or diagnostics
  - or basic research that is explicitly targeted at LMIC needs.

Hepatitis B

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

- **Basic research:** This only includes basic research that is explicitly targeted at LMIC needs, such as that related to HBV epidemiology and genetics in LMIC contexts (e.g. epidemiology of HBV drug resistance or vaccine escape mutants in LMICs).
- **Drugs:** only includes LMIC-specific costs for label-expansion clinical trials of new drugs, reformulations for LMIC use (e.g. curative therapies; drugs for preventing mother-to-child transmission of HBV; long-acting treatment formulations), registration of suitable drugs in LMICs, or preclinical research targeted at developing such products.
- **Biologics:** only includes R&D for biologics being developed specifically for LMIC needs, or in support of registration of biologics in LMICs. Such biologics must at a minimum provide coverage across HBV genotypes prevalent in LMICs (A, B, C, D, E, F, H and/or I).

NB Hepatitis B data is collected via the G-FINDER neglected disease survey.

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:
  - drugs, microbicides, vaccines, biologics, or diagnostics to address two or more STIs.
  - or basic research that is explicitly targeted at LMIC needs.
- **Drugs:** only includes R&D for therapeutic drugs for multiple STIs. Preventive drugs (and microbicides) 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 drugs, microbicides, vaccines, biologics, or diagnostics to address other STIs that disproportionately affect populations in LMICs, such as trichomoniasis, chancroid, Mycoplasma genitalium, lymphogranuloma venereum, granuloma inguinale (donovanosis).

Maternal health conditions

Maternal iron-deficiency anaemia

The scope of the inclusion of funding for maternal iron-deficiency anaemia R&D is currently restricted in the following area:

- **Diagnostics:** only includes point-of-care diagnostics applicable to LMIC contexts.

Post-partum haemorrhage (PPH)

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

- **Devices and combinations:** Only includes devices and combinations to treat PPH by targeting the underlying pathophysiology (e.g. uterine atony). Devices and combinations 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 WH targeted funding. These devices are excluded.

Pre-eclampsia and eclampsia

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

- **Basic research:** only includes basic research that is related to:
  - Drugs, diagnostics or biologics;
  - or disease pathogenesis;
  - or natural history, 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:** This only includes R&D for drugs to prevent and/or treat pre-eclampsia and/or eclampsia that offer improvements over existing products and therapies. It also includes R&D for a novel or existing (re-purposed) drugs and research into magnesium sulphate dosing regimens.

Inclusion of modelling

In 2023 (collecting FY2022 data), language describing modelling and related activities where they are designed to inform knowledge about the health issue or development of products for the health issue was added to the G-FINDER survey scope.

Renaming diagnostic R&D stages

In 2024 (collecting FY2023 data), the diagnostics R&D stages, ‘diagnostics & preclinical’ and ‘clinical evaluation’ were renamed ‘early development’ and ‘late development’ to align our categorisation with terminology commonly used across the diagnostics landscape.

Scope changes

In 2024, the WH scope was extended to include abortion, endometriosis, menopause, polycystic ovary syndrome, uterine fibroids, maternal iron-deficiency anaemia and preterm labour. A new product category of “dietary supplements” was added for all maternal health conditions (preeclampsia, post-partum haemorrhage, preterm labour and maternal iron-deficiency anaemia).

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SCOPE BY PRODUCT

I. BASIC RESEARCH

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

1. NATURAL HISTORY AND EPIDEMIOLOGY

Basic mechanisms of disease transmission or development

Disease prevalence in relation to human genotype, strain variation, and inoculation rates

Genetic diversity and phylogeny

1.1 Epidemiological research on the roles of human behaviour and effects of specific host
1.2 genotypes on disease transmission

1.3 Epidemiological research on host genetic factors influencing the prevalence of disease
1.4 (e.g. sickle cell, HLA type, Rh factor) or the impact of disease in select host genotypes

1.5 Epidemiological research on the distribution of a pathogen that is NOT related to the development of a specific product

1.6 Epidemiological research on the prevalence of morbidity and mortality due to the disease that is NOT related to specific product development

1.7 Epidemiological research on antigenic variability; population studies of human immunity
1.8 to the disease

1.9 Epidemiology for drug resistance or evolutionary studies on resistance development for established, existing drugs

1.10 Epidemiological research on the genetic evolution of a disease (e.g. variants and drug resistance) with the assistance of mathematical modelling where it is NOT linked to routine surveillance activities

2. 2.1 IMMUNOLOGY OF DISEASE

2.2 Defining signalling pathways of immune function (mechanisms of systemic and/or
2.3 mucosal immunity)

2.4 Interaction and impact of the signalling pathways with the pathogen

2.5 Development of assays or tools potentially useful for drug, vaccine, or microbicide research and development

2.6 Identification of immune correlates of protection, including *in vivo* and *in vitro* studies on
2.7 the protective immune response (cellular, humoral and/or mucosal)

Investigating the immune response to particular antigens; studies of specific antigens or immunogens proposed as vaccine candidates

Development of animal models to determine immune correlates of protection

3.1 Genetics of the immune response to the disease and effects of antigen polymorphism
3.2 or genetic diversity on specific vaccine candidates (as recognised from field studies)
3.3
3.4

3. BIOLOGY OF DISEASE

Structure and morphology of different developmental stages of the pathogen

Host-parasite interactions and biology

Biology of invasion of host cells (entry mechanisms)

Localisation of pathogen proteins or antigens

Development of culture and purification tools to assist in the study of the pathogen

Descriptions of pathogenic species and characterisation of strains or subtypes in animal models (course of infection, susceptibility of different hosts)

In vitro studies of interactions between the pathogen and other infectious agents

4. BIOCHEMISTRY OF THE PATHOGEN

Metabolism and nutrition

Protein sequencing, enzymology, and protein and enzyme characterisation (including antigen analysis)

Signal transduction; translation, processing, and export of proteins

Glycosylation, Glycosylphosphatidylinositol (GPI) anchors, transporters, ion channels, mitochondrial metabolism, and electrophysiology studies

Influence of the pathogen on host-cell biochemistry

Characterisation of antigen/protein diversity of pathogenic strains and subtypes

Characterisation of proteins and molecular basis for host-cell invasion

Analysis and characterisation of drug-resistant strains, and studies probing drug resistance mechanism/s or pathways

Non-specific research on the pathogen or host targets to identify potential drug, vaccine, or diagnostic targets (i.e. target identification)

5. GENETICS OF THE PATHOGEN

Studies on chromosomes; genomic maps; genetic crosses Cloning and sequencing of genes; cDNAs for functional proteins (including drug targets and vaccine candidates)

Expression of proteins from cloned genes; RNA analyses

Control and timing of gene expression; post-transcriptional processing

Analysis and characterisation of genes involved in drug resistance

Genetics of antigenic variability

Techniques for the genetic transformation of the pathogen

Tests for genotyping the pathogen for laboratory use

6. BIOINFORMATICS AND PROTEOMICS

Microarray analysis

Genome annotation - gene predictions

Comparative genomics, sequence alignment, genome assembly

Variation, single nucleotide polymorphisms (SNPs)

Database applications, data mining tools

Structural and functional genomics

Structural and functional proteomics

Proteome analysis, protein structure alignment

7. PATHOPHYSIOLOGY AND DISEASE SYMPTOMS

Clinical diagnosis and clinical observations of the disease presentation and pathophysiology

The role of nutritional status in determining disease severity and treatment effectiveness

Histopathology of the disease

The mechanisms of pathology of the disease; including, the role of the host immune system, and expression of adhesion molecules

7.1 Development of improved animal models to study disease pathophysiology, to evaluate the biological properties of drugs and microbicides

7.2 Identification of biomarkers for diagnostics or therapeutic monitoring

7.3 Studies of the mechanisms by which particular susceptible/resistant mammalian host genotypes exert their effect

7.4 Research on the effects of host co-morbidities and secondary effects of pathogen invasion

7.5 Interactions between the disease and other relevant concurrent infections, including determining timing and establishment of infection

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7.8

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7.9

II. DRUGS

Research activities and processes necessary to develop and improve new small molecule compounds or repurposed drugs specifically intended to address WH 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.

It 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 designed to prevent two or more STIs are considered by G-FINDER to be multi-purpose preventive technologies (MPTs)*

8. DISCOVERY AND PRECLINICAL

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

8.1 Target validation, characterisation, and selection

8.2 *In silico* discovery and development activities for drugs, including the use of pharmacometrics and mechanistic models

8.3 High throughput screening, lead optimisation

8.4 Studies supporting safety & tolerability testing in animal models and looking at *in vitro* correlates of *in vivo* protective response

8.5 Development of analytical tests for assaying drugs, including the development of animal models

8.6 Research on drugs from natural products; identification and characterisation of active ingredient

8.7 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

8.8 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

Development of tests for drug susceptibility of the pathogen for research purposes

Drug pharmacokinetic, toxicity and metabolism studies *in vitro* and in animal models, including bioavailability, adsorption, metabolism, and excretion (ADME) studies

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

8.9

8.10 Preparation of Investigational New Drug (IND) application for regulatory submission

8.11 Optimisation and manufacturing of new formulations to support label-expansion* for new patient sub-populations (e.g. infants, pregnant women)

9. 8.12 8.13 CLINICAL DEVELOPMENT - PHASE I

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

Phase Ia single ascending dose studies to determine pharmacokinetics, pharmacodynamics and maximum tolerated dose

9.1 Phase Ib multiple ascending dose studies to determine the pharmacokinetics, pharmacodynamics, safety and tolerability of multiple doses

9.2 Trials of food effect or drug-drug interactions

9.3

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

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

11.2 Regulatory standard clinical trials to assess effectiveness of a new drug against current 'gold standard'

11.3 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)

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

* 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.

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:

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 WH issues, or the health of target populations at trial sites.

Preliminary studies of morbidity and mortality at potential clinical trial sites, where these studies are directly linked to planned product trials.

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

12.2

12.3

13. CLINICAL DEVELOPMENT - UNSPECIFIED

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

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)

13.1

Further pharmaceutical development to generate the final clinical formulation, dosage form and other Chemistry and Manufacture Control (CMC) activities required for regulatory submission.

13.2

Compiling of all non-clinical and clinical data for submission of a New Drug Application (NDA) to regulatory authorities

13.3

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.

13.6

13.7 Transmission modelling to inform clinical trial design and therapeutic administration strategies for drugs in clinical development.

In silico clinical trials designed to assess safety and/or efficacy of drugs in clinical development

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

14.2

14.3

14.4 Pharmacovigilance and post-registration studies of newly registered drugs to assess adverse reactions, toxicology and safety.

14.5

Effectiveness studies and head-to-head comparator studies of newly registered drugs (with other therapies or interventions)

Cost-effectiveness studies of newly registered drugs

Treatment interactions and population level studies (of newly registered products e.g., pharmaco-epidemiological and resistance studies)

Behavioural research post-registration of new drugs relating to risk assessment, factors affecting adherence to protocol, provider compliance, and product acceptability.

14.8 Case history reports and assessment of long-term prophylaxis using newly registered drugs in communities in LMICs

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III. DIETARY SUPPLEMENTS

Definition: *Dietary supplements are products that include one or more of the following dietary ingredients: a vitamin, a mineral, a herb or other botanical, an amino acid, any other substance used to supplement the diet by increasing total dietary intake, or combination of any of the above. Nutraceuticals (foods that produce some type of physiological benefit) and functional foods (foods 'enriched' to provide a physiological benefit that the unmodified food cannot) are also considered to be dietary supplements. Dietary supplements are intended to be taken by mouth as a pill, capsule, tablet, or liquid (IV formulations, e.g. IV iron, are considered to be drugs) and their regulatory process focuses on safety and labelling rather than showing pre-market efficacy. There are exceptions for dietary supplements like nutraceuticals which may have a physiological benefit or for supplements that are used to treat or prevent a medical condition where more rigorous clinical testing is undertaken including efficacy studies. In contrast, a drug has an active ingredient with a pharmacological effect and will undergo more regulatory scrutiny. For inclusion, dietary supplements also need to be dosed formulations.*

Inclusions:

Research activities and processes necessary to develop and improve new or repurposed dietary supplements specifically intended to address WH issues; including dietary supplement design, preclinical and clinical development, and other activities essential for successful dietary supplement development and uptake.

Only includes R&D for dietary supplements that will be suitable for use in LMICs.

15. DISCOVERY AND PRECLINICAL

Research activities targeted at discovering and optimising investigational dietary ingredients, including the processes needed to allow new supplements to proceed to human trials; including:

15.1

15.2 Target validation, characterisation, and selection

15.3 *In silico* discovery and development activities for dietary ingredients, including the use of mechanistic models

15.4 High throughput screening, lead optimisation

15.5 Studies supporting safety & tolerability testing in animal models and looking at *in vitro* correlates of *in vivo* protective response

15.6 Development of analytical tests for assaying dietary ingredients, including the development of animal models

15.7 Research on dietary ingredients from natural products, identification and characterisation of components that are intended to have a biological effect or provide health benefits

15.8 Measurement of the activity of potential dietary ingredients *in vitro* and in animal models; including safety and efficacy studies necessary to satisfy regulatory requirements if the dietary supplement may be used to "diagnose, treat, cure, or prevent any disease."

15.9 Dietary supplement pharmacokinetic, toxicity and metabolism studies *in vitro* and in animal models, including bioavailability, adsorption, metabolism, and excretion (ADME) studies

Chemistry and synthesis of dietary supplements, 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 dietary ingredients to proceed to human trials

Preparation of application for regulatory submission (if the dietary supplement may be used to "diagnose, treat, cure, or prevent any disease."

Optimisation and manufacturing of new formulations (including new combinations) to support new use of a dietary supplement in new patient sub-populations (e.g. infants, pregnant women)

15.10

16. CLINICAL DEVELOPMENT - PHASE I

15.11

Clinical trials to determine safety and tolerability of investigational dietary supplement in a small group of patients or healthy volunteers; including:

Phase Ia single ascending dose studies to determine pharmacokinetics, pharmacodynamics and maximum tolerated dose

Phase Ib multiple ascending dose studies to determine the pharmacokinetics, pharmacodynamics, safety and tolerability of multiple doses

16.1 Trials of food effect, dietary influence or dietary supplement-drug interactions

16.2

17. CLINICAL DEVELOPMENT - PHASE II

16.3

Clinical trials to determine the efficacy, safety and therapeutic dose of investigational new dietary supplements in a small set of human subjects (up to several hundred); These only apply to dietary supplements which claim to treat or prevent a medical condition and include:

Phase IIa proof of concept studies to demonstrate clinical efficacy or biological activity

17.1 Phase IIb dose-finding studies to determine dose with optimum biological activity with

17.2 minimal adverse effects

18. CLINICAL DEVELOPMENT - PHASE III

Clinical trials to demonstrate efficacy in a trial population large enough to provide statistical significance (from several hundred to several thousand); these only apply to dietary supplements which claim to treat or prevent a medical condition and include studies to support the registration of dietary supplement formulations with such claims or label-expansion (expansion of claims) of already registered dietary supplements.

18.1

18.2 Regulatory standard clinical trials to assess effectiveness of a new dietary supplement against current 'gold standard'.

18.3 Regulatory standard clinical trials that investigate efficacy of an existing dietary ingredient to a new disease or patient group (e.g. pregnant women or HIV-positive patients) or support a formal registration for label expansion.

Regulatory standard clinical trials that investigate efficacy of an existing dietary supplement to new use, such as intermittent preventative therapy and pre-exposure prophylaxis or support formal registration for label expansion.

19.1

19. CLINICAL DEVELOPMENT - BASELINE EPIDEMIOLOGY

19.2

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:

Epidemiological studies directly linked to the conduct or support of clinical trials of products in development to assess or validate the epidemiology or incidence of WH issues or the health of target populations at trial sites.

Preliminary studies of morbidity and mortality at potential clinical trial sites, where these studies are directly linked to planned product trials.

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

20. CLINICAL DEVELOPMENT - UNSPECIFIED

Other costs required to support clinical testing of investigational new dietary supplements as needed for regulatory approval (when they are intended to "diagnose, treat, cure, or prevent any disease."); including:

19.3

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

20.1 Further pharmaceutical development to generate the final clinical formulation, dosage form and other Chemistry and Manufacture Control (CMC) activities required for regulatory submission (if the dietary supplement intends to diagnose, treat or prevent a disease).

20.2 Compiling of all non-clinical and clinical data for submission to regulatory authorities

20.3 Behavioural research prior to registration relating to risk assessment, factors affecting adherence to protocol, and product acceptability (if the dietary supplement intends to diagnose, treat or prevent a disease).

20.4

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 (if the dietary supplement intends to diagnose, treat or prevent a disease).

20.6 Transmission modelling to inform clinical trial design and therapeutic administration strategies for dietary supplements in clinical development.

20.7 *In silico* clinical trials designed to assess safety and/or efficacy of dietary supplements in clinical development

21. POST-REGISTRATION AND POST-MARKETING STUDIES

Studies relating to the detection, monitoring, evaluation, and prevention of adverse events associated with marketed dietary supplements. Since dietary supplements do not require a formal regulatory approval before being brought to market, efficacy and pharmacovigilance studies occur voluntarily and after commercialization. For dietary supplements intended to "diagnose, treat, cure, or prevent any disease", this section includes post-registration studies relating to the detection, monitoring, evaluation, and prevention of adverse events associated with newly approved dietary supplements so as to bridge the gap between highly controlled clinical trials intended for regulatory approval and the largely uncontrolled use of new dietary supplements by patients. Also includes studies conducted after regulatory approval that assess dietary supplements effectiveness in the wider population or which are necessary to support product use in LMICs.

21.1

21.2

21.3 Pharmacovigilance and post-registration studies of newly registered or marketed dietary supplements to assess adverse reactions, toxicology and safety.

21.4

21.5 Effectiveness studies and head-to-head comparator studies of newly registered or marketed dietary supplements (with other therapies or interventions, to validate health claims or explore new benefits)

Cost-effectiveness studies of newly registered or marketed dietary supplements.

Treatment interactions and population level studies (of newly registered or marketed products e.g., pharmaco-epidemiological and resistance studies)

Behavioural research post-registration of new dietary supplements relating to risk assessment, factors affecting adherence to protocol, provider compliance, and product acceptability.

Case history reports and assessment of long-term prophylaxis using newly registered or marketed dietary supplements in communities in LMICs.

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IV. MICROBICIDES

21.6

Research activities and processes necessary to develop and improve topical microbicides intended to prevent transmission; including microbicide discovery or design, preclinical and clinical development, and other activities essential for successful microbicide development and uptake.

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

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

22. DISCOVERY AND PRECLINICAL

Research activities targeted at identifying, optimising, and characterising investigational microbicides and including the processes necessary to allow lead compounds to proceed to human trials; including:

22.1 Specific research aimed at discovery of topical applications for microbicide use (e.g. vaginal defence enhancers, surfactants, entry/fusion inhibitors and replication inhibitors)

22.2 Target validation, characterisation, and selection

22.3 *In silico* discovery and development activities for microbicides, including the use of pharmacometrics and mechanistic models.

22.4 Preclinical evaluation of microbicide candidates including determination of acceptable formulation and delivery modes

22.5 Studies supporting safety & tolerability testing in animal models and looking at *in vitro* correlates of *in vivo* protective response.

22.6 Developing reagents and standardised methods to assess microbicide-induced immune response in animals and humans.

22.7 Optimisation of microbicide candidates, bioprocess development, formulation, and mode of delivery of novel prevention tools for broad international use (cheap, easy to produce, stable, easy to administer) including production of Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP)-grade product for regulatory toxicology studies.

22.8 Preparation of an Investigational New Drug (IND) application for regulatory submission

23.1

23. CLINICAL DEVELOPMENT - PHASE I

23.2

Clinical trials to determine the safety of investigational new microbicides for the first time in human subjects (up to one hundred), including:

Phase Ia single ascending dose studies to determine pharmacokinetics, pharmacodynamics and maximum tolerated dose.

Phase Ib multiple ascending dose studies to determine the pharmacokinetics, pharmacodynamics, safety and tolerability of multiple doses.

24. CLINICAL DEVELOPMENT - PHASE II

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

Phase IIa proof of concept studies to demonstrate clinical efficacy or biological activity.

Phase IIb dose-finding studies to determine dose with optimum biological activity with minimal adverse effects.

25. CLINICAL DEVELOPMENT - PHASE III

24.1
24.2

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

Regulatory standard clinical trials to assess effectiveness of novel microbicide products.

26. CLINICAL DEVELOPMENT - BASELINE EPIDEMIOLOGY

25.1

Studies evaluating potential trial site populations to confirm disease incidence, prevalence, or exposure risk, and which serve as the foundation for determining the optimal collection, analysis, interpretation and presentation of clinical trial data, including:

Epidemiological studies directly linked to the conduct or support of clinical trials of microbicides in development, to assess or validate the epidemiology of disease, disease incidence, or health of target populations at trial sites.

26.1

Preliminary studies of morbidity and mortality at potential clinical trial sites, where these studies are directly linked to planned microbicide trials.

26.2

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

26.3

27. CLINICAL DEVELOPMENT - UNSPECIFIED

Activities and processes associated with clinical testing of investigational new microbicides to demonstrate safety and efficacy in human subjects (as needed for regulatory approval), together with other costs required to support such clinical trials, including:

27.1

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

27.2

Further microbicide development to generate the final clinical formulation, dosage form and other Chemistry and Manufacture Control (CMC) activities required for regulatory submission.

27.3

27.4

Compiling of all non-clinical and clinical data for submission of a New Drug Application (NDA) to regulatory authorities

27.5

Behavioural research prior to registration relating to risk assessment, factors affecting adherence to protocol and product acceptability.

27.6

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.

27.7

Transmission modelling to inform clinical trial design and therapeutic administration strategies for microbicides in clinical development.

In silico clinical trials designed to assess safety and/or efficacy of microbicides in clinical development

28. POST-REGISTRATION STUDIES

Studies relating to the detection, monitoring, evaluation, and prevention of adverse events associated with newly approved microbicides so as to bridge the gap between highly controlled clinical trials intended for regulatory approval and the largely uncontrolled delivery of new microbicides; including:

	Studies conducted after regulatory approval that assess microbicide effectiveness in the wider population or which are necessary to support product use in LMICs
	Pharmacovigilance and post-registration studies of newly registered microbicides to assess adverse reactions, toxicology and safety
28.1	Effectiveness studies and head-to-head comparator studies of newly registered microbicides (with other therapies or interventions)
28.2	Cost-effectiveness studies of newly registered microbicides
28.3	Treatment interactions and population level studies (of newly registered preventive microbicides e.g., pharmaco-epidemiological and resistance studies)
28.4	Behavioural research post-registration of new microbicides relating to risk assessment,
28.5	factors affecting adherence to protocol, provider compliance, and product acceptability
28.6	Case history reports and assessment of long-term prophylaxis using newly registered microbicides in communities in LMICs
28.7	

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V. VACCINES

Research activities and processes necessary to develop and improve investigational vaccines specifically intended to prevent infection or disease or pregnancy; 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.

29. DISCOVERY AND PRECLINICAL

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

29.1	
29.2	Studies supporting novel vaccine design, including target validation & candidate optimisation
29.3	
29.4	*In silico* discovery and development activities for vaccines, including the use of pharmacometrics and mechanistic models
29.5	Development of animal models to assist in vaccine design and testing
29.6	Evaluation of vaccine technologies (e.g. adjuvants, delivery systems) to improve the immunogenicity of an identified candidate
29.7	Preclinical safety and immunogenicity studies with candidate vaccines, including use or
29.8	development of functional assays
	Preclinical animal studies, challenge models and addressing the correlation between *in vitro* models, animal models and field results
29.9	Studies on the genetics of the immune response to selected antigens as vaccine candidates, optimisation of animal models and correlates to clinical results
	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
	Research on safety and regulatory considerations (e.g. validation of preclinical assays to permit registration)

Preparation of an Investigational New Drug (IND) application for regulatory submission

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

30. CLINICAL DEVELOPMENT - PHASE I

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

29.1a
29.1

Phase Ia studies assessing safety, dosing, and immunogenicity in human volunteers

Phase Ib studies assessing safety, dosing, and immunogenicity in clinically exposed or high-risk populations

30.1
30.2

31. 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:

Phase IIa challenge studies

Phase IIb safety and preliminary efficacy studies in exposed populations or those at high-risk of infection

31.1
31.2

32. 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:

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

33. 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:

33.1

33.2 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

33.3

Preliminary studies of morbidity and mortality at potential clinical trial sites, where these studies are directly linked to planned preventive vaccines trials

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

34.1

34. CLINICAL DEVELOPMENT - UNSPECIFIED

34.2

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

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)

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

Compiling all non-clinical and clinical data to obtain a Biologics License from regulatory authorities

Behavioural research during clinical trials relating to risk assessment, factors affecting adherence to protocol, and product acceptability

34.3 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

34.4 Transmission modelling to inform clinical trial design and therapeutic administration strategies for vaccines in clinical development

34.5 *In silico* clinical trials designed to assess safety and/or efficacy of vaccines in development

34.6

35 34.7 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.

35.1 Pharmacovigilance and post-registration studies of newly registered preventive vaccines to assess adverse reactions, toxicology and safety

35.2 Effectiveness studies and head-to-head comparator studies of newly registered preventive vaccines (with other therapies or interventions)

35.3 Cost-effectiveness studies of newly registered preventive vaccines

35.4 Treatment interactions and population level studies (of newly registered preventive vaccines e.g., pharmaco-epidemiological and resistance studies)

35.5 Behavioural research post-registration of new preventive vaccines relating to risk assessment, factors affecting adherence to protocol, provider compliance, and product acceptability

35.6 Case history reports and assessment of long-term prophylaxis using newly registered preventive vaccines in communities in LMICs

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VI. BIOLOGICS

Research activities and processes necessary to develop and improve investigational biological agents and therapeutic vaccines specifically intended to treat infection or prevent pregnancy; including design, preclinical and clinical development, and other activities essential for successful development and uptake. This includes broadly neutralising monoclonal antibodies (bNAbs); polyclonal antibodies; and other bio-therapeutics such as peptide-, DNA- and RNA-based synthetic molecules. In 2020 (collection of FY2019 data), the 'vaccines (therapeutic)' category was renamed 'biologics' to reflect the distinction between traditional preventive vaccine technologies, and biologics and therapeutic vaccines.

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

36. DISCOVERY AND PRECLINICAL

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

36.1 Studies supporting novel biologic or therapeutic vaccine design including target validation and candidate optimisation

36.2 *In silico* discovery and development activities for biologics, including the use of pharmacometrics and mechanistic models

36.3 Evaluation of biologic technologies (delivery systems) to improve the delivery of an identified candidate

36.4 Preclinical safety and tolerability studies with candidate biologics or therapeutic vaccines, including use or development of functional assays

36.5 Preclinical animal studies, challenge models, and studies addressing the correlation between *in vitro* models, animal models and field results

36.6 Studies on the genetics of the immune response to selected antigens as biologic or therapeutic vaccine candidates, optimisation of animal models and correlates to clinical results

36.7 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 biologic to proceed to human trials

36.8 Research on safety and regulatory considerations (e.g. validation of preclinical assays to permit registration)

36.9 Preparation of an Investigational New Drug (IND) application for regulatory submission

36.10 Optimisation of biologic or therapeutic vaccine candidates for global use (cheaper, more stable, ease of administration, addition of LMIC-specific targets)

37. CLINICAL DEVELOPMENT - PHASE I

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

37.1 Phase Ia studies assessing safety, dosing, and tolerability in human volunteers

37.2 Phase Ib studies assessing safety, dosing, and tolerability in clinically exposed or high-risk populations

37.3 Phase I studies to examine safety, tolerability and pharmacokinetics of biological drugs such as a monoclonal antibody or a fully human polyclonal immunoglobulin

38. CLINICAL DEVELOPMENT - PHASE II

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

38.1 Phase IIa challenge studies

38.2 Phase IIb safety and preliminary efficacy studies in exposed populations or those at high-risk of infection

39. 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 biologics or therapeutic vaccines; including:

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

40. 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:

Epidemiological studies directly linked to the conduct or support of clinical trials of biologics or therapeutic vaccines in development, in order to assess or validate the epidemiology of disease, disease incidence, or health of target populations at trial sites

40.1 Preliminary studies of morbidity and mortality at potential clinical trial sites, where these studies are directly linked to planned biologics or therapeutic vaccine trials

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

40.3

41. CLINICAL DEVELOPMENT - UNSPECIFIED

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

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

41.2 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

41.3 Compiling all non-clinical and clinical data to obtain a Biologics License from regulatory authorities

41.4 Behavioural research during clinical trials relating to risk assessment, factors affecting adherence to protocol, and product acceptability

41.5 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

41.6 Transmission modelling to inform clinical trial design and therapeutic administration strategies for biologics in clinical development

41.7 *In silico* clinical trials designed to assess safety and/or efficacy of biologics in clinical development

42. POST-REGISTRATION STUDIES

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

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

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VII. 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).

43. EARLY DEVELOPMENT

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:

43.1	
43.2	
43.3	Validation, characterisation, and selection of targets suitable for diagnostic use
43.4	*In silico* biomarker and antigen discovery and development activities, including immune system interaction models
43.5	
43.6	Validation of new diagnostic markers or biomarkers
43.7	Development and testing of stable, easy-to-use diagnostic tests (e.g. improved sample collection/preparation, cheaper ELISA assays), including manufacturing design
43.8	New or improved diagnostics for disease staging and therapy decisions
	New or improved diagnostics to identify specific target populations
	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
	Creation of reference material banks

44. LATE DEVELOPMENT

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:

	Clinical efficacy trials
	Small-scale testing in humans to establish sensitivity and specificity and utility
	Technical evaluation of tests and studies evaluating product performance
	Establishment of product specifications, kit development and quality assurance
	Submission of relevant data to regulatory authorities for approval
44.1	
44.2	Assessment & validation of trial sites to carry out product trials
44.3	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)
44.4	
44.5	
44.6	
44.7	

45. 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:

	Larger-scale demonstration studies (assessing specificity, sensitivity and utility of the diagnostic test)
45.1	
	Cost-effectiveness studies assessing the diagnostic test
45.2	
45.3	Identification of pitfalls of the technology and studies of safety measures needed to support the technology
45.4	Studies to determine at what level of the health care system the technology is applicable (e.g. reference labs, regional labs)
45.5	
45.6	Identification of training needs
45.7	Collecting evidence for expanding the use of a diagnostic tool in different countries
45.8	Development of equipment and customer support documents
45.9	Head-to-head comparator studies (with current gold standard) and in the context of existing diagnostic algorithms
45.10	Behavioural research relating to risk assessment, factors affecting diagnostics use, and user acceptability (patient and provider)
	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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VIII. DEVICES AND COMBINATION PRODUCTS

Definitions:

*A **device** (in the context of this survey) 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 or removal of a contraceptive (e.g. intrauterine inserter), to control post-partum haemorrhage (e.g. tools to assist bimanual compression), or to clear HPV infection or treat cervical lesions (e.g. handheld thermal ablation devices).To be classified as a "device" in the G-FINDER survey, the technology must not contain a pharmaceutical element.*

*A **combination product** (in the context of this survey) is defined as the combination of an instrument, appliance, or other similar article with a **pharmaceutical element** which are intended to prevent*

pregnancy, the transmission of HIV or other STIs, or to halt bleeding associated with PPH. To be classified as a "combination product", the therapeutic properties of the product must only be achieved when the instrument and pharmaceutical element are used in conjunction – i.e. the instrument is involved in the delivery of the drug or biologic (e.g. contraceptive implant, hormone- or antiviral-releasing vaginal ring, oxytocin releasing microarray patch) and would not provide protection independently.

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).

46. 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:

46.1	Engineering analysis and testing, computational simulation, or biocompatibility testing including immunogenicity and carcinogenicity testing
46.2	Animal model testing of devices and combination products
46.3	Development and testing of heat stable, easy to use devices and combination products, including manufacturing design
46.4	New or improved devices and combination products for specific target populations
46.5	Creation of reference material banks

47. 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:

47.1	Studies to determine the safety and tolerability of a device or combination product
47.2	Studies to determine the PK/PD of a combination product

48. CLINICAL DEVELOPMENT - PHASE II

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

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

49. 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:

Regulatory standard clinical trials to assess effectiveness of a new device or combination product against current 'gold standard'

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

49.1

49.2

50. CLINICAL DEVELOPMENT - UNSPECIFIED

Other costs required to support clinical testing of investigational new device and combination products as needed for regulatory approval; including:

Early and traditional feasibility studies to evaluate device or combination product design with respect to clinical safety, functionality, and efficacy

50.1 Pivotal studies to provide definitive evidence of the safety and efficacy of a device or combination product

50.2 Infrastructure and site development costs directly associated with the conduct of clinical trials for device or combination product development in LMICs (e.g. refurbishment of

50.3 hospital wing, vehicle purchase, generators, training and community relationship building)

50.4 Further pharmaceutical development to generate the final clinical formulation, dosage form and other Chemistry and Manufacture Control (CMC) activities required for regulatory submission

50.5 Compiling of all non-clinical and clinical data for submission of a New Drug Application (NDA) to regulatory authorities

50.6 Behavioural research **prior to registration** relating to risk assessment, factors affecting

50.7 adherence to protocol, and product acceptability

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

51. OPERATIONAL RESEARCH

51.1

Operational procedures and implementation activities associated with novel devices and combination

51.2 *products, which are necessary to support global public health use; including:*

51.3

51.4 Larger-scale demonstration studies (assessing utility of devices and combination products in LMICs)

51.5 Cost-effectiveness studies

51.6 Identification of pitfalls of the device or combination product and studies of safety

51.7 measures needed to support the product

51.8 Identification of training needs

Collecting evidence for expanding the use of a device or combination product in different countries

Development of equipment and customer support documents

Head-to-head comparator studies and in the context of existing treatment algorithms

Behavioural research relating to risk assessment, factors affecting device and combination product use, and user acceptability (patient and provider)

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

52. 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.

51.9

Pharmacovigilance and post-registration studies of newly registered devices and combination products to assess adverse reactions, toxicology and safety

52.1 Effectiveness studies and head-to-head comparator studies of newly registered devices and combination products (with other therapies or interventions)

52.2 Cost-effectiveness studies of newly registered devices and combination products

52.3 Treatment interactions and population level studies (of newly registered products e.g., pharmaco-epidemiological and resistance studies)

52.4 Behavioural research post-registration of new devices and combination products

52.5 relating to risk assessment, factors affecting adherence to protocol, provider compliance, and product acceptability

52.6 Case history reports and assessment of long-term prophylaxis using newly registered devices and combination products in communities in LMICs

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IX. MULTIPURPOSE PREVENTION TECHNOLOGIES (MPTS)

Definition:

To be an MPT, a product must have at least two of the following WH 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 WH 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, microbicides, devices, and combination products. Eligible investments include product discovery or design, preclinical 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.

53.1

53.2

Only includes R&D to develop MPTs suitable for use in LMICs (e.g. heat stable, easy to use)

53. MULTIPURPOSE PREVENTION TECHNOLOGIES (MPTS)

Drugs

See section II for a full outline of the R&D activities included under this product category

Microbicides

See section III for a full outline of the R&D activities included under this product category

Biologics

See section V for a full outline of the R&D activities included under this product category

Devices and combination products

See section VIII for a full outline of the R&D activities included under this product category

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53.3

53.4

X. R&D FOR MORE THAN ONE WOMEN'S HEALTH ISSUE

54. 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.

55. ADJUVANTS AND IMMUNOMODULATORS

Adjuvants and immunomodulators are substances formulated as part of a vaccine to improve, modulate, or potentiate the immune response. These include compounds such as potassium aluminium sulfate, oil in water emulsion composed of squalene (MF59), MatrixM and Cytosine phosphoguanin (CpG 1018).

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 WH issues

Examples of R&D for adjuvants and immunomodulators included in the survey scope:

i. Understanding the innate or adaptive immune response, e.g. discovery of pathogen-associated molecular patterns (PAMPs)
ii. Development of animal model to determine an adjuvant's mechanism of action
iii. Developing a systematic approach to adjuvant discovery (e.g. predictive *in vitro* assays)
iv. High throughput screening to identify potential adjuvants

56. BIOLOGICS-RELATED PLATFORM TECHNOLOGIES

Biologics-related platform technologies include research on developing biotechnology processes, including identification, optimisation and manufacturing of biopharmaceuticals such as monoclonal antibodies, nucleic acid-based therapeutics (siRNA and oligonucleotides) and viral vector-based therapeutics which can be adapted for more than one pathogen.

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 user-friendly biologics-related platform technologies suitable for use in developing countries
c) The resulting research findings or leads must be accessible to organisations developing pharmaceutical or biological products for WH issues

Examples of R&D for biologics-related platform technologies included in the survey scope:

i. Development of transgenic animals for production of humanised monoclonal antibodies

ii. Development of T cell or innate immunity platforms with the capability of producing therapeutics for multiple infectious diseases
iii. PBMC-based neutralization testing of recombinant monoclonal antibodies from multiple pathogens
iv. Development of systems for more efficient and cost-effective stem cell creation for biological therapies for multiple potential diseases (including pregnancy related such as preeclampsia).

57. DRUG-RELATED PLATFORM TECHNOLOGIES

Drug-related platform technologies include research focusing on developing broad-spectrum therapeutics, including small molecule and host-directed agents, and drug delivery technologies and devices such as long-acting and subcutaneous drug delivery systems.

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
c) The resulting research findings or leads must be accessible to organisations developing pharmaceutical or biological products for WH issues

Examples of R&D for drug-related platform technologies included in the survey scope:

i. Development of methods to enhance oral bioavailability of poorly water-soluble drugs
ii. Discovery and optimisation of mechanisms for controlled release (e.g. micro-array patches, vaginal rings, or implant technologies as standalone products).

58. VACCINE-RELATED PLATFORM TECHNOLOGIES

Vaccine-related platform technologies include research on developing platforms, such as viral vectors (replicating and non-replicating) and nucleic acid-based platforms (DNA and mRNA) or vaccine development process innovation, such as thermostabilisation processes which can be employed for multiple target vaccines. It also includes research purely focusing on the delivery of a finished product, such as vaccine microarray patches.

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 research aimed at developing cheaper, faster, more user-friendly vaccine platform or delivery technologies, suitable for use in resource-limited settings.
c) The resulting research findings or leads must be accessible to organisations developing pharmaceutical or biological products for WH issues

Examples of R&D for vaccine-related platform technologies included in the survey scope:

i. Development of novel delivery technologies applicable to multiple vaccines, such as needle-free high-density microarray patch, intra-nasal or inhalable vaccine delivery platforms, and mucosal vaccine delivery system
ii. Development of a plant-based sub-unit vaccine delivery system

59. CORE FUNDING OF A MULTI-DISEASE 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 WH 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 STIs, but the donor does not know how much has been allocated to each disease or issue.

60. UNSPECIFIED WH 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 WH areas above.

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

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XI. OUT OF SCOPE (EXCLUDED FROM THE SURVEY)

61. GENERAL EXCLUSIONS

The G-FINDER WH survey only captures investments that support R&D for products that are suitable for addressing WH 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:

62. GENERAL SUPPORTIVE, NUTRITIONAL AND SYMPTOMATIC THERAPIES

62.1 Anti-pyretics, painkillers

63. IN-KIND CONTRIBUTIONS

63.1 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

64.1

64. ADDITIONAL EXCLUSIONS FOR PRIVATE SECTOR INVOLVEMENT

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

65.2

65. NON-PRODUCT R&D EXCLUSIONS

65.3 Clinical studies not linked to development of a new product

Protocol studies, clinical trials, behavioural research, and post-registration evaluation using established, available products (not linked to formal label-expansion trials of new products)

Epidemiological surveillance and monitoring studies that are not directly linked to product development. For example, routine DSS (Demographic Surveillance System) activities

66. HEALTH SERVICES AND ACCESS RESEARCH

Any clinical study not linked to development of a product

Disease management studies, studies of community attitudes, knowledge and practice in relation to WH issues, and STI control programs

Health care service studies in relation to delivery of WH care

Design of treatment and control programs appropriate to local prevailing conditions

66.1 Implementation and evaluation of large-scale WH programs operated through health care services, government ministries, non-governmental organizations (NGOs), etc.

66.2 Advocacy, community education and policy activities related to use, access, or roll-out of new product

66.3

66.4

66.5

67 66.6 OPERATIONAL PROGRAMME ASSESSMENT

Reviews on the status of WH product development

Studies on the economic impact of WH issue morbidity and mortality on communities

67.1 Studies on the economics of WH issue primary prevention including mathematical modelling of economic impact

67.2

67.3 Mathematical modelling of the disease (e.g. transmission, immune response) where it is linked to routine surveillance programmes

67.4 Fostering collaboration between academia, industry, government agencies, and NGOs

67.5

68. GENERAL CAPACITY BUILDING (HUMAN INFRASTRUCTURE)

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

The following capacity building activities are therefore excluded:

68.1 Building academic research capacity; improving existing academic capacity (except where directly linked to development of a specific product)

68.2 Providing training opportunities; strengthening R&D institutional capacity; developing and maintaining personnel (except where directly linked to development of a specific product)

68.3 Major infrastructure development (e.g. design, construction, and validation of large-scale manufacturing facilities)

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