REPRODUCTIVE HEALTH:
R&D FOR THE DEVELOPING WORLD

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**ACRONYMS**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
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</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>Australian ARC</td>
<td>Australian Research Council</td>
</tr>
<tr>
<td>Australian NHMRC</td>
<td>Australian National Health and Medical Research Council</td>
</tr>
<tr>
<td>BCI</td>
<td>Biodegradable contraceptive implant</td>
</tr>
<tr>
<td>DALY</td>
<td>Disability adjusted life year</td>
</tr>
<tr>
<td>DC</td>
<td>Developing country</td>
</tr>
<tr>
<td>Dutch DGIS</td>
<td>Dutch Ministry of Foreign Affairs – Directorate General of Development Cooperation</td>
</tr>
<tr>
<td>EAG</td>
<td>Expert Advisory Group</td>
</tr>
<tr>
<td>Gates Foundation</td>
<td>Bill &amp; Melinda Gates Foundation</td>
</tr>
<tr>
<td>GSK</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>HIC</td>
<td>High-Income Country</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>Indian ICMR</td>
<td>Indian Council of Medical Research</td>
</tr>
<tr>
<td>LMIC</td>
<td>Low- and Middle-Income Country</td>
</tr>
<tr>
<td>MIPS</td>
<td>Monash Institute of Pharmaceutical Sciences</td>
</tr>
<tr>
<td>MPT</td>
<td>Multipurpose Prevention Technology</td>
</tr>
<tr>
<td>PATH</td>
<td>Program for Appropriate Technology in Health</td>
</tr>
<tr>
<td>PDP</td>
<td>Product development partnership</td>
</tr>
<tr>
<td>PPH</td>
<td>Post-partum haemorrhage</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>Research and development</td>
</tr>
<tr>
<td>STI</td>
<td>Sexually transmitted infection</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>UK DFID</td>
<td>UK Department for International Development</td>
</tr>
<tr>
<td>UK MRC</td>
<td>UK Medical Research Council</td>
</tr>
<tr>
<td>US</td>
<td>United States</td>
</tr>
<tr>
<td>US CDC</td>
<td>US Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>US NIH</td>
<td>US National Institutes of Health</td>
</tr>
<tr>
<td>USAID</td>
<td>US Agency for International Development</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
The survey

The first G-FINDER reproductive health survey reports on 2013 global investment into research and development (R&D) for new reproductive health products for developing countries (DCs). Data collection for this report was linked to the G-FINDER neglected disease survey.

Reproductive health is a broad concept that covers the reproductive processes, functions and system at all stages of life. Although many reproductive health problems in DCs are not due to R&D gaps, some are. The purpose of this report is to capture those investments specifically aimed at reproductive health R&D gaps in DCs.

There are many commercial R&D investments into new reproductive health products for developed markets. While these investments target women in developed countries, they may also benefit women in low- and middle-income countries (LMICs). At the other end of the spectrum are R&D investments that are specifically aimed at DC needs. These funds are intended to meet the needs of women living in LMICs who suffer disproportionately from unintended pregnancies, death and disability during pregnancy and childbirth, sexually transmitted infections (STIs), and other problems related to the reproductive system and sexual behaviour. Funding may be aimed at developing new or adapted products that are more affordable, heat stable, or easier to deliver; or at establishing or improving the safety and efficacy of products in DC groups such as HIV-positive patients, or patients with co-infections such as tuberculosis.

However, these distinctions are not always clear-cut and it is sometimes difficult to determine if an investment is DC-specific, or how DC-specific it may be. Therefore, we convened and consulted an international Expert Advisory Group (EAG) composed of experts in reproductive health and reproductive health R&D. This resulted in the following list of DC-specific reproductive health R&D ‘gap’ areas for inclusion in this report:

- Drugs for post-partum haemorrhage (PPH)
- Drugs, devices and combination products for contraception
- Drugs for the treatment of syphilis and diagnostic tests for multiple STIs
- Multipurpose Prevention Technologies (MPTs)
- Platform technologies for reproductive health
- Core funding for reproductive health R&D organisations.

Findings

In 2013, reported funding for DC-specific reproductive health R&D was nearly $88m. The majority of this ($63m, 71%) went to developing-world focussed contraceptives. The pharmaceutical industry was the largest funder in this area, accounting for $33m (53%), followed by the philanthropic sector ($17m, 26%) and the public sector ($13m, 20%).
All other areas received less than $10m each: $9.2m (10%) went to core funding of reproductive health R&D organisations; $6.5m (7.4%) went to MPTs; $3.5m (3.9%) went to PPH; $1.8m (2.0%) went to platform technologies for reproductive health; and $0.4m (0.5%) went to non-HIV STIs. Some areas received no in-scope funding at all, including syphilis drugs, ultra-short acting contraceptive drugs and permanent contraceptive drugs.

All sectors provided significant investments into DC-specific R&D for reproductive health, with industry investing $36m (41%), the public sector $27m (30%) and philanthropy $25m (29%). Each sector invested the highest proportion of its funding into developing world-focussed contraceptive R&D. After industry, the top three funders (the Gates Foundation, the US Agency for International Development and the Indian Council for Medical Research) together provided almost half of total funding ($41m, 47%).

In terms of funding to the organisations developing DC-specific reproductive health products, almost half ($40m, 45%) went to the pharmaceutical industry (the vast majority of which was self-funding). Just under a quarter ($21m, 24%) of R&D funding went to product development partnerships and intermediaries, while academics received $19m (21%) and public developers the remaining $8.3m (9.4%). Apart from industry, the two largest product developers by value of funding were FHI 360 ($14m, 16%) and the Population Council ($13m, 15%).
INTRODUCTION

Reproductive health is a broad concept that covers the reproductive processes, functions and system at all stages of life. It involves access to comprehensive services such as family planning, skilled attendance at birth, emergency obstetric care, and the prevention and treatment of sexually transmitted infections (STIs), including HIV/AIDS.

Some persistent reproductive health problems in developing countries (DCs) are not due to research and development (R&D) gaps – for example, they can be due to weak health systems, cultural barriers or lack of information. However, in many cases, R&D gaps remain a problem. The purpose of this report is to capture those investments specifically aimed at reproductive health R&D gaps in DCs, where the need is greatest.

Distinguishing commercial from non-commercial R&D

There are many commercial R&D investments into new reproductive health products for developed markets. For instance, there is demand for contraception containing natural oestrogen in High-Income Countries (HICs) to reduce the risk of venous thromboembolism, particularly for obese women. While these investments target women in developed countries, where obesity is one of the most important public health issues, they may also benefit women in Low- and Middle-Income Countries (LMICs) where obesity is an emerging issue. Nevertheless, R&D investments like these are excluded from this report since they are clearly driven by, and targeted at, HIC markets.

At the other end of the spectrum are R&D investments that are specifically aimed at DC needs. These target women living in LMICs who suffer disproportionately from unintended pregnancies, death and disability during pregnancy and childbirth, STIs, and other problems related to the reproductive system and sexual behaviour. Funding may be aimed at developing new or adapted products that are more affordable, heat stable, or orally or vaginally administered rather than intravenously or intramuscularly; or at establishing or improving the safety and efficacy of products in DC groups such as HIV-positive patients, or patients with co-infections such as tuberculosis. These investments are clearly DC-specific and are therefore included in this report.

However, while people in HICs and LMICs can and do have specific reproductive health needs, there are also shared reproductive health needs that span low-, middle- and high-income economies – in these cases, it can be difficult to determine if an investment is DC-specific, or how DC-specific it may be. In such cases, our key filter was the question: Would this R&D investment have continued if DCs no longer existed? If the answer was ‘even without DCs, we would still do this R&D’, the investment was excluded (it was clearly not DC-specific). If the answer was ‘without DCs we would have no reason to do this R&D’, the investment was included as it was clearly DC-specific.

Given the described complexities in distinguishing between investments targeting developed countries from investments targeting DCs, particularly in ‘shared’ areas, we convened and consulted an international Expert Advisory Group (EAG) composed of experts in reproductive health and reproductive health R&D (see Annexe 2). They were asked to nominate and then filter a list of reproductive health issues based on the criteria outlined in Figure 1, and using the filter question noted above as a final decider.
This process resulted in the list of DC-specific reproductive health R&D ‘gap’ areas and product ‘gap’ areas for inclusion in this report seen in Table 1. Some of these product areas were restricted to prevent DC-specific data being swamped by ‘white noise’ from commercial R&D investments (e.g. for contraceptive drugs, only products specifically designed for LMIC settings were included). Basic research was also excluded since this early-stage research cannot be allocated to a specific developed or developing country application.

Table 1. G-FINDER reproductive health areas, products and technologies

<table>
<thead>
<tr>
<th>Reproductive health area</th>
<th>Drugs</th>
<th>Devices</th>
<th>Combinations</th>
<th>Diagnostics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-partum haemorrhage</td>
<td>R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-HIV sexually transmitted infections (STIs)</td>
<td>R</td>
<td></td>
<td>R</td>
<td></td>
</tr>
<tr>
<td>Syphilis (including congenital syphilis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple STIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraceptives</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td></td>
</tr>
<tr>
<td>Multipurpose Prevention Technologies</td>
<td></td>
<td></td>
<td></td>
<td>Y</td>
</tr>
<tr>
<td>Platform technologies for reproductive health</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Core funding of a reproductive health R&amp;D organisation</td>
<td></td>
<td></td>
<td></td>
<td>Y</td>
</tr>
</tbody>
</table>

*‘R’ denotes a restricted category where only some investments are eligible, as defined in Annexe 4.

*‘Y’ denotes a category where a reproductive health area, product or technology is included in the survey.

We note that the scope of G-FINDER is limited to R&D. Although we recognise the vital importance of activities such as operational and implementation research, community education and general capacity building – as well as the very substantial investments made into these areas – they are nevertheless outside the scope of this report. We also exclude investment into general therapies such as painkillers since these cannot be designated to reproductive health only.

For further information on the methodology of this survey, refer to Annexe 1.
OVERALL FUNDING

Nearly $88m was invested into R&D of in-scope reproductive health products in 2013. The majority ($63m, 71%) of this funding went to contraceptives, with other areas each receiving less than $10m.

Around $4.0m (4.6% of the total) was reported to the survey as ‘unspecified reproductive health R&D’: these were grants that could not be easily apportioned to a single area. As a result, reported funding for some reproductive health areas and products will be slightly lower than actual funding, with the difference being included as ‘unspecified reproductive health R&D’ funding.

Table 2. DC-specific reproductive health R&D funding 2013

<table>
<thead>
<tr>
<th>Reproductive health area</th>
<th>US$</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraceptives</td>
<td>62,541,252</td>
<td>71</td>
</tr>
<tr>
<td>Core funding of a reproductive health R&amp;D organisation</td>
<td>9,150,512</td>
<td>10</td>
</tr>
<tr>
<td>Multipurpose Prevention Technologies</td>
<td>6,499,667</td>
<td>7.4</td>
</tr>
<tr>
<td>Unspecified reproductive health R&amp;D</td>
<td>4,015,639</td>
<td>4.6</td>
</tr>
<tr>
<td>Post-partum haemorrhage</td>
<td>3,463,744</td>
<td>3.9</td>
</tr>
<tr>
<td>Platform technologies for reproductive health</td>
<td>1,787,664</td>
<td>2.0</td>
</tr>
<tr>
<td>Non-HIV sexually transmitted infections</td>
<td>408,879</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>87,857,358</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
### CONTRACEPTIVES

Women in both developed and developing countries need safe and effective contraception, and three-quarters of women in DCs who seek to avoid unplanned pregnancy already use a safe and effective method. However, this means that a quarter of all women in DCs needing contraception – 225 million women – still have an unmet need for safe and effective contraception.\(^1\)

The unmet need is greatest in poor countries (low and lower-middle income countries account for about 75% of the developing world unmet need\(^1\)) and this results in around 74 million unintended pregnancies in DCs each year.\(^1\) As described by the Guttmacher Institute, addressing this unmet need would prevent 52 million unintended pregnancies per year, including 21 million unplanned births, 24 million abortions (of which 16 million may be unsafe\(^3\)) and 6 million miscarriages.\(^1\) It would also prevent 500,000 newborn deaths per year, and 70,000 maternal deaths per year. Most of the latter reduction would take place in sub-Saharan Africa, the region with the highest levels of both mortality during pregnancy and childbirth, and the highest unmet need for modern contraception.\(^1\)

There are many reasons why women in DCs do not or cannot use modern contraceptive methods, only some of which are due to R&D gaps.\(^3,4\) For instance, women (or their partners) may be opposed to contraception; or they may want contraception but be unaware or distrustful of existing effective methods, unable to afford them, or unable to access them (for example, because products are out of stock).

However, in other cases, an R&D gap is the problem. For instance, available contraceptives can be unsuitable for women in DCs because of their side effects, potential health risks or incompatibility with breast-feeding; or because their design leads to higher costs or requires administration by a highly-trained provider or using speciality equipment, something that can be very difficult for women in poor, remote or unstable settings. It is funding specifically aimed at these R&D gaps that this survey seeks to capture.

Current R&D gaps for DC-specific contraceptives include:

- New contraceptives that are usable on demand (that is, around the time of intercourse, and potentially without a partner’s knowledge or cooperation)
- Contraceptives that are safe to use while breast-feeding
- New long-acting, reversible contraceptives
- Non-hormonal contraceptives
- Non-surgical permanent contraception.

All new methods need to be affordable, well-tolerated and easy to deliver if they are to be useful and used, particularly by poorer women and in poorer countries. They might include devices (for example, intrauterine devices and diaphragms), drugs or drug/device combinations.

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<table>
<thead>
<tr>
<th>TOTAL SPEND ON DC-SPECIFIC CONTRACEPTIVE R&amp;D IN 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>$62.5 MILLION</td>
</tr>
</tbody>
</table>

225 million women in developing countries have an unmet need for safe and effective contraception.
Total funding for DC-specific contraceptive R&D was just under $63m in 2013. More than three-quarters of funding was for combination products, which received $49m (78%). Drugs received $7.6m (12%) and contraceptive devices the remaining $6.0m (9.6%). Within drug R&D, two-thirds of funding went to short-acting drugs ($5.1m), a quarter to long-acting drugs ($1.9m) and the remainder to unspecified drug R&D ($0.6m). There is also a need for ultra-short acting, and for permanent contraceptive drugs, but neither of these areas received in-scope funding in 2013.

The pharmaceutical industry provided more than half of developing world-focussed contraceptive R&D funding ($33m, 53%). Philanthropic funders invested just over a quarter of the total ($17m, 26%) – almost all of which ($16m) was from the Gates Foundation. The public sector provided the remaining $13m (20%), with US Agency for International Development (USAID) providing half of this ($6.4m).

**Figure 2. Contraceptive R&D funding by product type 2013**

**Figure 3. Contraceptive R&D funding by sector 2013**
CASE STUDY – A LONGER-ACTING INJECTABLE CONTRACEPTIVE

FHI 360, a US-based product development partnership (PDP), is currently evaluating candidates for a longer-acting injectable contraceptive for women in the developing world. The project aims to develop a single-use, pre-packaged product that would provide women with six months of contraception from a single, affordable injection.

Injectable contraceptives are used by over 40 million women globally, and make up over one-third of modern contraceptive use in the least developed countries. However, available technologies only provide protection for 1-3 months, requiring between 4 and 12 visits a year to a health professional. This can be difficult in resource poor settings, contributing to discontinuation rates of over 40% for injectable contraception in some countries.

An injectable contraceptive lasting six months would reduce the number of times a woman needs to interact with a health provider, thus increasing contraceptive access for women across the developing world and improving compliance and continuation rates, resulting in fewer unintended pregnancies. A pre-filled, single-use injectable could be easily used by health workers with limited training, could potentially be self-administered and would eliminate the possibility of disease transmission through needle re-use.

Established in 2011, FHI 360 is active in health research, advocacy, policy and programmatic work in over 70 countries. The development of a longer-acting injectable contraceptive is a part of its Contraceptive Technology Innovation initiative, which includes an R&D portfolio of family planning technologies. After issuing a global call for proposals in 2012, FHI 360 identified four potential longer-acting contraceptive candidates for further evaluation. All are currently in the proof-of-concept stage, and a finished product is possible by 2021. Funding for the injectable is provided by the Gates Foundation.
MULTIPURPOSE PREVENTION TECHNOLOGIES

For the scope of this survey, G-FINDER defined MPTs as: a product that combines a platform technology or contraceptive device with one or more drug/s, and addresses two or more reproductive health indications.

The potential benefit of MPTs would be very high in DCs, especially in poorer countries in Africa where women bear a significant burden of HIV, STIs and unintended pregnancies. In sub-Saharan Africa, women account for approximately 60% of all HIV infections, and 53 million women have an unmet need for safe and effective contraception. Women in Africa suffered around 39 million new cases of chlamydia, gonorrhoea and trichomoniasis in 2005.

MPTs could allow women and girls to address multiple sexual and reproductive health issues with one product. There is potential for MPTs to include vaccines, contraceptives, microbicides and drugs. MPTs can include combinations that target contraception, HIV/AIDS or other STIs such as syphilis, gonorrhoea, chlamydia, trichomoniasis, hepatitis B, herpes or human papillomavirus. MPTs can increase efficiencies for end-users, donors, procurers and providers by providing simultaneous protection against multiple health risks while also meeting women’s sexual and reproductive health needs.

MPTs needed are:

- Contraceptive device + HIV drug/s
- Contraceptive device + STI drug/s
- Contraceptive device + STI + HIV drug/s
- Contraceptive device or platform technology + STI + HIV + contraceptive drug/s.

A total of $6.5m was invested in MPT R&D in 2013. The majority of funding for MPTs came from the public sector ($6.2m, 96%), with the philanthropic sector providing the remaining $0.3m (3.9%).

There were four public funders of MPT R&D – with US funders providing the vast majority ($5.8m, 93% of public funding). All of the funding from the philanthropic sector was from the Gates Foundation.
CASE STUDY – INTRAVAGINAL CONTRACEPTIVE RING FOR RELEASE OF LEVONORGESTREL AND TENOFOVIR

CONRAD, a US-based PDP, is leading the development of an intravaginal contraceptive ring that also provides protection against HIV and herpes simplex virus-2 infection. The ring is designed to stay in place for three months, continuously releasing the contraceptive drug levonorgestrel and the antiretroviral tenofovir.12

Women often lack decision-making power for reproductive health in DCs. Condoms are the only available method that provides protection from both unwanted pregnancy and infection; however, use of male condoms tends to be controlled by men.13 Vaginal rings are intended to transfer the decision to use prevention products to women. The vaginal ring provides ongoing contraceptive protection that offers a reliable advantage over contraceptives that need to be used at the time of intercourse.14

Studies have shown that tenofovir is effective in preventing HIV infection, but current drug delivery mechanisms are not well-suited to DCs. In pill form, tenofovir requires high doses and must be taken daily. CONRAD’s vaginal ring is designed to deliver a high dose of tenofovir continuously over 90 days.14

The vaginal ring is being co-developed with researchers from the McCormick School of Engineering and Applied Science, and the Department of Obstetrics and Gynecology at Northwestern University Feinberg School of Medicine.14 Phase I clinical trials to evaluate the safety and acceptability of the product began in October 2014, with completion planned for November 2015.15

Established in 1986, CONRAD is based at the Eastern Virginia Medical School.16 CONRAD aims to develop safe, affordable contraceptive and microbial products that are acceptable in resource-poor settings. CONRAD conducts preclinical research and clinical trials, and partners with industry organisations to bring new products to market.17 CONRAD receives funding for the vaginal ring from USAID.
FINDINGS

Post-partum haemorrhage (PPH) is commonly defined as a blood loss of 500ml or more within 24 hours of giving birth and affects approximately 2% of all women giving birth. It is the leading cause of mortality associated with pregnancy and childbirth in most low-income countries. In Asia and sub-Saharan Africa, PPH is associated with 30% of such deaths. In 2010, PPH was responsible for 58,000 deaths and 3.3 million disability adjusted life years (DALYs) in the developing world.

Intravenous or intramuscular injection of oxytocin is the accepted gold standard for prevention and treatment of PPH, and is an essential medicine recommended by the World Health Organization (WHO). However, it is not suited to many DC settings. Current formulations of the drug are not stable at room temperature, therefore they require refrigeration to maintain efficacy – often a problem in low resource settings. A skilled health worker is also needed to administer oxytocin, but globally, 40 million births a year are without a skilled attendant, including half of all births in sub-Saharan Africa and South Asia.

Misoprostol is an alternative treatment for both prevention and treatment of PPH. While it is less effective than oxytocin, it is heat stable and can be given orally. However, there is controversy regarding its use in PPH treatment, due to a lack of evidence of its efficacy and potential side effects. The WHO recommends that misoprostol only be given to treat PPH in the absence of any other treatment or if all other measures fail.

Other alternatives include oxytocin analogues and blood clotting drugs used to halt bleeding.

Current DC-specific R&D gaps for PPH include:

- Formulations of oxytocin and oxytocin analogues that are heat-stable and do not require intravenous or intramuscular administration
- Blood clotting drugs that affect uterine bleeding specifically and that are appropriate for DC settings.

DC-specific R&D for drugs to treat PPH received $3.5m in 2013. Just over three-quarters of this was provided by the pharmaceutical industry ($2.6m, 76%). The Wellcome Trust, the only philanthropic funder, provided a further $0.8m (22%); with the remaining $0.1m (2.4%) from the UK Medical Research Council (MRC), the sole public funder.
CASE STUDY – INHALED OXYTOCIN

GlaxoSmithKline (GSK) is collaborating with Monash University to develop a powder formulation of oxytocin that can be inhaled from a simple, disposable device. This technology has the potential to prevent millions of cases of PPH as it overcomes the limitations that make currently available formulations of oxytocin inappropriate for many DC settings.

Unlike injected oxytocin, the dry oxytocin formulation remains effective at temperatures up to 50°C, so can be used in virtually all climates without need for refrigeration. The single-use nasal spray can be used outside a health facility by basically skilled health workers, or potentially self-administered.

Early development of the inhaled oxytocin was undertaken at the Monash Institute of Pharmaceutical Sciences (MIPS). In September 2014 the technology was licensed to industry partner GSK to bring the research from preclinical through to trial stage.

Based at Monash University in Australia, MIPS was established in 2008. MIPS undertakes basic and translational drug discovery, drug delivery and drug development research and has long-term collaborative research programs with more than 20 biotechnology and pharmaceutical companies. GSK is a multinational pharmaceutical company with commercial operations in over 150 countries and manufacturing facilities in 36.

Following the 2014 co-development agreement between Monash University and GSK, funding has been committed for early-stage development from The McCall MacBain Foundation, Grand Challenges Canada and the Planet Wheeler Foundation.
Non-HIV sexually transmitted infections (STIs) are a major global cause of acute illness, infertility, stigma, long-term disability and death, and have serious medical and psychological consequences for millions of men, women and infants. According to the WHO, there were 93 million estimated new cases of the most prevalent STIs globally in 2008: 60 million cases of trichomoniasis, 21 million cases of gonorrhoea, 8.3 million cases of chlamydia and 3.4 million cases of syphilis.

A significant challenge in the control of STIs is accurate and timely diagnosis. Current methods for early diagnosis can be unsuitable for resource-constrained settings as they require trained staff, laboratory infrastructure and/or might be costly or lengthy. The WHO has estimated that a combined test for chlamydia and gonorrhoea requiring no laboratory infrastructure would save more than 4 million DALYs, and prevent more than 17 million new gonorrhoea and chlamydia infections and more than 212,000 HIV infections over four years, even when used only among sex workers in sub-Saharan Africa, China, and South-East Asia.

Current R&D gaps for non-HIV STIs include:

- Low-cost, rapid, reliable, easy to use point-of-care diagnostics specifically designed for low-resource settings, and able to diagnose more than one STI
- Oral, single-dose drugs for syphilis.

Less than half a million dollars ($0.4m) was invested in R&D for DC-specific non-HIV STIs in 2013, all going to diagnostics for multiple STIs. No in-scope funding was reported for syphilis drug R&D.

There were only two grants reported for diagnostics: one from the US National Institutes of Health (NIH, $0.23m, 55%) for multiple STIs, and the other from the US Centers for Disease Control and Prevention (CDC, $0.18m, 45%) for syphilis and HIV.
PLATFORM TECHNOLOGIES FOR REPRODUCTIVE HEALTH

R&D into technologies that can be applied to a range of areas, but is not yet focused on a single reproductive health area or product, is classified as platform technology R&D. Examples include implants and technologies that can be used for the controlled release of drugs, but are not yet developed as a product with a specific drug. Once a platform technology is focused on a specific need (for example, it is being developed in combination with a specific drug), then it is classified either as a contraceptive combination or MPT.

Total funding for DC-specific reproductive health platform technology R&D was $1.8m in 2013. The majority of this ($1.5m, 83%) was from the Gates Foundation, with USAID providing a further $0.3m (14%) and industry the remaining $0.1m (3.5%).

CASE STUDY – BIODEGRADABLE CONTRACEPTIVE IMPLANT

A biodegradable contraceptive implant (BCI) that will offer women an 18-month family planning option is currently being developed by FHI 360, a US-based PDP. As with existing implant technology, the BCI will be implanted under the skin and continuously release hormones for long-term contraception but, unlike existing implants, it will safely break down in the body at the end of the device’s effectiveness period.

Contraceptive implants are an increasingly popular means of family planning in a number of DCs, as they offer highly effective, long-term protection. However, the device must be removed when pregnancy is desired, or at the end of the device’s duration of effectiveness. Implant removal requires a procedure by a skilled health worker, which may not be easily accessible for women in low-resource settings. A biodegradable implant is designed to eliminate the need for device removal after the effectiveness period.

Early proof-of-concept testing for the BCI is now underway. FHI 360 is leading the development of the new platform in partnership with novel drug delivery developers Orbis Biosciences and Yale University.

R&D for the BCI is conducted under FHI 360’s Contraceptive Technology Innovation Initiative. Launched in 2013, this initiative is focused on delivery of affordable mid-to-long term contraceptive options for low resource settings. USAID is funding the BCI project.
CORE FUNDING OF REPRODUCTIVE HEALTH R&D ORGANISATIONS

Funding for R&D organisations that work in multiple reproductive health areas, and that could not be accurately allocated to a specific reproductive health area, was reported as core funding. Funding to an organisation involved in multiple reproductive health areas that could be earmarked to a specific area or product, was included under that specific area.

Organisations focussed on DC-specific reproductive health R&D received $9.2m in core funding in 2013. Two public funders – the Indian Council of Medical Research (ICMR) and UK Department for International Development (DFID) – provided over three-quarters of this ($7.1m, 77%). The remaining $2.1m (23%) was from the Gates Foundation, the only philanthropic organisation to provide core funding to a DC-focussed reproductive health R&D organisation in 2013.
Industry, the public sector and philanthropy each provided significant investments into DC-specific R&D for reproductive health. The majority of public sector funding ($21m, 78%) was from HICs. Contraceptives received the highest proportion of each sector’s R&D funding, including the vast majority of industry funding ($33m, 93%), two-thirds of philanthropic funding ($17m, 66%) and just under half of public funding ($13m, 48%).

After industry (where investments are aggregated into a single figure), the top three funders – the Gates Foundation, USAID and the Indian ICMR – together provided almost half of total funding ($41m, 47%), with the Gates Foundation investing more than twice as much as any other organisation (excluding industry). The remaining organisations invested less than $3.6m (4.0%) each.

Some funders invested across a wide range of reproductive health R&D areas. For example, the Gates Foundation funded R&D for MPTs, contraceptives and platform technologies, as well as providing core funding to multi-focus reproductive health R&D organisations. Others funded a wide range of reproductive health areas by virtue of providing their investment as core funding to a multi-focus reproductive health R&D organisation. For instance, the Indian ICMR provided all its funding ($5.9m) as core funding to its own internal research institutes; and UK DFID gave its entire investment ($1.1m) as core funding to Grand Challenges Canada.

Other organisations funded only one or two specific reproductive health R&D areas. For instance, the Dutch DGIS only funded contraceptive R&D.
CASE STUDY – THE GLOBAL IMBALANCE IN DC-SPECIFIC REPRODUCTIVE HEALTH R&D

Although both Europe and the US provide substantial funding for programmatic, operational and capacity development work for reproductive health in DCs, the US appears to have a much stronger focus on funding R&D for new products compared with Europe.

In 2013, the US accounted for 87% ($77m) of reported global funding for DC-specific reproductive health R&D – over fifteen times the investment of Europe. Only three European countries reported reproductive health R&D funding to G-FINDER – the Netherlands, the UK and Norway – totalling $4.7m (5.3% of the global total).

The largest funder from Europe, the Dutch DGIS ($2.5m), accounted for over half of all European funding. By comparison, there were several large funders from the US, including the Gates Foundation ($24m), who accounted for almost a third of US funding, followed by USAID ($11m) and the US NIH ($3.6m).

While the number of funders from each region were comparable (five organisations each from the US and Europe, excluding industry), the number of grants from US-based funders was over six times that of European funders.

India was the only LMIC to report DC-specific reproductive health R&D funding, but its investment of $5.9m (6.7% of total), was more than that of Europe combined. The Indian ICMR accounted for all of this, providing self-funding to two internal research institutes. We note, however, that Indian investments tend to be focussed on domestic needs, and not all products are qualified for broader global use.

Globally, the only other reporting country to invest in DC-specific reproductive health R&D was Australia, with $0.5m (0.5% of total), although we note that some major developing countries who may have significant investments do not report to this survey, such as China.

Figure 11. Regional funding for DC-specific reproductive health R&D 2013
DEVELOPERS OF DC-SPECIFIC REPRODUCTIVE HEALTH PRODUCTS

Almost half ($40m, 45%) of total funding to conduct R&D for DC-specific reproductive health products went to the pharmaceutical industry, although much of this ($36m, 91%) was industry’s own self-funding. Just under a quarter ($21m, 24%) of R&D funding went to PDPs and intermediaries, while academics received $19m (21%) and public developers – such as government research institutions – received the remaining $8.3m (9.4%).

On top of the pharmaceutical industry’s self-funding, a small additional amount of grant funding came from others ($3.7m, 9.4% of industry funding) – the majority of which came from the Gates Foundation ($2.9m, 77%).

Academic institutes were largely funded through grants from the public ($8.3m, 45%) and philanthropic ($8.1m, 43%) sectors, although they also funded a small amount of their own R&D ($2.1m, 12%).

The philanthropic sector provided almost two-thirds ($13m, 62%) of PDP and intermediary funding, with the remainder coming from the public sector ($8.1m, 38%).

The majority of funding for public developers was internal investment ($6.1m, 74%), with the rest from other funders in the public sector ($1.2m, 14%) and philanthropic funders ($1.0m, 12%).

The major research organisations by value of funding were FHI 360 ($14m, 16%), the Population Council ($13m, 15%), the Indian ICMR ($5.9m, 6.7%) and the Program for Appropriate Technology in Health (PATH, $3.5m, 3.9%). All other product developers received less than $2.0m (this excludes industry).

Figure 12. Recipients of DC-specific reproductive health R&D funding 2013
CASE STUDY – THE POPULATION COUNCIL

Formed in 1952, the US-based Population Council is a non-government global health research organisation specialising in reproductive health, HIV and youth development. Partnering with governments, the pharmaceutical industry and civil society groups, the Population Council conducts basic research and clinical trials for new health technologies, and links with service delivery systems in over 50 countries, as well as working to license products for DC use. Over 120 million women have utilised contraceptive implants and intrauterine devices developed by the Population Council.

The Population Council was a major recipient of reproductive health R&D funding in 2013, accounting for 15% of all funding. The majority ($11m, 87%) was invested into R&D for contraceptives and the remainder ($1.7m, 13%) for MPT R&D.

The Population Council is developing several first-of-its-kind family planning technologies targeted at the developing world. These include a one-year contraceptive vaginal ring employing Nestorone® and ethinyl estradiol which will provide long-acting, reversible contraception, and is designed to be initiated and controlled by women; and a one-year long-acting, reversible male contraceptive implant, also in early-stage development. In collaboration with Antares Pharma, the Population Council have also completed Phase II trials on a transdermal contraceptive gel that can be absorbed through a woman’s skin to provide immediate contraceptive protection.

Almost half (48%) of the Population Council’s funding comes from USAID for the support of developing world-focussed contraceptive and MPT projects. A further 30% comes from the Gates Foundation for the development of affordable and acceptable intravaginal ring technology and 5.2% from the US NIH for contraceptives and MPTs. The remaining 16% is self-funded by the Population Council directly, for translational work along the product development continuum.
ANNEXE 1: METHODOLOGY

Data collection

Data was collected via a reproductive health R&D module which was linked to the G-FINDER neglected disease survey. In consultation with our international Expert Advisory Group (EAG, see Annexe 2), organisations involved in reproductive health R&D were identified for participation. These organisations were asked to report every in-scope reproductive health R&D grant they had disbursed or received in 2013.

Thirty-one organisations reported reproductive health R&D data in the first year of the G-FINDER expansion into reproductive health (see Annexe 3 for a list of survey participants).

All respondents used the same definitions, categories and inclusion/exclusion criteria (see Annexe 4). We only accepted primary grant data. If accurate primary data was not available, we did not substitute secondary data or estimates.

Data was collected over a six-week period from May to June 2014, during which intensive follow-up and support were provided to key participants.

Data from participating multinational pharmaceutical companies and small pharmaceutical and biotechnology firms was aggregated in order to protect their confidentiality.

Survey scope

As discussed in the Introduction, commercial R&D investments into new reproductive health products for wealthy markets were excluded from this report since they are driven by, and targeted at, populations in HICs. People in LMICs may benefit from these investments, but the research would still be done even if DCs did not exist.

This report only includes R&D investments specifically targeting men and women in LMICs. This R&D work may be aimed at developing new or adapted products that are more affordable, heat stable, or deliverable via oral or vaginal routes rather than intravenously or intramuscularly; or at establishing or improving the safety and efficacy of products for patients who are also affected by diseases that disproportionately affect LMICs such as HIV/AIDS, malaria or tuberculosis.

Given the complexities in distinguishing between investments targeting HICs from investments targeting LMICs, we worked closely with our EAG to identify reproductive health issues specific to DC settings. This process resulted in the following list of reproductive health R&D areas: PPH, contraceptives, non-HIV STIs, MPTs, platform technologies for reproductive health and core funding of a reproductive health R&D organisation.

Some of these R&D areas were restricted to only include DC-specific investments (e.g. for contraceptive drugs, only products specifically designed for LMIC settings were included). Basic research was also excluded since this early-stage research cannot be allocated to a specific developed or developing country application.

Funding for the development of MPTs that include a microbicide – previously included in the neglected disease G-FINDER report as HIV/AIDS microbicides R&D – is now included in this report. Other R&D funding for HIV/AIDS is reported in the annual neglected disease G-FINDER report.
Handling of financial data

The collection principles used by the G-FINDER survey to handle key financial data were also used to handle the data included in this report. These principles included:

- Survey recipients were asked to enter grant-by-grant expenditures incurred during their financial year (as opposed to the 2013 calendar year) that had the largest overlap with 2013. PDPs and other intermediaries and product developers were also asked to enter grant-by-grant revenue during the same period.
- Only expenditures were included, as opposed to commitments made but not yet disbursed or ‘soft’ figures such as in-kind contributions, costs of capital, or funding estimates.
- All figures are reported in 2013 US dollars. Any data entered by survey participants in their local currency was converted to US dollars based on the 2013 average annual exchange rate as reported by the IMF.

Survey tool and process

In order to be as consistent and comprehensive as possible across the range of reproductive health conditions surveyed, we followed two core principles:

1. Only primary data reported by the funders, PDPs and other intermediaries, and product developers themselves was included in the survey. If this data was not available, it was not supplemented with secondary data or estimates.
2. All primary grant data was collected using the same online/offline reporting tool and inclusion/exclusion framework for all survey recipients.

Survey tool

Survey participants were asked to enter every DC-specific reproductive health R&D investment they had disbursed or received in their financial year 2013 into a password-protected online database, including the grant amount, grant identification number, a brief description of the grant and the name of the funder or recipient of the grant. They were also asked to confirm their organisation details such as role in funding (e.g. funder, fund manager, product developer), financial year, currency used, type of organisation (e.g. private sector firm, academic institution, PDP, multilateral organisation), and country where they were located.

Each grant was entered using a three-step process where the survey recipient had to choose (1) a specific reproductive health condition; (2) a product type (e.g. drugs, diagnostics); and (3) a research type within the product (e.g. discovery and preclinical, clinical development); according to pre-determined categories (see Annexe 4). Where survey recipients could not provide data to this level of detail, they were asked to provide the finest level of granularity they could.

If survey recipients were not able to allocate the grant to a single condition in step 1, three options were available:
• ‘Platform technologies for reproductive health’
• ‘Core funding of a reproductive health R&D organisation’ (e.g., funding to an organisation working in multiple reproductive health areas, where the expenditure per area was not known to the funder)
• If survey recipients were not able to allocate the grant to a single product in step 2 or a single research type in step 3, they had the option to select ‘Unspecified reproductive health R&D’.

Data cleaning

Survey closure was followed by a period of intensive cleaning, cross-checking, and organising of the complex dataset collected.

All grants were verified through a four-step process:

1. Each grant was reviewed against our inclusion criteria. Over 355 grants were manually checked for correct allocation
2. Grants identified as borderline in terms of scope were reviewed in consultation with the EAG
3. Automated reconciliation reports were used to cross-check ‘disbursed’ funding reported by funders against ‘received’ funding reported by recipients
4. Uncovered discrepancies were resolved through direct contact with the funder and recipient to identify the correct figure. In the few cases where discrepancies still remained, the funder’s figures were used.

Limitations to interpretation

As with all surveys, there are limitations to the data presented. Potential limitations include:

Survey non-completion

Although strenuous efforts were made to identify all organisations active in reproductive health R&D, some reproductive health R&D funding might not have been captured because organisations were not identified and therefore were not invited to participate, or were invited to participate, but did not respond.

While data from major public funders is close to 100% complete, private sector investments might be under-reported due to the lack of company participation. Only five companies reported DC-specific reproductive health R&D data in 2013. Also, the lack of participation from DC firms means likely under-reporting in reproductive health areas where these firms are active.

Response rate

Differing levels of responsiveness between organisations and countries may also skew the findings. For instance, the Australian location of the G-FINDER group may have encouraged higher levels of responsiveness from Australian funders, while funders in non-English speaking settings may have been less enthusiastic in their levels of response. This is not known to have occurred.
Time lags in the funding process

Time lags exist between disbursement and receipt of funding, as well as between receipt of funds and the moment they are actually spent. Thus, grants by funders will not always be recorded as received by recipients in the same financial year and there may be a delay between R&D investments as reported by G-FINDER and actual expenditure on R&D programmes by product developers and researchers.

Inability to disaggregate investments

Funding allocated to some conditions and products may be underestimated due to:

- Organisations working across multiple reproductive health conditions: Core funding grants to organisations working on multiple conditions are not counted within the funding figures for specific conditions
- Investments for multiple conditions: When funders were unable to disaggregate grants for multiple reproductive health conditions within scope, these investments were included in the ‘Unspecified reproductive health R&D’ category. This methodology was followed to prevent double-counting investments
- Investments in shared areas: When funders were unable to disaggregate grants for developed markets from investments into DC-specific products, these investments were excluded. This might have led to under reporting.

Missing data

We can only report the data as it is given to us. Although strenuous efforts were made to check the classification, accuracy and completeness of grants, data might have been incorrectly entered or funders may have accidentally omitted some grants. We believe, however, that the checks and balances built into the process mean that such mistakes, if present, will have a minor overall impact.
## ANNEXE 2: EXPERT ADVISORY GROUP MEMBERS

<table>
<thead>
<tr>
<th>MEMBER</th>
<th>ORGANISATION</th>
<th>TITLE</th>
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<tbody>
<tr>
<td>Jane Hutchings</td>
<td>Program for Appropriate Technology in Health (PATH)</td>
<td>Director, Reproductive Health</td>
</tr>
<tr>
<td>Judy Manning</td>
<td>Office of Population and Reproductive Health, Global Health Bureau, United States Agency for International Development (USAID)</td>
<td>Biomedical R&amp;D Team Lead</td>
</tr>
<tr>
<td>Malcolm McNeil</td>
<td>UK Department for International Development (DFID)</td>
<td>Senior Health Adviser, Research and Evidence Division</td>
</tr>
<tr>
<td>Susan Meikle</td>
<td>Gynecologic Health and Disease Branch, The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH)</td>
<td>Program Director, Pelvic Floor Disorders</td>
</tr>
<tr>
<td>Lori Newman</td>
<td>Department of Reproductive Health and Research, World Health Organization: Special Programme of Research, Development and Research Training in Human Reproduction (WHO/HRP)</td>
<td>Medical Officer, Sexually Transmitted Infections Team</td>
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<tr>
<td>Matthew Reeves</td>
<td>National Abortion Federation</td>
<td>Medical Director</td>
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<tr>
<td>Morven Roberts</td>
<td>UK Medical Research Council (MRC)</td>
<td>Programme Manager for Global Infections and Global Health Trials</td>
</tr>
<tr>
<td>Malabika Roy</td>
<td>Indian Council for Medical Research (ICMR)</td>
<td>Head, Division of Reproductive Child Health</td>
</tr>
<tr>
<td>Joseph Speidel</td>
<td>Bixby Center for Global Reproductive Health, University of California, San Francisco</td>
<td>Professor, Department of Obstetrics, Gynecology &amp; Reproductive Sciences</td>
</tr>
<tr>
<td>Marleen Temmerman</td>
<td>Department of Reproductive Health and Research, World Health Organization: Special Programme of Research, Development and Research Training in Human Reproduction (WHO/HRP)</td>
<td>Director, Reproductive Health and Research</td>
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<tr>
<td>Kirsten Thompson</td>
<td>Bixby Center for Global Reproductive Health, Project Director</td>
<td>University of California, San Francisco</td>
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<tr>
<td>John Townsend</td>
<td>Population Council</td>
<td>Vice President and Director, Reproductive Health</td>
</tr>
<tr>
<td>Kirsten Vogelsong</td>
<td>Bill &amp; Melinda Gates Foundation</td>
<td>Senior Program Officer, Contraceptive Development</td>
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## ANNEXE 3: SURVEY RESPONDENTS

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<tr>
<th>Organisation name</th>
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<tr>
<td>• Australian National Health and Medical Research Council (NHMRC)</td>
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<td>• Australian Research Council (ARC)</td>
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<td>• Becton, Dickinson and Company</td>
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<tr>
<td>• Bill &amp; Melinda Gates Foundation</td>
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<tr>
<td>• Brazilian Ministry of Health, Department of Science and Technology (DECIT)</td>
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<td>• CONRAD</td>
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<td>• Female Health Company*</td>
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<td>• FHI 360</td>
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<td>• Gynuity Health Projects</td>
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<tr>
<td>• Indian Council of Medical Research (ICMR)</td>
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<tr>
<td>• Indian Department of Biotechnology, Ministry of Science and Technology (DBT)</td>
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<tr>
<td>• Institut Pasteur</td>
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<tr>
<td>• Institute of Tropical Medicine Antwerp/Prince Leopold Institute of Tropical Medicine (ITM)</td>
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<tr>
<td>• ISGlobal, including Spanish Clinical Foundation for Biomedical Research (FCRB) and Barcelona Centre for International Health Research (CRESIB)</td>
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<tr>
<td>• Mexican National Institute of Public Health (INSPI)</td>
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<td>• MicroCHIPS</td>
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<td>• MSD</td>
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<td>• Population Council</td>
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<tr>
<td>• Program for Appropriate Technology in Health (PATH)</td>
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<td>• RemovAID</td>
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<tr>
<td>• South Africa Medical Research Council (MRC)</td>
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<tr>
<td>• Swiss National Science Foundation (SNSF)</td>
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<tr>
<td>• Swiss Tropical &amp; Public Health Institute</td>
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<tr>
<td>• UK Department for International Development (DFID)</td>
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<tr>
<td>• UK Medical Research Council (MRC)</td>
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<tr>
<td>• United States Agency for International Development (USAID)</td>
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<tr>
<td>• Universal Access to the Female Condom (UAFEC)*</td>
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<tr>
<td>• US Centers for Disease Control and Prevention (CDC)</td>
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<td>• US National Institutes of Health (NIH)</td>
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<tr>
<td>• World Health Organization: Special Programme of Research, Development and Research Training in Human Reproduction (WHO/HRP)</td>
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<td>• The Wellcome Trust</td>
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* Denotes organisations where data was only received via the HIV Vaccines and Microbicides Resource Tracking Working Group
ANNEXE 4: SUMMARY OF REPRODUCTIVE HEALTH R&D REFERENCE DOCUMENT

The full R&D reference document is lengthy and detailed, therefore a summary is presented here. Please also refer to Table 1, which outlines the reproductive health areas and products included in the G-FINDER survey.

I. Post-partum haemorrhage

Drugs

Research activities and processes necessary to develop and improve new drugs specifically designed to prevent or treat post-partum haemorrhage; including drug discovery or design, preclinical and clinical development and other activities essential for successful drug development and uptake.

IMPORTANT: ONLY includes R&D on uterotonic drugs specifically designed for low-income settings. Such a drug must: a) be heat stable; and b) not require intravenous administration.

Research areas included were as follows:

- Discovery and preclinical
- Clinical development
- Phase IV/ pharmacovigilance studies
- Baseline epidemiology directly linked to trials of products in development.

II. Contraceptives

Drugs

Research activities and processes necessary to develop and improve new drugs specifically designed to prevent pregnancy.

IMPORTANT: ONLY includes R&D to develop, optimise, and validate contraceptive drugs for use in resource-limited settings (more affordable, more reliable, ease of use in the field); including drug discovery or design, preclinical and clinical development and other activities essential for successful drug development and uptake.

This category includes R&D into new contraceptive drugs delivered without devices. If a new drug was to be delivered as part of a device, data was entered into the ‘Combinations’ for Contraceptives section.

Contraceptive drugs were classified according to their duration:

- **Ultra Short/Immediate:** on-demand method that requires action at the time of intercourse for efficacy (e.g. emergency contraception)
- **Short:** methods that work for <1 year but do not require action at the time of intercourse (e.g. injectable hormones)
- **Long:** methods that work for >1 year
- **Permanent:** irreversible methods.
Research areas included were as follows:

- Discovery and preclinical
- Clinical development
- Phase IV/ pharmacovigilance studies
- Baseline epidemiology directly linked to trials of products in development.

**Devices**

A device is an instrument, apparatus, appliance, implant, or other similar or related article, intended to be used to control conception. This article does not achieve its primary intended purpose through chemical action within or on the body and is not dependent upon being metabolised for the achievement of any of its primary intended purposes. An example would be condoms.

**IMPORTANT:** If a new device also included a drug, data was entered in the ‘Combinations’ section for Contraceptives. If a new device was not the final product used to control conception but is a technology used to deliver other products, data was entered in the ‘Platform technologies for reproductive health section’. An example would be development of ring or patch technologies.

Research areas included were as follows:

- Discovery and preclinical
- Clinical evaluation
- Operational research for devices.

**Combinations**

Research activities and processes to develop or improve a product that combines a platform technology or contraceptive device with one or more contraceptive drug/s.

Eligible investments included product discovery or design, preclinical and clinical development and other activities essential for successful product development and uptake.

**IMPORTANT:** ONLY includes R&D to combine previously developed platforms/devices with previously developed drugs to create a new or improved combination contraceptive product. If a project was to develop a platform technology, data was entered in the ‘Platform technologies for reproductive health’ section.

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**III. Non-HIV sexually transmitted infections**

This does not include investments into HIV/AIDS R&D. HIV/AIDS investments are included in the G-FINDER report on neglected disease R&D funding (http://policycures.org/g-finder2014.html).

**Drugs for syphilis (including congenital syphilis)**

Research activities and processes necessary to develop and improve new compounds specifically designed to prevent, cure or treat syphilis, including congenital syphilis; including drug discovery or design, preclinical and clinical development and other activities essential for successful drug development and uptake.

**IMPORTANT:** ONLY includes R&D on drugs specifically designed for low-income settings. Such a drug must: a) be oral; and b) single dose.
Research areas included were as follows:

- Discovery and preclinical
- Clinical development
- Phase IV/ pharmacovigilance studies
- Baseline epidemiology directly linked to trials of products in development.

**Diagnostics for multiple STIs**

Research activities and processes necessary to develop, optimise, and validate diagnostic tests for multiple STIs for use in resource-limited settings; including discovery and design, preclinical and clinical evaluation, and other activities essential for successful deployment for public health use.

**IMPORTANT:** ONLY includes R&D on diagnostics specifically designed for low-income settings. Such a diagnostic must a) diagnose more than one STI; b) diagnose at least two of the following eight STIs: syphilis, gonorrhoea, chlamydia, trichomoniasis, hepatitis B, herpes, HIV, and HPV and c) be affordable, fast, reliable and easy to use in the field.

Research areas included were as follows:

- Discovery and preclinical
- Clinical evaluation
- Operational research for diagnostics.

**IV. Multipurpose Prevention Technologies**

Research activities and processes to develop or improve a product that combines a platform technology or contraceptive device with one or more drug/s, and addresses two or more reproductive health indications. Combination products entered here include drugs to prevent, treat or cure HIV/AIDS or the sexually transmitted infections included in G-FINDER (syphilis, gonorrhoea, chlamydia, trichomoniasis, hepatitis B, herpes and HPV). Some examples of combinations that were entered here are:

- Contraceptive device + HIV drug/s
- Contraceptive device + STI drug/s
- Contraceptive device + STI + HIV drug/s
- Contraceptive device or platform technology + STI + HIV + contraceptive drug/s.

Eligible investments included product discovery or design, preclinical and clinical development and other activities essential for successful product development and uptake.

**IMPORTANT:** ONLY includes R&D to combine previously developed platforms/devices with previously developed drugs to create a new or improved combination product. If a project was to develop a platform technology, data was entered in the ‘Platform technologies for reproductive health’ section.

**V. Platform technologies for reproductive health**

Any technology to facilitate the delivery of reproductive health products in a resource-limited setting, such as technologies to extend the duration of action of steroidal contraceptives, skin applications to improve acceptability, and technologies for controlled release of drugs etc (e.g. dendritic cell systems, emulsions, novel viral vectors, sprays, patches and needle-free devices).
This category had **strict restrictions**. It ONLY included funding for R&D which met these two conditions:

- It was conducted by **public, philanthropic or not-for-profit entities**
- It was research that was **not yet directed towards a specific disease or product**.

**VI. Core funding of a reproductive health R&D organisation**

This category was used if core funding or non-earmarked funding to an organisation that researches and develops products for multiple reproductive health areas included in G-FINDER had been disbursed, but the survey participant did not know how funding had been invested by that organisation.

**Example:**

Core funding had been allocated to an organisation that was developing both contraceptives and STI diagnostics, but the donor did not know how much had been allocated to each R&D area.

**VII. Unspecified reproductive health R&D**

This category was **ONLY** used when funding met the R&D scope criteria set out in this document, but the survey participant did not have enough information to allocate the funding to one of the specific reproductive health areas above.
ANNEXE 5: REFERENCES


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