

### 3 Are current global investments in rectal microbicide research adequate to move from promise to product?

#### Summary

IRMA's resource tracking analysis and scientific-agenda setting have identified the following:

- Between 2007–2010, global spending on rectal microbicide (RM) research totalled U.S. \$25 million. Of this amount, the U.S. public sector contributed 91.6%, European public sector contributions represented 5.3%, and the philanthropic sector contributed 3.0%.
- In 2010, global spending on RM research will be approximately U.S. \$7.2 million.
- An estimate of U.S. \$10 million invested annually from 2011–2014, increasing to U.S. \$44 million annually from 2015–2020, would allow for the field to develop and advance at least two candidates forward to late-stage testing (Phase IIb/III).
- Compared to 2010 levels, annual global spending on RM research must increase by 40% for the next four years (2011–2014), and it must increase at least six-fold in the years 2015–2020.

#### 3.1 Methodology

In 2010, IRMA updated the resource tracking exercise it conducted in 2006, and revised its estimates of the funding required to expand and maintain a healthy research pipeline of rectal microbicide (RM) candidates.

IRMA identified RM research funding levels for 2007–2010 through the following methods:

- Snowball sampling, starting with RM researchers known through the IRMA network;
- Searching for all relevant projects through the U.S. National Institutes of Health (NIH) Research Portfolio Online Reporting Tool (RePORT);
- Contacting the other funders identified through the 2006 tracking exercise directly;
- Contacting the European Research Directorate-General; and,
- Reviewing the compiled list for accuracy and completion with each of these stakeholders.

The HIV Vaccines and Microbicides Resource Tracking Working Group was established in 2004 to generate data on global investments in preventive HIV vaccine and microbicide research and development, and policy and advocacy activities. In 2006, the Working Group expanded its tracking efforts to include other experimental HIV prevention options, such as adult male circumcision, herpes simplex virus 2 suppression, and pre-exposure prophylaxis (PrEP). In its 2009 report, the Working Group provided an estimate of total RM spending for research and development: U.S. \$5 million in 2008. Given the scope of the overall resource tracking exercise, it was unable to provide specific details on RM investments, projects, and studies.

In close consultation with microbicide researchers, IRMA projected the required funding needed to maintain a robust RM research pipeline. The assessment of resources devoted to RM research for all of 2010 is a projection based on information available in the first quarter of the year.

#### Data limitations

While basic science and clinical research on vaginal microbicides are crucial to the eventual development of a safe and effective RM, this survey tracks research focussed specifically on the research and development of products for rectal use. A calculation of the limited resources directed toward RM policy and advocacy initiatives, while important, is not included here.

Commercial sector involvement in RM research is quite limited. There are some in-kind contributions, such as the provision of antiretrovirals (ARVs) to research institutions to test as potential RM candidates; however, the commercial sector often is unwilling to reveal actual dollar investments publicly. While the estimates provided in this document do not include contributions from the commercial sector in 2007-2010, we acknowledge that companies like Gilead have made their products available without cost. Gilead's active participation in deliberations regarding microbicides and PrEP also benefits the field.



“We must have multiple options for the prevention of HIV for the simple reason that different people may benefit from different methods. Prevention works better if we can choose what is best for us, not just one or two limited choices. Having multiple options for HIV prevention is a human rights issue, an LGBT rights issue, as much as it is a health issue.”

**Sunil Babu Pant**  
Member, Constituent Assembly  
and Parliament of Nepal  
Kathmandu, Nepal

### 3.2 Reminder: Results from IRMA's previous resource tracking exercise in 2006

In 2006, IRMA conducted a resource tracking exercise to determine both the total level of funding provided globally for RM research between 2000 and 2006, and to estimate the level of funding required to bring a small number of candidates through all stages of research over the following 10 years.

IRMA found that total investments in RM research between 2000 and 2006 were U.S. \$34 million. Disbursements in 2006 were U.S. \$7.2 million.

Between 2000 and 2006, the U.S. public sector contributed 97.4% of overall investments. The philanthropic and commercial sectors accounted for 2.6% of spending. No evidence of specific RM investments could be uncovered from member states of the European Union, other countries, or multilaterals during this period.

In 2006, IRMA estimated annual spending of at least U.S. \$35 million would be required over 10 years—totalling U.S. \$350 million—to realise a comprehensive RM research programme. Based on this estimate, yearly investments would have needed to increase five-fold from 2006 levels.

### 3.3 Investment in rectal microbicide research: Trends from 2007–2010

IRMA found that U.S. \$25 million was spent on RM research between 2007 and 2010. During this period the U.S. public sector contributed almost U.S. \$22.9 million (91.6% of global funding), European public funding sources contributed approximately U.S. \$1.3 million (5.3%), and the philanthropic sector contributed a little over U.S. \$750,000 (3.0%).

**Public sector investments from 2007–2010:** U.S. \$24.2 million from public sources was invested in RM research. The U.S. NIH contributed over U.S. \$22.5 million and the California HIV/AIDS Research Program, funded by the State of California, contributed almost U.S. \$400,000. The European Commission provided U.S. \$1.3 million through a project funded by the Seventh Framework Programme (FP7).<sup>1</sup>

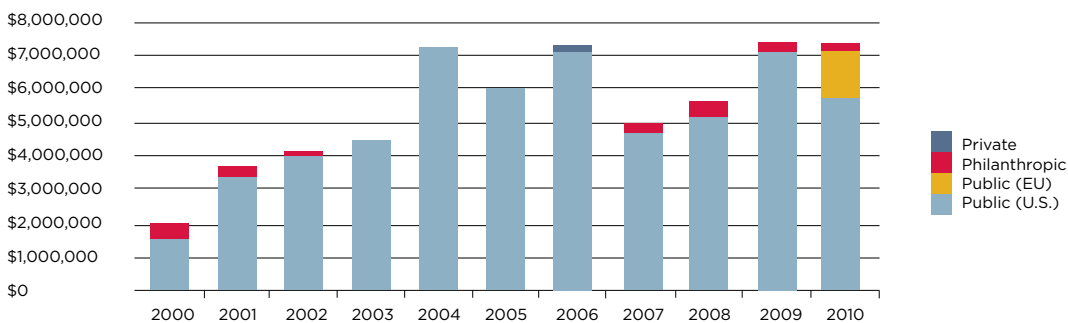
**Philanthropic sector investments from 2007–2010:** amfAR–The Foundation for AIDS Research, contributed over U.S. \$750,000, and has been the primary philanthropic investor in RM research for over a decade.

**Commercial sector investments from 2007–2010:** As mentioned, IRMA was unable to quantify private sector investments in RM research for this period. However, there have been valuable in-kind contributions from companies such as Gilead and others.

When combined with the data from the earlier IRMA resource tracking exercise, total investments in RM research show a modest increase from 2000–2003, followed by fluctuations hovering between U.S. \$5–7 million per year from 2004–2010.

The level of funding over the next few years is likely to remain stable due to recently announced projects in the U.S. and Europe. The Combination HIV Antiretroviral Rectal Microbicide (CHARM) Program will receive U.S. \$11 million over five years, starting in 2010. The project entitled “Microbicide Safety and Acceptability in Young Men” will receive U.S. \$6.5 million over four years, also starting in 2010. Both projects are funded by the U.S. NIH, and are dedicated specifically to RM research. The Combined Highly-Active Antiretroviral Microbicides (CHAARM) Programme will receive 12 million euros (approximately U.S. \$16 million) over five years from the European Commission's Seventh Research Framework Programme, starting in 2010. Part of its work will focus on RM research. See Sections 2.2–2.4 for descriptions of these three programmes.

#### RECTAL MICROBICIDE RESEARCH SPENDING BY YEAR (2000–2010), IN U.S. DOLLARS



Over the 11-year period of investments in RM research IRMA has tracked, the public sector has provided 97.3% of the funding (mostly from the U.S.), the philanthropic sector has provided 2.5% of funding, and the commercial sector has provided 0.2%.

1. The Framework Programmes are the main financial tools through which the European Union supports research and development activities covering almost all scientific disciplines.

## RECTAL MICROBICIDE RESEARCH SPENDING BY SECTOR (2000–2010), IN U.S. DOLLARS

	PUBLIC	PHILANTHROPIC	COMMERCIAL	TOTAL
Investment	58.1 million	1.5 million	0.1 million	59.7 million
Percentage	97.3%	2.5%	0.2%	100%

### 3.4 Estimated funding needs and resource gap for 2011–2020

In consultation with leading researchers in the field, IRMA calculated approximate annual funding needs for RM research and development over the next 10 years (2011–2020), based on the following:

#### ASSUMPTIONS AND TARGETS

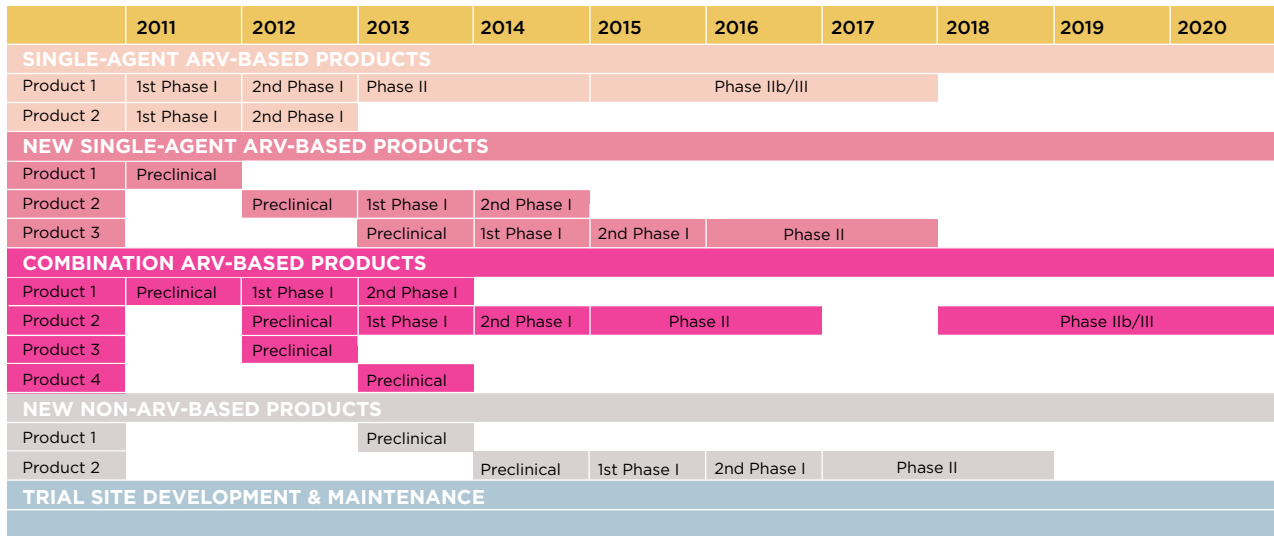
Existing ARV-based products	Two single-agent antiretroviral vaginal microbicide candidates will be tested for rectal safety, and one of the two candidates will eventually be tested for rectal use in a large-scale efficacy trial.
New ARV-based products	Three new microbicide candidates based on ARVs will be developed over the next 10 years, and two will advance as far as Phase I/II safety testing.
Combination products	Four microbicide candidates combining more than one active ingredient—for example two different classes of ARVs—will be formulated and tested for rectal use over the next 10 years, and one of these candidates will eventually be tested for rectal use in a large-scale efficacy trial.
Non-ARV-based products*	Two new microbicide candidates that are not based on ARVs will be developed over the next 10 years, and one will be formulated and tested for rectal safety.
Trial site development	Trial site development and maintenance will occur over the next 10 years to prepare for and support clinical trials of RM candidates. This work would most likely be conducted in North America, Latin America, and the Asia-Pacific region.
Developments in the HIV prevention field	The current standard prevention package offered to clinical trial participants will not change significantly. If this prevention package changes—for example if PrEP is shown to be effective and is routinely offered to trial participants—a significant expansion of resources will be required to conduct large-scale RM trials. Comprehensive prevention packages result in fewer seroconversions among trial participants, and trials would need to run longer and/or recruit more participants to reach the number of seroconversions required to assess an intervention's efficacy.
More funding, more researchers, more research projects	New, dedicated investments in RM research will allow a greater number of projects to be conducted by an increasing number of researchers from various fields, and from various parts of the world.
Cost of research**	Discovery, preclinical evaluation, and formulation will cost a minimum of U.S. \$1-2 million for each experimental product.
	Phase I trials will cost approximately U.S. \$1.5 million and last around nine months. Each viable product will undergo two Phase I trials.
	Phase II trials will cost about U.S. \$3 million and may last one and a half years.
	Phase IIb/III trials will cost at least U.S. \$120 million and last at least three years.
	Trial site development and maintenance work is variable but can cost U.S. \$2 million per year.

\* Ideally, RMs should be safe, effective, acceptable, and accessible for use by all persons who engage in anal intercourse. Currently, research into new prevention technologies focusses largely on oral and topical products that contain some of the same ARVs used for treatment by persons living with HIV. These products are unlikely to be appropriate for use by someone who is HIV-positive, because the use of such products may generate drug-resistant virus which would limit treatment options. This is of special concern in the developing world where alternatives to first-line drug regimens are not yet a reality. Both ARV-based and non-ARV-based products should be developed to meet multiple user needs, including the prevention needs of people living with HIV and those who are HIV-negative. It is concerning that there are no non-ARV-based microbicide formulations in efficacy trials, and very few in early pre-clinical and clinical development at the moment.

\*\* These cost estimates were developed in consultation with leading researchers in the field, and with input from the Alliance for Microbicide Development, which has been developing its own estimates of the average cost of each stage of microbicide research.

The following chart illustrates how the various classes of candidate microbicides, described in the assumptions from the table above, would progress through development and testing from 2011–2020.

### MODEL OF RECTAL MICROBICIDE DEVELOPMENT PORTFOLIO EVOLUTION (2011–2020)

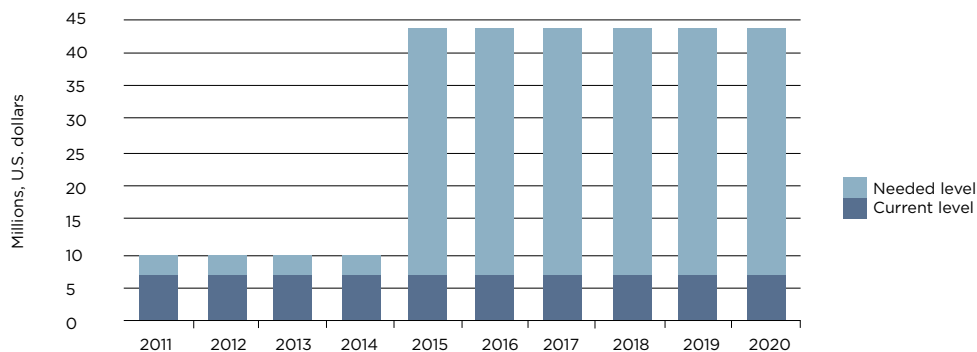


### 3.4.1 Increased funding required

Based on the assumptions, targets, and estimated costs described, and applying these estimated costs to the theoretical research portfolio illustrated in the Gantt chart above, IRMA anticipates that U.S. \$10 million are required annually over each of the next four years (2011–2014), followed by U.S. \$44 million annually from 2015–2020, to ensure an adequate number of candidates are pursued from bench to clinical efficacy trials.

In other words, compared to the 2010 spending level of U.S. \$7.2 million, annual global spending on RM research must increase by 40% for the next four years (2011–2014), and it must increase at least six-fold in the years 2015–2020 to ensure a minimum of two candidates reach late-stage testing.

### ANNUAL RECTAL MICROBICIDE RESEARCH FUNDING NEEDS (2011–2020)



### 3.4.2 More diverse funding required

For the 2007–2010 timeframe, IRMA was only able to identify four RM-specific funders: the U.S. NIH, the European Commission (through FP7), amfAR, and the California HIV/AIDS Research Program (funded by the State of California). In 2010, they collectively contributed U.S. \$7.2 million to RM research.

By way of comparison, in 2008, a more extensive array of donors from around the world provided U.S. \$244 million to general microbicide research. RM research is included in that total, accounting for approximately 2.2% of microbicide funding that year. An even broader array of donors provided U.S. \$868 million to HIV vaccine research.

IRMA applauds the donors that have supported new prevention technology research and calls for a greater number of donors to support microbicide, vaccine, and PrEP studies.



“There will be continued commitment of the NIAID DAIDS Prevention Sciences Program to the development and deployment of a safe, acceptable and effective rectal microbicide, through support of investigator initiated research. Specifically in the field of rectal microbicides, we expect to see the development of rectal-specific formulations for microbicides, as well as a movement toward creating rectal microbicides with more than one active ingredient (combination microbicides).”

**Jim Turpin**

Microbicides Research Branch,  
National Institutes of Health  
Bethesda, U.S.

Developing the diversity of RM funders would not only increase the amount of resources available, but would ensure greater sustainability as well. Given that the domestic HIV epidemics in many donor countries primarily affect gay men and other MSM, and are driven by unprotected anal intercourse, the funding disconnect is rather unfortunate. RMs would provide an important prevention option for their citizens as well as people from around the world.

Past and current contributions to vaccine and microbicide research have come largely from the development and foreign affairs budgets of individual countries. While funding for RM research could feasibly draw from these same sources, financial support through the domestic health and research budgets of these countries would also be quite appropriate considering their epidemic profiles. With the exception of the U.S. and the European Commission, these funding streams remain dry.

Obviously, given the relative infancy of RM research and development, hundreds of millions of dollars are not required annually. The RM funding scenario laid out here calls for very modest sums, and would have a significant impact for millions of women and men around the world who engage in AI. **Reducing other line items in the prevention portfolio to enhance funding for RMs is not acceptable. Appropriate funding must be allocated for all new prevention technologies.**