The NIH must NOT leave us behind: We demand funding for microbicides research

As members and allies of International Rectal Microbicide Advocates (IRMA), we express our gratitude for NIH leadership in the field of HIV prevention research and our strong support for the continuation of robust NIH funding for the research and development of a range of HIV prevention tools, including not only long-acting systemic products such as vaccines, implants and injectables, but also topical on-demand products such as vaginal and rectal microbicides. Sexually active women and men around the world who are vulnerable to HIV require a range of choices for protection.

Withdrawing funding support for research and development of topical on-demand HIV prevention tools is irresponsible from a financial perspective, illogical from a scientific perspective, and short-sighted from a strategic perspective.

Microbicide research is fiscally responsible

We fully support funding for the development of long-acting systemic products. Doing so at the expense of other classes of products however, is a serious mistake. Funding on-going development of topical on-demand products is a sound investment.

Each year, vaccines receive significantly more funding than microbicides. The Resource Tracking for HIV Prevention Research and Development Working Group estimates that between 2000-2016, US$12.8 billion was spent globally on vaccine R&D, while only US$3.0 billion was spent on microbicides—four times less. This disparity keeps getting larger. In 2016, vaccines received five times more funding than microbicides globally (US$868 million versus US$167 million). Despite such a glaring disparity, a vaginal ring is already under regulatory review and is being tested further for multi-purpose use, while a potential vaccine regimen is still being tested and optimized in clinical trials.

In 2016, the US contributed 84% of the global funding in microbicides R&D. Purely from a business angle, it is irresponsible to discontinue investment in an area that shows such promise and seems poised to produce dividends.

Microbicide research is evidence-based science

In addition to the vaginal ring mentioned above, a number of studies testing candidate vaginal and rectal microbicide products are underway.

Looking at rectal microbicides specifically, a tenofovir gel has already shown promise in an international phase II trial. By early 2020 no less than eight safety studies testing candidate products should be completed. These include a variety of formulations: inserts, suppositories, and gels with applicators, but also behaviourally congruent formulations such as douches and lube-like products. The active ingredients include five different antiretrovirals (ARVs) as well as one non-ARV-based product. Two of these products will be tested for multi-purpose use (HIV and STI endpoints) and for dual compartment use (vaginal and rectal).

STI rates are increasing in many populations vulnerable to HIV. Products that could reduce the incidence of both HIV and STIs would be valuable. Many of the proposed long-acting systemic products (i.e., oral PrEP, injectables, implants, vaccines) will only target HIV and will not be active against other STIs. Products that could

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be formulated to be multi-purpose should be developed, including topical gels, suppositories, inserts, douches, enemas, and vaginal rings. Furthermore, women the world over utilize an array of contraceptive options. Products co-formulated to address HIV prevention and contraception—and potentially other STIs—are highly desired by women. A birth control indication for a product that also offers HIV protection could reach women who see themselves at low risk for HIV but high risk for unintended pregnancy.

However, given the timing of the NIH funding cycle, a decision to drop support for ongoing research into topical products would effectively stop this work in its tracks, just as we are poised to get answers about several potentially promising products. Indeed while the studies currently running will continue to operate, it is unclear whether and how the products they are testing could move forward without ongoing NIH support.

**Microbicide research is strategic**

It is foolish to put all our eggs in one basket, or in one category of products. We need long-acting systemic products that don’t require daily administration, just as we need topical on-demand products that don’t require an intense clinical interface and long-term commitment. People want different modalities to suit a wide variety of circumstances.² We know from the experience of the contraceptive field that the more options we provide to people, the more sexual acts are protected.³ The answer to adherence challenges is more options from a variety of product classes, not less.

No single product or class of product will meet all the needs of all vulnerable people over their life courses nor be the answer to ending the epidemic. We recognize the challenges inherent in topical products. However, long-acting systemic products are not without their own significant operational and implementation challenges. For example, injectables such as Cabotegravir will require clinic visits every two months for injections, and taking an oral dose for four weeks before the first injection and for a year after discontinuing the injections.⁴,⁵ For people attracted to this modality because they don’t wish to take a daily pill, this is a major challenge.

We recognize that long-acting systemic products present one way to deal with the adherence obstacles faced by some users. Offering products that users find desirable, that are behaviourally congruent, and that enhance pleasure could be equally effective at dealing with adherence challenges faced by others. Communities tell us they want products that fit their life circumstances. Many are interested in products that can be used only when needed, thereby avoiding systemic exposure to drugs for long periods of time.

Finally, there are significant opportunity costs associated with dropping the research into topical on-demand products now. Commentary to date seems to reflect an unscientific faith in the certainty of efficacy trials being currently conducted—for which results are still several years away. While they’ve shown promise, long-acting injectables could yet fail to demonstrate sufficient efficacy and serious challenges may not be seen until implementation is attempted. We still don’t know if monoclonal antibodies or current vaccine candidates will prove useful. It is imperative we continue research into topical on-demand products as viable alternatives in the meantime. However, without ongoing funding support, microbicide research infrastructure and the substantial body of knowledge within microbicide scientists will have been lost or become obsolete and momentum and time will be lost—the microbicide field may wither and die. Whether to broaden HIV

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³ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4168565/
⁴ Oral PrEP will be used in conjunction with injectables both before the initial injection and after the last injection. Before: Because there is no way to remove the drug once injected, a 4-week “lead-in” strategy using an oral form of the active drug will be utilized to establish safety parameters. After: Following the final injection, drug concentration will slowly diminish, providing less and less protection against HIV. Oral PrEP would be recommended to reduce the risk of infection during this period and (if infection were to occur) to reduce the risk of resistance in the face of low drug levels.
prevention choices or to keep topical options alive should injectable PrEP fail to demonstrate protective efficacy years from now, it will be extraordinarily difficult (if not impossible) to revitalize the microbicide program if we discard the opportunities at hand to develop desperately needed new HIV and STI prevention tools.

It is critically important that the upcoming funding announcement be designed strategically to leverage retention of the expertise and infrastructure necessary to pursue expanded safety and efficacy assessment of the most promising topical products to emerge from currently funded clinical studies.

Again, we fully support funding for the development of long-acting systemic HIV prevention options. Topical on-demand products, including vaginal and rectal microbicides, are also a wise investment equally worthy of sustained funding support.

We the undersigned demand a continued commitment to the research and development of microbicides. We demand appropriate, sustained funding for these activities.

Founded in 2005, IRMA is a Chicago-based global network of over 1,200 advocates, policymakers and leading scientists from six continents working together to advance a robust rectal microbicide research and development agenda—from basic science to behavioural research. IRMA’s goal is to support the creation of safe, effective, acceptable and accessible rectal microbicides for cisgender and transgender women and men around the world who engage in anal intercourse. IRMA partners with other advocacy organizations around the world to help advance rectal microbicide research.

Microbicides are products that could be used in the vagina or rectum to reduce the risk of HIV infection. These products could also be formulated to reduce the risk of STI infection and/or unintended pregnancy.