WHOSE CHOICE IS IT ANYWAY?

Analysis of Comments to and Responses from NIH’s 2017 Refining the HIV Research Enterprise Request for Input on Research Priorities
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Special thanks to AIDS Foundation of Chicago for providing funding for this initiative and to Lauren Glodowski for incorporating over 300 pages of material into the word cloud featured in this report.

WORD CLOUD METHODOLOGY:
A statistical text analysis program was used to analyze the frequency of words appearing throughout the contents of the 330 pages of material received through the FOIA request. Frequencies were quantified for words, acronyms and phrases (with the exception of general terms such as research, support) appearing at least three times throughout this material. Data were then translated into size groups, so that increasing word size is indicative of a greater number of mentions throughout the content. The result of this analysis is the word cloud on the cover of this report.
This report is dedicated to Dan Bigg, the brilliant visionary who founded and led the Chicago Recovery Alliance. Dan died at home on August 21, 2018.

A brave, beautiful and truly revolutionary harm reduction advocate, Dan, in all his compassionate, loving, crazy, creative, strategic, maddening, relentless, rumpled, dog-hair-covered splendor, is responsible for directly and indirectly saving the lives of countless thousands of people who inject drugs – in Chicago and around the world.


He was also one of my most important mentors, one of the very first people who supported my microbicide advocacy, not thinking I was crazy, totally “getting it.” In fact, he provided a small grant that allowed me to attend my first-ever microbicide conference – in London, 2004. The next year, a small group of advocates and I founded IRMA.

I am forever indebted to Dan for believing in me, for challenging me, for arguing with me, laughing with me, and for laying down one of the first bricks on my microbicide path. I know he’d want me to continue fighting – whoever, wherever, whenever, however – giving ‘em hell to help ensure HIV prevention options that address the messy complexity of human beings, that meet us where we are, that respect us, that give us a range of choices based on what we desire, and that support “any positive change.”

I love you Mister Bigg.

**JIM PICKETT**

**CHAIR, INTERNATIONAL RECTAL MICROBICIDE ADVOCATES**
International Rectal Microbicide Advocates (IRMA) and our many partners and allies believe we need an array of HIV prevention options, and that the development of safe, effective, acceptable and accessible vaginal and rectal microbicides remains an important priority.

However, microbicides are under threat.

Every seven years, the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), revisits its HIV prevention and treatment research priorities and competitively renews its funding of the HIV clinical trials networks operating in the United States and across the world. To help determine focus and priorities for the networks from 2021 through 2027, NIAID launched a request for input in early 2017 that it promised would be transparent and meaningful.

After input was collected, NIAID presented its proposal for refining the HIV clinical research networks in early 2018. The new proposal did NOT support the research and development of user-controlled, short-acting, non-systemic microbicide options, and focused solely on long-acting and systemic formulations (such as vaccines and injectables and implants). They note they will support multi-purpose prevention products if they are presented with a highly efficacious product. If the level of efficacy must compete with a systemic product, the bar may be impossible to reach.

Given that the US government provides the lion’s share of global funding for rectal and vaginal microbicide research (84% of global funding to be precise), these prevention research priorities will likely mean the end of the microbicides/topical prevention field.

Concerned with the lack of transparency surrounding the request for input, AIDS Foundation of Chicago (AFC) filed a Freedom of Information Act (FOIA) request to obtain copies of all comments submitted during the input phase, as well as all responses from NIAID. The goal was to determine how NIAID’s proposed US-taxpayer-funded plan reflected input received—or not. We analyzed the 330 pages of comments received through the FOIA request, as well as any additional “missing” content that we were able to trace. This represents 120 unique submissions from advocates, researchers, academics, elected officials, research networks and industry, mostly from the US and several African countries, as well as 56 responses from NIAID.

The vast majority of submissions (79%) expressed either explicit support for HIV prevention choices and/or continuing microbicides research, or implicit
support through alternative foci, such as maintaining the current research network structure (which includes the Microbicide Trials Network), the importance of meaningful community engagement in the research process or the need for social-behavioral research.

More specifically, many respondents mentioned the need for HIV prevention choices and/or options. Several comments included references to the need for an HIV prevention toolbox, that one size does not fit all, or that different people have different needs at different times. There were several explicit references to needing user-initiated, short-acting and on-demand products such as microbicides, in addition to systemic products, as well as comparisons to lessons learned from the contraception field.

Many respondents either explicitly or implicitly expressed wanting to see the development of microbicides continue. Comments included references to leveraging the success of the dapivirine ring and pursuing promising products currently in the research pipeline (vaginal and rectal microbicides, and multi-purpose technologies). Also included were concerns about the possible limitations of systemic approaches and the potential delays in the introduction of new products if alternative options are not pursued. Putting all of our eggs into one basket could very well be overly optimistic and keep our HIV prevention method mix from expanding by neglecting various research directions.

Many respondents mentioned both vaginal and rectal microbicides, including a variety of possible topical formulations. They also mentioned several specific features they value in microbicide formulation and delivery mechanisms including:

- The capacity for production as multi-purpose technologies—products that could prevent not only HIV, but also unplanned pregnancies and/or sexually transmitted infections (STIs).

- HIV prevention options that users—especially women, girls, and other receptive partners—can control, including in cases where discretion is desired.

- Products that are short-acting and can be used on-demand at the time of sex, including the possibility of intermittent use during sporadic periods when the user is sexually active.

- Products that are non-systemic and that can be used without
overburdening the user or the healthcare system.

Products that are behaviourally congruent—meaning that they build on existing practices such as rectal douching or the use of lubricants during sex—to enhance their acceptance and uptake.

The vast majority of those who submitted input—whether from the US or from around the world—unequivocally supported the ongoing and targeted development of on-demand topical products, including a range of vaginal and rectal microbicides that could prevent HIV, STIs and unplanned pregnancy among a range of communities, including young women and gay men.

NIAID’s responses were often contradictory. While nominally espousing the language of choice and prevention options for women and other vulnerable groups, the NIAID responses demonstrated an uncompromising and patronizing stance towards microbicides and the development of tools that are specifically designed to meet the needs of those who are most vulnerable—and they belied a deep hostility towards those who call for that choice.

In those responses, NIAID stated that they “will continue to support development of topical HIV prevention products.” At the same time, they provide a list of conditions under which that would need to happen—which includes several complex, possibly scientifically unattainable criteria that by definition effectively exclude microbicides. This is disingenuous “support,” both cynical and hypocritical.

We are particularly troubled to see that the letter submitted during the input process by the leadership of the HIV Prevention Trials Network (HPTN)—which will be the strongest or only contender bidding for the entity leading non-vaccine HIV prevention research—makes absolutely no mention of the intention to continue the work or incorporate the priorities and expertise of the Microbicide Trials Network (MTN). Indeed, there is no mention of microbicides or non-systemic on-demand products, and not a word about the need for options, choices, or a range of tools to meet the needs of various communities.

It is not too late to change or influence the priorities proposed by the NIH. We must mobilize as a community of prevention consumers, advocates, researchers and policy-makers and continue to voice the need for research that leads to an array of prevention options for those who need them most. In an era where the mantra is for options that fit people’s lives versus those...
that people must fit into their lives, the current approach will not allow us to adequately respond to the HIV prevention crisis we face.

To the NIH and the HPTN leadership, we say this: There is a vocal, aware, interested constituency for microbicides and we are watching what you do. We will not allow our voices to be sidelined. There is too much at stake. We look forward to working together as fully engaged and committed partners in a revitalized HIV prevention research enterprise that encompasses a broad range of potential options to meet our varied and complex HIV prevention and sexual health needs.

Please consult the “What You Can Do” section at the end of this report to take action TODAY.
International Rectal Microbicide Advocates (IRMA), a project of AIDS Foundation of Chicago (AFC), was founded in 2005. Since that time, there has been an enormous amount of change in the field of HIV prevention research and in our world generally. On a positive note, the remarkably high efficacy of antiretroviral drugs (ARVs) for prevention has been demonstrated, both for oral PrEP (now approved and subsidized in several countries) and through treatment leading to viral suppression or “undetectability” (U=U, Undetectable = Untransmittable). As of August 2018, the microbicide field has successfully completed the first-ever Phase II study of a rectal microbicide, is awaiting regulatory review of a vaginal ring that prevents HIV among women, and has several other rectal, vaginal and multipurpose products in development.

However, microbicides are under threat. Given that the US government provides the lion’s share of global funding for rectal and vaginal microbicide research (84% of global funding, to be precise), the prevention research priorities recently announced by the National Institutes of Health (NIH) could mean the end of the microbicides/topical prevention field. Instead of supporting the development of multiple complementary approaches to HIV prevention, the NIH is proposing a narrow focus on long-acting systemic prevention options (such as vaccines and long-acting injectables and implants) but not user-controlled, on-demand, non-systemic options such as vaginal or rectal microbicides (including films, gels, inserts, lubricants, rectal douches, vaginal rings, and suppositories).

IRMA and our many partners and allies believe we need an array of HIV prevention options, and that the development of safe, effective, acceptable, accessible and desirable vaginal and rectal microbicides remains an important priority. This includes multi-purpose technologies.
Every seven years, the National Institute of Allergy and Infectious Diseases (NIAID), a component of the NIH, revisits its HIV prevention and treatment research priorities and competitively renews its funding of the HIV clinical trials networks operating in the United States and across the world. To help determine focus and priorities for the networks from 2021 through 2027, NIAID launched a request for input, dubbed “Refining the HIV Research Enterprise,” in early 2017 that it promised would be transparent and meaningful. Scientists, advocates, policy makers and other stakeholders were encouraged to “think big about new opportunities for innovation and discovery” and to provide input into the structure of the clinical trials networks and proposed priorities for HIV prevention and treatment research. NIAID specifically asked stakeholders to provide feedback on NIH’s HIV/AIDS research strategy (vaccines, non-vaccine HIV prevention and therapeutics) and on network structure and administration.

In terms of strategy and non-vaccine prevention, NIAID asked stakeholders to consider the following questions:

- NIH articulated its priorities for HIV/AIDS research in 2015. In your view, what can the HIV research enterprise do now to achieve these goals?

- What are some of the considerations to take into account as NIH develops the next iteration of HIV research priorities?

- How can we capitalize on the opportunities for synergy among these research areas?

- How can we foster the desire for the use of non-vaccine prevention tools, encourage their uptake, and optimize adherence to their use?

- What has not been understood about the needs of those at risk of HIV infection in this regard?

- Within the current areas of emphasis in HIV prevention, what advances will the field have achieved by the end of the current grant cycle in 2020? What important questions will have been answered?

- The research enterprise is working toward proof-of-concept and licensure for safe, easy-to-use non-vaccine prevention strategies that are highly effective and accepted by women, men, and adolescents. How will this trajectory change over the next 10 years, assuming some concepts succeed and move on to licensure?
What social and behavioral science research questions need to be addressed to underpin future concept and product discovery?

The research community has made incredible strides in preventing perinatal transmission of HIV. What are the most pressing research questions that remain in this area?

Stakeholder input was solicited through an online portal on the NIAID website and via direct email to Dr. Carl W. Dieffenbach, Director of the Division of AIDS, NIAID. Input was collected through November 30, 2017 and NIAID presented its current proposal for refining the HIV clinical research networks to the NIAID AIDS Research Advisory Committee (ARAC) on January 29, 2018. Echoing what NIH leadership had been suggesting throughout 2017 in presentations, webinars, blogs and personal conversations, the new proposal did not support the research and development of user-controlled, short-acting, non-systemic microbicide options, and focused solely on long-acting and systemic formulations. Dr. Dieffenbach described how the MTN would be eliminated, with all non-vaccine HIV prevention research to occur at a prevention trials network. Community members, including IRMA’s Jim Pickett, provided testimony—all urging NIAID to continue microbicide research, reiterating what they and many others had expressed via the portal and through other public means. You can view the proceedings online here.

During the public comment period in 2017, IRMA developed and broadly circulated a statement emphasizing the need for prevention choices to meet the various needs of multiple vulnerable communities, sought endorsements, and encouraged others to submit their own comments to NIAID. An additional letter outlining the important role microbicides would play in cisgender and transgender women’s ability to reduce HIV acquisition was circulated by AFC. Ultimately, 306 organizations and 527 individuals from all parts of the world endorsed these two statements.

AFC also coordinated efforts to develop a Congressional letter in the US House of Representatives. Led by Congresswoman Jan Schakowsky (D-IL), 18 members of Congress signed this letter strongly endorsing continued microbicide research and development.

As noted above, despite NIAID’s statements requesting input from stakeholders, it became clear in the middle of 2017, well before the November 30 deadline for providing input, that NIAID leadership had already decided it would be cutting support for research into on-demand HIV/STI topical microbicide prevention options. After the public comment
period concluded, advocates, including IRMA, asked NIAID for an opportunity to review all the input that came in through the portal and via email, as well as all official responses. This request was denied. Concerned with the lack of transparency surrounding the request for input, AFC filed a Freedom of Information Act (FOIA) request to obtain copies of all comments submitted during the input phase as well as all responses from NIAID. The goal was to determine how NIAID’s proposed US-taxpayer-funded plan reflected input received—or not.

Essentially, did stakeholders who provided input voice support for HIV prevention modalities that included non-systemic, short-acting, user-controlled methods or did they mirror NIAID’s narrow focus and only indicate an interest in long-acting, systemic products? Perhaps they voiced support for a range of products that include both short- and long-acting modalities, those delivered locally and systemically, and both user-controlled methods and those delivered in clinic?

NIAID is currently preparing Funding Opportunity Announcements (FOAs), which are set to be made public for “fair and open” competition, with awards expected in late 2020.
Through its FOIA request, AFC obtained a copy of comments submitted to NIAID during the input phase and NIAID’s responses to comments. There were more than 330 pages in all.

Yet, while reviewing the FOIA documents, we were deeply concerned to discover that a number of submissions were missing. Within a small group of six people, we were personally aware of no less than 10 missing submissions, including:

- Letters from the scientific advisory board of the NIH-funded DREAM project, AVAC and a group of young women from East and Southern Africa, in addition to at least four other letters
- Several comments that were submitted into the web portal during an IRMA meeting in New York

Were some of the submissions deliberately omitted from the FOIA documents? Was some input not received due to technical problems with the web portal? Conversations with our peers and observations about the pattern of missing submissions suggest at least part of the problem is the latter, but the former could also be a problem. One thing is clear: the mechanism for input was inadequate and not all stakeholders were heard.

Compounding the problem was the very unfortunate lack of transparency. Despite repeated calls from stakeholders to make submitted comments public, and despite stating in some of their written responses that NIAID would post the input they received on their website, this was never done. Getting access to the input submitted to NIAID required advocates filing a FOIA request.

We analyzed 330 pages of comments received through the FOIA request, as well as any additional “missing” content that we were able to trace. Unfortunately, we have no way of knowing how many other comments might have gone missing nor the views expressed in these comments.
DEMOGRAPHICS OF RESPONDENTS

Respondents represented the following constituencies: (Please note that some respondents represent more than one constituency.)

- Advocates/Community (47)
- Researchers/Academics (34)
- Elected Officials (19)
- Research Networks (4)
- Industry (2)
- Unknown (24)

Respondents came from the following countries and regions:

- 73 from the US
- 27 from Africa (including 10 from Uganda, 5 from South Africa, 2 from Kenya, 2 from Zimbabwe, 1 from South Sudan, 1 from Tanzania and 6 from unspecified African countries)
- 20 Unknown

SUBMISSIONS BY THE NUMBERS

We analyzed 120 unique submissions, including those we obtained through FOIA and the “missing” input we were able to trace.

- 95 submissions (79%) relate to Key Themes as described in Table A and below.
- 25 submissions (21%) relate to other topics beyond the scope of our inquiry. We did not analyze these submissions.

Of the 95 submissions related to Key Themes:

- 84 submissions (88%) express explicit support for HIV prevention choices and/or continuing microbicides research.
- The other 11 letters (12%) implicitly express support for choices and continuing microbicide research, through a focus on maintaining
the current research network structure (which includes the MTN), Good Participatory Practice (GPP) or the need for social-behavioral research.

Of note, 70% of all submissions (whether relating to a Key Theme or not) expressed explicit support for HIV prevention choices and/or continued microbicides research.

Table A summarizes the number of times each Key Theme is mentioned throughout submissions. Please note that each submission could mention more than one theme.

### TABLE A: SUMMARY OF KEY THEMES

<table>
<thead>
<tr>
<th>THE NEED FOR PREVENTION CHOICES</th>
<th>SPECIFIC POPULATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choice/Options</td>
<td>59</td>
</tr>
<tr>
<td>117 total mentions of need for choices</td>
<td></td>
</tr>
<tr>
<td>Continue microbicide research</td>
<td>58</td>
</tr>
<tr>
<td>65 total mentions of microbicides</td>
<td></td>
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<tr>
<td><strong>PRODUCT RELATED COMMENTS</strong></td>
<td><strong>OTHER CALLS TO NIAID</strong></td>
</tr>
<tr>
<td>Microbicide-Vaginal</td>
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<tr>
<td>Microbicide-Rectal</td>
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<tr>
<td>Microbicide-Both</td>
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<tr>
<td>MPTs - Pregnancy</td>
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<tr>
<td>MPTs - STIs</td>
<td>5</td>
</tr>
<tr>
<td><strong>PRODUCT FEATURES</strong></td>
<td></td>
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<tr>
<td>Women-Controlled</td>
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<td>User-Controlled</td>
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<tr>
<td>On-demand/Short-term</td>
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<tr>
<td>Non-Medicalized</td>
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<tr>
<td>Behaviourally Congruent</td>
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<tr>
<td><strong>TOTAL MENTIONS</strong></td>
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</tr>
<tr>
<td><strong>TOTAL REFERENCES</strong></td>
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<tr>
<td><strong>TOTAL MENTIONS OF MPTs</strong></td>
<td>29</td>
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<tr>
<td><strong>TOTAL MENTIONS OF MICROBIDES</strong></td>
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</tbody>
</table>
ANALYSIS OF KEY THEMES
THE NEED FOR PREVENTION CHOICES

CHOICE/OPTIONS
Many respondents either explicitly or implicitly mentioned the need for HIV prevention choices and/or options. Several comments included references to the need for an HIV prevention toolbox, that one size does not fit all, or that different people have different needs at different times. There were several explicit references to needing user-initiated, short-acting and on-demand products such as microbicides, in addition to systemic products, as well as comparisons to lessons learned from the contraception field. Some of the comments included:

The family planning field has demonstrated time and time again that providing women with a variety of methods to meet their needs and preferences results in greater product use and satisfaction and fewer unintended pregnancies. This same principle is applicable to the field of HIV prevention.

WOMEN’S HEALTH ADVOCATES (GLOBAL)

We want choices—we are all different and we want different tools so we can choose what suits us best.

YOUNG WOMEN’S GROUP (EAST AND SOUTHERN AFRICA)

Whether it comes to what type of birth control they are using, or the way that they are preventing or treating their HIV, women WANT options!!! Please don’t go down the path of eliminating these other options; the ramifications could be highly negative towards the future of women’s health.

FAMILY PLANNING RESEARCHER (US)

No single method can be expected to stop HIV. Additional methods are required to widen the choices available for more people to be protected from HIV and MTN is making a significant contribution to make this dream a reality.

ACADEMIC (ZIMBABWE)
Topical on-demand products like microbicides are essential to ensure that people who are vulnerable to HIV have options that meet their needs. All prevention avenues should be pursued—vaccines, long-acting systemic products such as injectables and implants, and topical on-demand products such as microbicides... People who are susceptible to HIV have expressed needing more, not fewer options, to meet a variety of prevention needs, desires, and contexts across their lifespan... If we are to end the HIV epidemic, an array of prevention options, including safe, effective, acceptable, and accessible microbicides must remain a priority at NIH.

**LEGISLATORS (US)**

Both our research in HIV and our experience in family planning clearly show that women need choices, and that different modalities will suit different women at different times of their lives... We need to meet women where they are and offer them choices that fit into their lifestyles, rather than dictating which methods are best for them.

**RESEARCHER (US)**

If research in sexual and reproductive health has taught us anything, it is that products must adapt to the needs of users; not the other way around. Microbicides are poised to do just that: provide options for an important market segmentation of people who want the option to use protection when they need it that is not systemic and requires no long-term commitment.

**RESEARCHER (US)**

Do NOT forget WOMEN who carry the majority of the burden of the HIV epidemic... Do not forget that CHOICE is not an option, it’s a must for ending this epidemic... Women MUST have choices. Men who have sex with men (MSM) and other vulnerable populations need choices too! ... Like for contraception, we have to provide method choice so coverage will be higher and better. Topical/non-systemic products are part of the choice we must provide to current and future users.

**RESEARCHER (US)**

Getting effective, acceptable microbicides into women’s hands is critical... We can’t wait for a vaccine and we can’t settle just for systemic methods like oral PrEP. Multiple options—including on demand microbicides that women can use as needed—must also be part of the picture... Lives depend on making tools that women want.

**COMMENTER**
CONTINUE RESEARCH ON MICROBICIDES

Many respondents either explicitly or implicitly expressed wanting to see that the development of microbicides continues. Comments included references to leveraging the success of the dapivirine ring and pursuing promising products currently in the research pipeline (vaginal and rectal microbicides, multi-purpose technologies). Concerns were expressed about the possible limitations of systemic approaches and the potential delays in the introduction of new products if alternative options are not pursued. Some of the comments included:

Refocusing the prevention research agenda solely on vaccines and long-acting systemic products at the cost of further development of microbicides is scientifically short-sighted, especially as injectable formulations under study have not yet been proven effective.

WOMEN’S HEALTH ADVOCATES (GLOBAL)

Many of our colleagues have expressed concern that dismissal of microbicides now would sell short years of investment in groundbreaking science, forgo novel technologies just as they are on the verge of achieving new successes and population-level impact, and dismiss the prevention needs of women, adolescent girls, men, and communities worldwide who currently have too few HIV prevention options.

WOMEN’S HEALTH ADVOCATES (GLOBAL)

Microbicides must continue to be a priority for the NIH research network agenda going forward—anything less would be either blind hope that other, yet-unproven strategies will be wildly successful (such wishful thinking has failed us all many times in HIV prevention) or a deliberate decision that the most vulnerable populations at risk for HIV, who may not ever be able to use other prevention tools, will not have access to the tools they need or want.

HIV PREVENTION RESEARCHERS (US)

We can’t dismiss the needs of the current generation in hopes of something that may or may not come to fruition for the generations to come. Is that ethical, especially when it’s not known the prospects of long-acting injectables and current vaccine candidates?
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.

**ADVOCATES AND RESEARCHERS (GLOBAL)**

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.

**LEGISLATORS (US)**

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... It is imperative we continue research into topical on-demand products as viable alternatives in the meantime.

**ADVOCATES AND RESEARCHERS (GLOBAL)**

I ask you to reconsider your exclusion of topical microbicides for PrEP from inclusion in future network research which you effectively ensure by requiring ‘systemic protection’... Respectfully, [this] seems an arbitrary requirement largely unsupported by evidence... Systemic protection as the cause for poor performance is only theoretical and other variables are far more powerful explanatory variables... A ‘systemic protection’ requirement effectively makes long-acting injectable cabotegravir the only PrEP option for most of the next decade, putting all the eggs into one very flimsy basket for now.

**HIV PREVENTION RESEARCHER (US)**

Removing the microbicides agenda doesn’t feel like it is in the interest of providing a mix of tools for HIV prevention in young women. I plead with the NIH to continue supporting all possible HIV prevention tools and options including long-acting products and the not-so-long-acting like microbicides.

**RESEARCHER (SOUTH AFRICA)**

The dapivirine vaginal ring is only the beginning, NOT the end of a new prevention tool for women... Adherence can be optimized by making rings MPTs for HIV/STIs and pregnancy prevention.

**RESEARCHER (US)**
PRODUCT-RELATED COMMENTS

MICROBICIDE-VAGINAL
Many respondents specifically mentioned vaginal microbicides. This includes references to the dapivirine ring, other potential vaginal rings and other topical formulations (e.g., gels, tablets, films). Comments included:

We love the idea of the ring... We would use it because it’s in and doesn’t bother us for a while... We would love the ring even more if you added a contraceptive. We understand that DAIDS is thinking not to put more research into other forms of rings like this and we don’t think that’s a good idea. We have seen it work for some women and that’s okay that it doesn’t work for all because it’s another tool, another choice.

YOUNG WOMEN - EAST/SOUTHERN AFRICA

We need more research in microbicides which can protect against pregnancy, STIs and HIV. Secondly most of the products available today are male-controlled so there is a need to produce a product that puts HIV prevention in the hands of women. Finally, young women are intermittently sexually active yet at a very high risk of HIV. We are kindly requesting for a product that can be used as and when needed during that activity.

COMMENTER (UGANDA)

MICROBICIDE-RECTAL
Many respondents specifically mentioned rectal microbicides. This includes references to various topical formulations, including douches, enemas, lubricants and suppositories, with comments like:

The desirability for an on demand, behaviorally-congruent PrEP product has been voiced loudly by the populations at greatest risk of HIV nationally and internationally, especially by young black MSM in the US for more than 10 years... Rectal microbicide products now in clinical development demonstrate the capability to meet these requirements.

RESEARCHER (US)

Rectal microbicides, especially those formulated as a rectal douche, have an important potential to prevent HIV transmission... Research on rectal microbicide douches is on the brink of offering important topical alternatives for individuals who reject systemic HIV prevention strategies (i.e., oral PrEP). Rectal microbicide douche development research is worthy of continued support.

RESEARCHER (US)
MPTs - PREGNANCY AND STIs  
Many respondents mentioned multi-purpose technologies, including products that could prevent not only HIV, but also unplanned pregnancies and sexually transmitted infections (STIs). Some of the comments included:

*STI rates are increasing in many populations vulnerable to HIV. Products that could reduce the incidence of both HIV and STIs would be valuable.*

**ADVOCATES AND RESEARCHERS (GLOBAL)**

As African women, we need more research in microbicides which can protect against pregnancy, STI and HIV at the same time.

**COMMENTER (AFRICA)**

Women need to have options in order to control their sexual health. This decision would eliminate the great potential for a future option: the combination of HIV prevention and contraception in the form of a vaginal ring. Please consider how vital these options are when deciding how to fund future HIV prevention research!

**CLINICIAN (US)**

MICROBICIDE-BOTH VAGINAL AND RECTAL  
Many respondents mentioned both vaginal and rectal microbicides, including a variety of possible topical formulations.

*The highest priority for topical approaches is to determine the effectiveness of the dapivirine ring now that modest efficacy has been demonstrated with per-protocol analyses indicating a strong association between adherence and efficacy... The second highest priority for topical approaches is to determine whether a rectal microbicide is effective.*

**RESEARCHER (US)**

I am concerned that the focus on systemic HIV prevention modalities compromises the very desirability that Dr. Dieffenbach calls for... For many, systemic products in any shape or form will never be considered desirable—especially in communities with significant medical mistrust, which are often the communities that most need an array of effective HIV prevention options. In terms of desirability, microbicides—including rectal and vaginal microbicides—may very well be the most valuable HIV prevention tools currently under study.

**RESEARCHER (US)**
PRODUCT FEATURES

WOMEN-CONTROLLED OR USER-CONTROLLED
Many respondents mentioned the need for HIV prevention options that users—especially women—can control, including in cases where discretion is desired. Among the comments were:

We need more products that will put the power of HIV prevention in the hands of women who are most at risk to HIV in Africa and yet have less power to negotiate for safer sex.

COMMENTER (AFRICA)

Microbicides offer a very important opportunity to develop a woman-centered HIV preventive tool... Why kill an idea when you are still looking for an answer?

ADVOCATE (UGANDA)

This is the beginning of more products to come that women can use so I think we need to keep the microbicide agenda alive... Women are the hardest hit by the HIV epidemic and finding a variety of methods that suit their lifestyles would be the best and microbicides present such a platform to develop products women can use.

RESEARCHER (UGANDA)

ON-DEMAND/SHORT-TERM
Many respondents mentioned the need for products that are short-acting and that can be used on-demand at the time of sex, including the possibility of intermittent use during sporadic periods when the user is sexually active. Comments included:

Young women, who are most at risk of contracting HIV, are only intermittently sexually active. They therefore need a product that can be used as and when needed.

COMMENTER

Systemic products under study (e.g., injectables and implants)... will never meet the needs of people who want—and need—easy-to-use, on-demand tools that readily fit into their lives and do not require systemic application.

RESEARCHER (US)
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.

Although there have been difficulties in development of topical products, particularly with adherence, there are areas (including enemas) that are behaviorally congruent and hold great promise. We can’t give up on this!

Advocates and researchers (Global)

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Advocates and researchers (Global)

Some respondents mentioned the appeal of products that are behaviourally congruent—meaning that they build on existing practices such as rectal douching or the use of lubricants during sex—to enhance their acceptance and uptake. Comments included:

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Advocates and researchers (Global)

Some respondents mentioned the need for products that are non-systemic and that can be used without overburdening the user or the healthcare system, with comments such as the following:

Some of us like the convenience of systemic coverage. But others of us... don’t want something that requires constant check-up. We want something that doesn’t stay in our bodies for a long time.

Young women - East/Southern Africa

We in Africa need a prevention package that can be empowering to the user and less dependent on a very ailing health care system.

Commenter (Africa)

There will always be a need for a woman-controlled method of HIV prevention that, unlike implants, injectables or vaccines, do not require medical services and have minimal systemic side effects.

Clinician (US)

Be behaviourally congruent

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Advocates and researchers (Global)

Although there have been difficulties in development of topical products, particularly with adherence, there are areas (including enemas) that are behaviorally congruent and hold great promise. We can’t give up on this!

RESEARCHER (US)
SPECIFIC POPULATIONS

Some respondents mentioned the HIV prevention needs of specific populations, including pregnant and breastfeeding women; adolescent girls and young women; gay men and other men who have sex with men (MSM); transgender men and women. Comments included:

*Invest more in microbicides so that more and more adolescent girls and young women are able to find a product that best suits their lifestyles and we can ultimately contribute towards reducing the number of new HIV infections.*

**COMMENTER (ZIMBABWE)**

*We have to continue listening to the community of gay, bisexual, same-gender-loving and other MSM. If we do, we’ll find more options to help us conquer this epidemic.*

**ADVOCATE (US)**

*The black men and transgender men and women of color who are served by [our organization] want more options for HIV prevention.*

**ADVOCATE (US)**

OTHER CALLS TO NIAID

DON’T COMBINE NETWORKS

Some respondents expressed a preference for the NIH not to combine existing HIV prevention networks, with comments such as:

*I have heard about the plan to dissolve the Microbicides Trials Network. However this is a blow to the African women who are faced with the HIV/AIDS burden... Let MTN live for it has understood best the African woman and how best to help her fight HIV.*

**CLINICIAN (UGANDA)**

*I am of the firm opinion that networks should not merge, and that there is still a strong need for ongoing work in microbicides... The population that I work with carries among the highest HIV burden in the world... We owe it to the population... to provide products that will possibly have greater effectiveness, or dual function (such as dapivirine ring with contraceptive), or that will last longer... Disintegration of this network would be a huge loss to the world with regards to HIV prevention.*

**RESEARCHER (SOUTH AFRICA)**
Maintain the HIV Prevention Trials Network (HPTN), HIV Vaccine Trials Network (HVTN), and Microbicide Trials Network (MTN), rather than combine all three networks into a single HIV prevention network... We are concerned that a single biomedical prevention research network will stymie the rigorous early-phase research necessary to advance promising compounds, formulations, and delivery technologies. Furthermore, given the wide range in study design, participant populations, site requirements that research into new preventive therapy, vaccines, and microbicides require, it may not be logical to combine these into a single network... Early-phase clinical research must still be prioritized, particularly in the areas of vaccine development and multi-purpose technologies. We are concerned that this work will be deprioritized with research network consolidation emphasizing integrated, large trials.

ADVOCATES (US)

GPP/STAKEHOLDERS ENGAGEMENT
Some respondents mentioned the need for the NIH-funded HIV prevention research networks to engage actively with community stakeholders, including underrepresented populations, trial participants and community organizations. This includes specific references to Good Participatory Practice (GPP).

We recommend that stakeholder engagement be added as a central pillar to all network and research structures.

ADVOCATES (GLOBAL)

Implementation of GPP guidelines for biomedical HIV prevention research or comparable guidance should be mandatory for all networks.

ADVOCATES (GLOBAL)

There is a critical need for women to hold key positions in the design and implementation of HIV prevention and treatment research... Low retention rates for women in HIV research studies are believed to be influenced by study designs intended for men, but that were later altered to accommodate women.

ADVOCATES (US)

SOCIAL/BEHAVIOURAL RESEARCH
Some respondents mentioned the need to support social and behavioural research, including in relation to adherence, user preference and epidemiology.
We believe it is too early to contract the scientific agenda of the networks based on our current knowledge of user preferences for HIV prevention options... There is a need for research that can tell us what people do and don’t want outside of the clinical trials, but that research has not been done.

ADVOCATES (GLOBAL)

I strongly believe there is still need to invest in research for HIV prevention options for women and to invest in understanding the social behavioural issues that impact on women’s use of study products.

ADVOCATE (UGANDA)

NIAID must meaningfully involve behavioral and social scientists in study leadership to help ensure that these bio-psycho-social factors are considered in study design, implementation, and follow-through.

ADVOCATES (US)

HOPING NIAID WILL LISTEN

Some respondents expressed the hope that NIAID would listen to civil society, community voices, and specific populations in various contexts that have an urgent need for an expanded range of HIV prevention options.

The redirection contradicts NIAID’s claims that developing tailored, safe, effective, and desirable prevention tools to meet people’s diverse prevention needs and contexts is a top priority.

WOMEN’S HEALTH ADVOCATES (GLOBAL)

We hope our views will be heard and considered because we don’t want our issues to go unnoticed. We would love if—in the future—we were asked first about our needs instead of just coming with the products researchers think will be best and then asking us if we would use them.

YOUNG WOMEN - EAST/SOUTHERN AFRICA

CALL FOR TRANSPARENCY

Some respondents called for greater transparency in the NIH’s decision-making process, including specific references to the consultation process.

It would be great to see all incoming comments posted in a public forum so that we can all participate in an informed discussion on future research priorities.

RESEARCHER (US)
ANALYSIS OF NIH RESPONSES

We analyzed 56 responses from NIAID.

There were 27 substantive responses to relevant submissions (of which 18 are identical responses to US Legislators), leaving 10 unique substantive responses (1 to Legislators plus 9 others).

The other 29 responses include brief acknowledgments of receipt of input, requests for permission to post submissions to the NIAID website (which we have noted never happened), and responses to submissions unrelated to our themes of interest (IMPAACT/maternal/pediatric research).

ANALYSIS OF KEY THEMES

CHOICE

NIAID responses stated that choice is fundamental to protection. They agreed with the idea of options, but said choice is not the endpoint—the tools must be effective.

We agree that choice is fundamental to protection, and NIAID is committed to supporting the development of an array of safe and effective tools that ultimately can be implemented at a scale that moves the needle on the pandemic, particularly for disproportionately affected groups like young women.

CARL DIEFFENBACH

Developing choices for HIV prevention is a smart approach to protecting diverse people and populations. However, choice itself is not the endpoint to which we strive. As stewards of federal investment in HIV research, it is crucial that any prevention tool demonstrate a high degree of safety and efficacy in preventing HIV.

CARL DIEFFENBACH

THE PREVENTION NEEDS OF WOMEN

NIAID stated it would support tools for disproportionately affected groups like young women, saying that women have been in a “blind spot” and that they are now a top priority. NIAID said products were needed that can be used discretely but that also fully protect women—not only during vaginal sex but also anal sex.
Throughout history, the needs of women have often been a blind spot in science. However, it is clear that women must be taken into account from the start of the research process to ensure their health needs are met, and ultimately to improve the health for all members of society. I want to assure you that funding the development of innovative HIV prevention products that work for women is a chief priority for NIH.

CARL DIEFFENBACH

To be clear, NIAID will continue to support development of topical HIV prevention products. Microbicides can be discreet, and they are applied by the user—important concepts for those who lack agency in relationships or face stigma for choosing to protect themselves… In particular, microbicides are thought to offer advantages for women, should a modality reach regulatory approval. That said, we need a focused discussion on what it means to fully protect women from HIV... if it is sufficient to only protect women during vaginal sex, when data indicate that rates of women engaging in vaginal and anal sex are increasing, especially for young women.

CARL DIEFFENBACH

Developing safe, effective and desirable prevention tools for women has been a longstanding goal for the National Institutes of Health, and is a top priority for the next iteration of the clinical research enterprise.

CARL DIEFFENBACH

FISCAL CONSTRAINTS AND THE BENEFITS OF ONE NETWORK
NIAID stated that due to fiscal constraints, they combined the HIV prevention clinical trials networks. They stated that in any case, one broad prevention network will ensure that the most innovative, effective, highest priority prevention strategies are evaluated. They state that this will also ensure that partnerships are built internally and with others like the pharmaceutical industry. They state that such partnerships will help to move products to market and to implement them to scale.

Integrating HIV prevention research in one network will ensure that the highest priority research is accomplished, allow for deeper collaborations and partnerships with network experts and other organizations like pharmaceutical companies, which are essential for getting successful products to market.

CARL DIEFFENBACH
SUPPORT FOR INNOVATIVE, MERITORIOUS CONCEPTS OF HIGHLY SAFE AND EFFECTIVE TOOLS?
NIAID stated that they’re not excluding microbicides, but the priority is systemic protection. They stated that they must invest wisely, which means in highly effective tools, and that they would support innovative, meritorious, promising concepts. On the one hand, they mentioned in some responses that this includes a multi-purpose vaginal ring that would prevent HIV and unplanned pregnancies, as well as rectal douches. On the other hand, they indicated that microbicides research is limited, that there is a need for prevention options beyond what’s currently being investigated, and that there is a need for innovation in the field. They stated that if innovation happens, they would consider supporting microbicides. However, they also asserted that microbicides have limited proven efficacy and that there is no proof that the most vulnerable groups would adhere to them—nor is there proof that they can provide systemic protection. They said we need something that provides equivalent protection to daily PrEP. NIAID stated that it needs to invest smartly and that it is not looking for something to protect a fraction of the population.

Highly meritorious proposals to study microbicides will be welcome at NIAID.

CARL DIEFFENBACH

We will also complete clinical studies currently underway. We need better, next-generation solutions to be designed and tested. This will require creativity and innovation beyond what is already in clinical studies.

CARL DIEFFENBACH

Should the ring be licensed, we will continue efforts with you and your colleagues to develop a multipurpose version of the ring for HIV prevention and contraception.

CARL DIEFFENBACH

NIAID is also interested in supporting the development of other innovative prevention strategies, such as the proposed concept from the Development of a Rectal Enema as Microbicide (DREAM) project... Additionally we need to remember that the most challenging aspects of HIV prevention products are acceptability and adherence. How this concept would be made available to young MSM not just in the United States but also in other regions of the world that could greatly benefit from it is an issue that warrants further discussion.

CARL DIEFFENBACH
The candidate microbicides currently in the research pipeline have limited proven efficacy, and it has not been demonstrated that the most vulnerable users would choose or adhere to these products. While there is a strong cry for these products as abstract tools, users become more reticent when confronted with the realities of using prototype products, even when marginally behaviorally congruent.

CARL DIEFFENBACH

There is no evidence to demonstrate that a rectally applied product that lacks the ability to penetrate system-wide will be able to offer effective protection. However, while systemic protection is critical, systemic delivery is not mandatory. I do acknowledge your position that this position effectively eliminates microbicide research in its current state, but I think this field is in need of a significant evaluation of what is actually desirable, practical, and provides protection equivalent to daily PrEP. The goal should not be to protect a fraction of the population, it should be to develop products that are highly desired, easy to use, and are able to confer safe and effective protection.

CARL DIEFFENBACH

NO FUNDING FOR COMMUNITY ENGAGEMENT

NIAID stated that there is no more funding available for community engagement and research literacy.

While the Be the Generation Bridge Project... complemented site and network-level community engagement activities by laying the groundwork in reaching people in many of these communities, and building research literacy and awareness, funding is no longer possible to support that type of effort.

CARL DIEFFENBACH
The NIH input phase has come to a close. Priorities for the next cycle of HIV prevention and treatment research (2021 – 2027) and the new structure for the prevention research clinical trials networks have all but officially been decided. Unfortunately, as our analysis demonstrates, they do not significantly reflect priorities expressed during the input phase by communities, advocates and researchers from across the globe, nor by communities, advocates, researchers and lawmakers within the US. Community concerns and priorities have been largely ignored.

In an era where user-centred design is being promoted and championed, it is disappointing that the next 7 years of NIH-funded research is not responding to the needs of those for whom these tools are critical. The vast majority of those who submitted input—whether from the US or from around the world—unequivocally supported the ongoing and targeted development of on-demand topical products, including an array of vaginal and rectal microbicides that could prevent HIV, STIs and unplanned pregnancy among a range of communities, such as young women and gay men.

NIAID’s responses to comments are contradictory. While nominally espousing the language of choice and prevention options for women and other vulnerable groups, the NIAID responses demonstrate an uncompromising and patronizing stance towards microbicides and the development of tools that are specifically designed to meet the needs of those who are most vulnerable —and they belie a deep hostility towards those who call for that choice.

In those responses, NIAID stated that they “will continue to support development of topical HIV prevention products.” At the same time, they provide a list of conditions under which that would need to happen—which includes several complex, possibly scientifically unattainable criteria that by definition effectively exclude microbicides. This is disingenuous “support,” both cynical and hypocritical.

We are particularly troubled to see that the letter submitted during the input process by the leadership of the HPTN—which will be the strongest or possibly only contender bidding to lead non-vaccine HIV prevention research—makes absolutely no mention of the intention to continue the work or incorporate the priorities and expertise of the MTN. Indeed, there is no mention of microbicides or non-systemic on-demand products, and not a word about the need for options, choices, a range of tools to meet the needs of various communities.
It is not too late to change or influence the priorities proposed by the NIH. We must mobilize as a community of prevention consumers, advocates, researchers and policy-makers and continue to voice the need for research that leads to an array of prevention options for those who need them most. In an era where the mantra is for options that fit people’s lives versus those that people must fit into their lives, the current approach will not allow us to adequately respond to the HIV prevention crisis we face.

To the NIH and the HPTN leadership, we say this: There is a vocal, aware, interested constituency for microbicides and we are watching what you do. We will not allow our voices to be sidelined. There is too much at stake. We look forward to working together as fully engaged and committed partners in a revitalized HIV prevention research enterprise that encompasses a broad range of potential options to meet our varied and complex HIV prevention and sexual health needs.
WHAT YOU CAN DO

Share the report widely through your networks and social media, using the following link tinyurl.com/whosechoiceanyway and hashtags as appropriate:

#fulltoolbox
#HIVpreventionoptions
#microbicides4all
#usercontrolled
#usercentereddesign
#ourpreventionchoices
#optionsforpeopleslives

Write to the NIAID/NIH and HPTN leadership to express your views. Feel free to use the key messages from this report as inspiration.

NIAID/NIH Leadership: Dr. Carl W. Dieffenbach, Director of the Division of AIDS, National Institute of Allergy and Infectious Diseases, National Institutes of Health (cdieffenba@niaid.nih.gov) and Dr. Anthony S. Fauci, Director of the National Institute of Allergy and Infectious Diseases, National Institutes of Health (afauci@niaid.nih.gov)

NIAID’s AIDS Research Advisory Committee (ARAC): Chairperson Dr. Cara Wilson (Cara.Wilson@ucdenver.edu). Contact information for other ARAC Committee members can be found at https://www.niaid.nih.gov/about/committees-aids-research

HPTN Leadership: Dr. Wafaa El-Sadr (wme1@columbia.edu) and Dr. Myron Cohen (myron_cohen@med.unc.edu), co-Principal Investigators