

## Microbicide Development Act

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### Introduction

The Microbicide Development Act is proposed legislation that was originally introduced in the House of the 106<sup>th</sup> Congress.<sup>1</sup> It was introduced in the House and the Senate of the 107<sup>th</sup>, 109<sup>th</sup> and 110<sup>th</sup> Congresses and the Senate of the 108<sup>th</sup> Congress.<sup>2,3,4,5</sup> The bill would substantially increase the US government's commitment to the research and development of Microbicides.

Microbicides are a class of products currently under development that a person could apply topically to prevent transmission of HIV and other infections. Microbicides could come in a variety of forms, including gels, creams, films, or rings that would release the drug slowly over days or weeks<sup>6</sup>.

Globally women make up 48% of all adults living with HIV/AIDS; in sub-Saharan Africa that percentage rises to 59%<sup>7</sup>. In the U.S., the Centers for Disease Control and Prevention (CDC) estimates that as many as 300,000 women are living with HIV<sup>8</sup>. Gender inequality plays a significant role in new infections among women and girls. Biological, social, cultural, and economic factors including sexual violence and survival sex make women and girls particularly vulnerable to HIV infection.<sup>9</sup> To combat this heightened vulnerability and sky rocketing infection rates, women need more HIV prevention options, particularly a form of HIV prevention they can control.

A prominent HIV prevention strategy around the globe is commonly known as ABC: Abstain from risky behavior, Be faithful, and use Condoms. This approach to prevention is very useful when applied with broad support from all levels of society. But, the ABC method is not feasible or realistic for many women across the

world who are not in a position to negotiate safe sex practices that could save their lives. Women are not always empowered to insist on fidelity and assuming a partner's faithfulness can put both women and men at increased risk for HIV. Similarly, correct and consistent condom use varies greatly between relationships. Condom use, which is often controlled by a man, tends to diminish between regular partners while risk for HIV infection may not decrease.<sup>10</sup> One of the great potentials for a microbicide is to provide another prevention tool that women and girls, who are being disproportionately affected by HIV, can control.

### What are Microbicides?

A technical definition of a microbicide is "a substance that can significantly reduce transmission of HIV and/or viral, bacterial, fungal, or protozoan sexually transmitted pathogens when applied topically to genital mucosal surfaces."<sup>11</sup> Although microbicide development is often focused on providing a prevention alternative for women and girls engaging in vaginal sex, microbicides have the potential to be used by any person engaging in receptive anal sex, regardless of gender. Potential microbicides take different approaches to preventing infection by HIV. According to the Alliance for Microbicide Development, there are seven different scientific mechanisms being studied in which a microbicide could prevent HIV infection.<sup>12</sup>

The seven mechanisms for prevention occur at different stages of possible HIV infection. One method is creating a physical barrier for HIV infection. A second approach is to inactivate or neutralize the virus before it passes the epithelium (layer of cells in the vaginal or rectal

cavity) and enters the body. A third microbical mechanism of action is to strengthen the body's natural defenses; this is known as a vaginal defense enhancer. A fourth method is by preventing other STI infections with a microbicide.<sup>13</sup> The next three means of preventing HIV infection with a microbicide occur after the virus has entered the body.

These three methods involve adapting current antiretroviral treatments for HIV into microbical forms. One method is to prevent the HIV virus from fusing with a potential host cell; compounds that do this are called fusion inhibitors. Another method is to prevent the virus from copying its RNA in a process known as reverse transcriptase; these compounds are known as reverse transcriptase inhibitors. The final method is to prevent the uptake of HIV infection by cells after the virus has passed into the body.<sup>14</sup> All of these avenues are presently being studied to find a safe and effective microbicide.

### **In the Pipeline**

Research to find a safe and effective microbicide is proceeding with numerous candidates in order to find a compound that will succeed in providing another form of prevention against HIV. According to the Alliance for Microbicide Development (AMD), there are approximately sixty microbicide candidates in various states of development. Of these sixty, forty-seven candidates have been verified and are being tracked by AMD.<sup>15</sup>

It takes on average between 10 and 12 years for an experimental drug to move through all the stages of research. There are four or sometimes five distinct stages of research; preclinical trials, phase I, phase II, phase III, and sometimes phase IV post market research. Preclinical research takes place in a laboratory and does not include any testing on human subjects. The preclinical phase lasts an average of three and a half years. If a candidate passes the preclinical stage it moves to phase I research to test safety and

dosage on less than 100 healthy volunteer subjects. Phase I research takes an average of one year. Phase II research is meant to evaluate effectiveness and look for side effects, this phase takes place with between 100-300 patient volunteer and last for about two years. Phase III research verifies effectiveness and continues to look for side effects in between 1000-3000 patient volunteers, this phase lasts an average of three years. If a candidate passes all these stages it goes to the US Food and Drug Administration (FDA) where it undergoes a review and possible approval process that takes about two and a half years. Some drugs and devices enter phase IV research after FDA approval to continue to evaluate the drug.<sup>16</sup>

There are thirty-six microbicide candidates in the preclinical phases of development and eleven other candidates that are in different phases of actual clinical trials.

Only two candidates are currently in the third and final phase of clinical trials. These two candidates are Carraguard gel and PRO 2000/5 gel both of which are fusion inhibitors. There are two further candidates in late phase two trials, Caprisa 004 (a reverse transcriptase inhibitor) and BufferGel (a vaginal defense enhancer). The five remaining candidates are in either early phase II or phase I trials.<sup>17</sup>

### **Microbicide Development Act**

The Microbicide Development Act, S. 823, HR 1420, would authorize increased funding for, and require better coordination among federal agencies conducting microbicide research, including the Centers for Disease Control and Prevention (CDC), the U.S. Agency for International Development (USAID), and the National Institutes for Health (NIH). The bill would also require coordinating agencies to submit a report to Congress verifying their collaboration and recorded progress. The Microbicide Development Act would also authorize the appropriation of necessary funding to support microbicide research for the

next two years. Currently Microbicides only represent 3% of the federal HIV/AIDS research budget.<sup>18</sup>

Finally, the bill would also establish a branch within the National Institute of Allergy and Infectious Diseases (NIAID) dedicated solely to the development of microbicides.<sup>19</sup>

### Funding Levels

Investment in Microbicide research and development has grown significantly in the past few years. In 2000, public and philanthropic investment in vaccine research totaled \$66 million. In 2004, that number rose to \$140 million. In 2004, the United States accounted for about 75% of total investments in microbicides. The majority of funding for microbicide research comes from the public and philanthropic sector. Presently, no major pharmaceutical company is investing substantially in microbicide Research and Development.<sup>20</sup>

USAID and the US Department of Health and Human Services allocate available funding for microbicide development. The estimated total of U.S. federal funding for microbicide research and development in FY 2007 is \$131,314,000, with \$91,714,000 going to HHS and \$39,600,000 going to USAID.<sup>21</sup> The monies going to HHS are further divided and sent to both the Centers for Disease Control and Prevention and the National Institute of Health. 70% of all United States funding for Microbicide research and development is through the National Institutes of Health (NIH). Unfortunately, the funding levels for microbicide research in FY 2007 are lower than those for FY2006, which had a funding level of \$131,520,000.<sup>22</sup>

### Conclusion

Microbicides have the potential to prevent millions of HIV infections around the world, therefore saving millions of lives. Microbicides also have the potential for great cost savings in HIV prevention, treatment, and care. There have been numerous studies which estimate the total

benefits of an effective microbicide. One study by the Global Public Health Working Group of the Microbicide Initiative looked at the impact an effective microbicide would have on different populations around the world.

The study looked at possible microbicides with different levels of efficacy against HIV and other STIs. These ranged from 40% efficacy against HIV and 0% efficacy against other STIs to 60% efficacy against HIV and 40% efficacy against other STIs. With these assumptions, the study estimated that 1,662,344 to 2,735,177 new HIV infections could be averted over three years.<sup>23</sup> These numbers are truly staggering when one considers that the world has never seen widespread and sustained diminishing of new HIV infections since the beginning of the epidemic. In addition to the benefits of preventing HIV infection among these millions of individuals, there are also massive economic benefits an effective microbicide would bring.

Using the same assumptions about differing microbicide efficacy, estimates of the cost savings to health systems are from \$1.77 billion to \$2.88 billion, over three years.<sup>24</sup> These estimates show that the benefits from even a low efficacy microbicide translate into millions of lives and billions of dollars saved.

### AIDS Action Position

- AIDS Action supports passage of the Microbicide Development Act of 2007 to substantially increase the US government's commitment to the development of microbicides.
- AIDS Action supports wide co-sponsorship of the Act.
- AIDS Action supports increased public and private resources and funding for Microbicide development.

<sup>1</sup>Microbicides Development Act of 2000, H.R. 3891, 106<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2000)

<sup>2</sup> Microbicide Development Act of 2001, H.R. 2405, 107<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2001) / Microbicide Development Act of 2001, S. 1752, 107<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2001)

<sup>3</sup> Microbicide Development Act of 2003, S. 859, 108<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2003)

<sup>4</sup> Microbicide Development Act of 2005, H.R. 3854, 109<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2005) / Microbicide Development Act of 2005, S. 550, 109<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2005)

<sup>5</sup> Microbicide Development Act of 2007, H.R. 1420, 110<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2007) / Microbicide Development Act of 2007, S. 823, 110<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2007)

<sup>6</sup> Global Campaign for Microbicides. (2006) *Frequently Asked Questions About Microbicides: Fact Sheet 2. Global Campaign for Microbicides*. Retrieved October, 2007, from Global Campaign for Microbicides Web Page: [www.global-campaign.org/clientfiles/FS2-FAQs-May05.doc](http://www.global-campaign.org/clientfiles/FS2-FAQs-May05.doc)

<sup>7</sup> The Henry J. Kaiser Family Foundation. (2007) *The Global HIV/AIDS Epidemic*. Retrieved October, 2007, from The Henry J. Kaiser Family Foundation Web page: [http://kff.org/hivaids/upload/3030\\_09.pdf](http://kff.org/hivaids/upload/3030_09.pdf)

<sup>8</sup> The Henry J. Kaiser Family Foundation. (2007) *Fact Sheet: Women and HIV/AIDS in the United States*, Retrieved October, 2007, from The Henry J. Kaiser Family Foundation Web page: <http://kff.org/hivaids/upload/6092-04.pdf>

<sup>9</sup> Global Coalition on Women and AIDS. (2006) *Increase Women's Control Over HIV Prevention: Fight AIDS*, Retrieved October, 2007, from Global Coalition on Women and AIDS Web page: <http://www.global-campaign.org/clientfiles/GCOWA-Briefing-Paper.pdf>

<sup>10</sup> Global Campaign for Microbicides. (2003) *Are people using condoms? Current evidence from Sub-Saharan Africa and Asia and the implications for microbicides*. Retrieved October, 2007, from Global Campaign for Microbicides Web page: <http://www.global-campaign.org/clientfiles/LSHTM-Condom.pdf>

<sup>11</sup> Alliance for Microbicide Development. (2007) *Microbicide Facts*. Retrieved October, 2007, from Alliance for Microbicide Development Web page: <http://www.microbicide.org/microbicideinfo/reference/microbicides.factsheet.pdf>

<sup>12</sup> Harrison, Polly. (2007). *Where do we go? Where do we need to go?* Retrieved October, 2007, from Global Health Council Web page: [http://www.globalhealth.org/images/pdf/events/p\\_harrison.pdf](http://www.globalhealth.org/images/pdf/events/p_harrison.pdf)

<sup>13</sup> Ibid

<sup>14</sup> Ibid

<sup>15</sup> Harrison, Polly. (2007). *Where do we go? Where do we need to go?* Retrieved October, 2007, from Global Health Council Web page: [http://www.globalhealth.org/images/pdf/events/p\\_harrison.pdf](http://www.globalhealth.org/images/pdf/events/p_harrison.pdf)

<sup>16</sup> Rados, Carol. (2003) *Inside Clinical Trials Testing Medical Products in People*. Retrieved October, 2007 from

the FDA Web site: [http://www.fda.gov/fdac/features/2003/503\\_trial.html](http://www.fda.gov/fdac/features/2003/503_trial.html)

<sup>17</sup> Alliance for Microbicide Development. (2007) *Microbicide Candidates in Ongoing Clinical Trials: Summary as of October 2007*. Retrieved October, 2007, from Global Health Council Web page: [http://www.globalhealth.org/images/pdf/events/handout3\\_101007.pdf](http://www.globalhealth.org/images/pdf/events/handout3_101007.pdf)

<sup>18</sup> Global Campaign for Microbicides. (2007) Sign on to S823 and HR 1420 The Microbicide Development Act of 2007. Retrieved October, 2007, from Global Campaign for Microbicides Web Page: [www.global-campaign.org/clientfiles/Legislators%20factsheet-MDA-Oct-2007.doc](http://www.global-campaign.org/clientfiles/Legislators%20factsheet-MDA-Oct-2007.doc)

<sup>19</sup> Microbicide Development Act of 2007, H.R. 1420, 110<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2007) / Microbicide Development Act of 2007, S. 823, 110<sup>th</sup> Cong. 1<sup>st</sup> Sess. (2007)

<sup>20</sup> Global Campaign for Microbicides (2007) Retrieved October 2007 from <http://www.global-campaign.org/economics.htm>.

<sup>21</sup> Alliance for Microbicide Development. (2007) *US Federal Government Funding FY 1997-2008*. Retrieved from the Global Health Council Web page: [http://www.globalhealth.org/images/pdf/events/handout1\\_101007.pdf](http://www.globalhealth.org/images/pdf/events/handout1_101007.pdf)

<sup>22</sup> Ibid

<sup>23</sup> Microbicide Initiative. (2001) *The Public Health Benefits of Microbicides in Lower-Income Countries Model Projections*. Retrieved October, 2007, from Public Health Working Group Web page: [http://www.global-campaign.org/clientfiles/rep7\\_publichealth.pdf](http://www.global-campaign.org/clientfiles/rep7_publichealth.pdf)

<sup>24</sup> Ibid