

March 6 - March 12, 2002

Microbe Managers Meet the Next Generation of HIV Prevention

By Joyce Lombardi

Two decades into the AIDS epidemic, condoms are still our only real defense against one of the biggest dangers of sex. They're cumbersome and they don't always work, but unless we abstain, they're all we've got. And if our partner refuses to use them, we've got nothing.

But what if there were another option, something like an invisible condom that would let us have safe skin-to-skin sex? Or a super-spermicide that could protect us from HIV, gonorrhea, herpes, chlamydia, vaginal infections, and even pregnancy, all at the same time? There might just be.

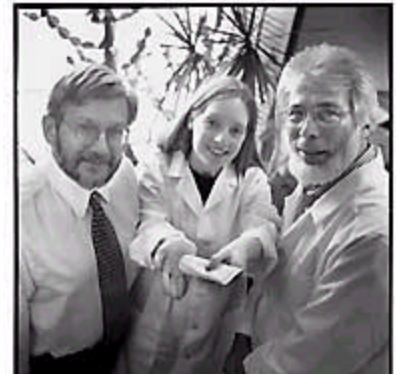
Its name is BufferGel and it is quietly being developed in a modest lab on the Homewood campus of Johns Hopkins University.

BufferGel is a clear, odorless goo. On the fingertips it feels like a cross between KY Jelly and hair gel. It is one of the most promising of a fledgling, experimental class of compounds called "microbicides," substances that, once applied inside the vagina, do battle with the viruses and bacteria that cause sexually transmitted diseases (STDs), including HIV.

There are about 60 microbicides currently in development by universities, nonprofit organizations, and small private firms around the world. Since none are on the market yet, most people haven't heard of microbicides. ("Could you spell that?" a public-relations rep at one Baltimore AIDS organization says when asked about them.) But those familiar with the potential of these germ-fighting gels, foams, and creams say they are revolutionary--and long overdue. "The development of a safe, effective microbicide would represent the most significant advance in women's reproductive health since the [birth-control] pill," says Lori Heise, a longtime women's-health advocate and current director of the Washington-based advocacy group Global Campaign for Microbicides. "It could do for infection what the pill did for fertility control for women 40 years ago in terms of putting power into their hands."

If the empowerment rhetoric sounds like just that, more and more AIDS and reproductive-health advocates familiar with the burgeoning field stand firm behind it.

"Have I heard of microbicides?" Lynda Dee, chairperson of AIDS Action Baltimore, practically barks into the phone. "Oh God, it's the only form of protection a woman can control herself! If a woman had a microbicide, she wouldn't have to worry about some big lug slapping her around



ReProtect directors Dr. Thomas Moench, Kristen Khanna, and Richard Cone proffer their product.

saying, 'We're gonna have sex without a condom whether you like it or not.' She could just put the stuff in, and he'd never even know."

The message of microbicide proponents distills down to this: Life-wrecking diseases like AIDS, gonorrhea, and chlamydia are proliferating because the current means of preventing them--using male or female condoms, being monogamous, or refusing sex--are simply not feasible for many of the world's women.

Consider, for example, a high-school girl in Baltimore whose 25-year-old boyfriend flies into a rage and accuses her of infidelity when she suggests he wear a condom. Or a young wife in Bombay who wants to get pregnant and so has unprotected sex with her husband, who visits prostitutes on the side.

Geeta Rao Gupta, president of the D.C.-based nonprofit International Center for Research on Women, read hundreds of such stories from around the world when she was directing a global research program on women and AIDS 12 years ago. "The thing that jumped out at me," she says, "was that women, whether illiterate or educated, poor or middle class, were asking for something they could control--perhaps unobtrusively, but which also allowed for skin-to-skin contact, which as we know is the cultural icon of intimacy."

No matter what their individual stories, one thing unites most of the 17.6 million women in the world currently living with HIV/AIDS. Most got infected by sex with a man. For many, that man was their husband.

"I was surprised to find out that, for women, one of the biggest risk factors worldwide for acquiring HIV is being married," says Kristen Khanna, business director for ReProtect LLC, the private company that makes BufferGel.

And AIDS among women is sharply on the rise. From 1997 to 2000, the proportion of females among worldwide HIV/AIDS cases climbed from 41 percent to 47 percent. In the United States, almost a quarter of all cases of full-blown AIDS in 1999 were women, compared to 7 percent in 1985. The statistics for teenage girls are particularly alarming: Six of every 10 U.S. teenagers with AIDS in 2001 were girls.

Poverty and powerlessness are partially to blame for these dismal numbers, but so is biology. Women's bodies, due to increased genital-tract surface area and the fragility of cervical cells, are thought to be more susceptible to infection than men's. One University of California study found that women were eight times more likely to contract HIV from vaginal intercourse than men were. A 1997 report by the Institute of Medicine, a Washington-based clearinghouse for health information, cites studies showing that women have a 90 percent chance of getting gonorrhea from one sexual encounter with an infected partner, while men have only a 20 percent to 30 percent chance. The bodies of teenage girls, whose cells are still developing, are especially vulnerable.

No one thinks that microbicides will be a magic bullet against AIDS. But most microbicide developers believe they can make a serious dent in the number of sexually transmitted diseases and unwanted pregnancies.

Khanna recently interrupted her own research on HIV transmission to work for ReProtect full time. "What inspires me," she says, "is the thought of having these [microbicide] products on the market, and then knowing they have contributed to healthier women and healthier families." If still a long time away, that expectation might not be far off the mark. A statistical analysis by the London School of Hygiene and Tropical Medicine concludes that a moderately effective (60 percent efficacy) microbicide, even if used in only half of sexual encounters by a fraction of women in the developing world, could reduce the number of new HIV infections by about 3 million over three years. That's roughly the number of people who died of AIDS worldwide in 2001.

"The modeling studies show that even a low-efficacy product could turn this epidemic around because, like a vaccine, it would help men and children as well as women," says Dr. Zeda Rosenberg, scientific director of the global nonprofit organization Family Health International and chairperson of a microbicide working group of the national HIV Prevention Trials Network. "It creates a domino effect."

The findings have thrilled those working on microbicides, whose efforts have yet to attract much attention outside the rarefied world of health research. "I get goose bumps as I say this," ICRW's Gupta says. "But now we have the hard data that makes the case for what women [have been] asking for for 10 years, for investing in microbicides."

Due to a confluence of hard-to-miss factors--the deepening AIDS crisis in the developing world, the stalled search for an HIV vaccine--this message is beginning to reach some important listeners. Melinda Gates has given almost \$50 million toward microbicide development; earlier this year, the philanthropist wife of Microsoft founder Bill Gates told *Newsweek* that she would be willing to give up some of her fiercely guarded privacy if it would help bring a microbicide to market more quickly. On World AIDS Day last December, actress Sharon Stone helped unveil stark red and white billboards put up by fashion designer Kenneth Cole directing viewers to a microbicide Web page hosted by the American Foundation for AIDS Research. On Capitol Hill, legislators in both houses of Congress have begun adding their names to the Microbicide Development Act, a 2-year-old attempt by U.S. Rep. Connie Morella (R-Md.) to jump-start national funding for microbicide research.

Meanwhile, back in a Hopkins lab in late January, ReProtect's staff is going about its daily work. Business director Khanna, eight and a half months pregnant, is having a final round of talks with local venture capitalists. Medical director Dr. Thomas Moench is on a conference call with researchers in Zimbabwe and India, two of six countries where BufferGel is slated to begin clinical trials. Managing director Richard Cone, a Hopkins biophysics professor, is helping a student measure the hydrogen-peroxide levels of vaginal secretions through the air-lock portals of an anaerobic chamber. (Disclosure: The author is a contract employee of Johns Hopkins' Bloomberg School of Public Health, a position she took shortly before completing work on this story. She has no ties to ReProtect, which employs Hopkins faculty but is an independent private company.)

The ReProtect scientists are all busy, very busy, but they are also waiting. They are waiting for hard data that shows that a microbicide, any microbicide, actually works. Such "proof of

concept," to use the industry term, could encourage reluctant pharmaceutical companies, private organizations, and governmental agencies to step forward and invest, thus opening the door for the entire field to advance.

"There were many people who tried to fly," Cone says, "but once the Wright Brothers succeeded, the development of airplanes sprang forth. It's the same thing with microbicides. When one is proven to work, it will provide the push for the entire field."

"At this point, it doesn't matter which product is first," says Kevin Whaley, a ReProtect partner and co-founder of the Alliance for Microbicide Development, a consortium of researchers and advocates formed in 1998. "We all just want a microbicide to be effective and be FDA-allowed." At the moment, through a combination of good science, good luck, and good contacts, BufferGel is further along the arduous research trail than any of the 60 or so other microbicides currently in development; it entered Phase III clinical trials for contraception in October and will start Phase III HIV trials later this year. Two other microbicides are now also undergoing these large-scale trials, which test a product's efficacy in humans and, as the last step before seeking U.S. Food and Drug Administration approval, are considered the make-or-break end game of the long, costly process of drug research. (Phases I and II test a product's safety in humans. BufferGel completed those tests--performed on women in the United States, India, Thailand, Malawi, and Zimbabwe--without a hitch.) Most other microbicide compounds are still in the lab-work or animal-testing stage.

What's more, BufferGel was also one of two microbicides selected by the highly competitive National Institutes of Health (NIH)-sponsored HIV Prevention Trials Network for tests involving 8,000 women in four countries in the developing world. (The other is Pro 2000, a viral inhibitor made by the small Lexington, Mass.-based biotech company Interneuron Pharmaceuticals.) That progress has been nine years in the making, since Cone, Moench, and Whaley formed ReProtect in 1993. None had a business background, but all were doing STD- and HIV-related research and felt a call to get more involved in prevention efforts.

"We wrote grant proposal after grant proposal," says Moench, a Hopkins-trained infectious-disease physician, "but we couldn't get funded. At the time, there was very little support from either the university or the NIH for what we were trying to do."

Hopkins and NIH have been supportive in recent years, Moench notes; ReProtect has received more funding from the federal agency than any other microbicide developer has. But a decade ago, the work they wanted to do was met largely with indifference in the scientific community. Few researchers were willing to step out of high-profile work, such as AIDS treatment and vaccine development, into the obscurity of a science that deals with vaginas, semen, and sexual taboos.

"Until recently, microbicide science was not considered real science," says Polly Harrison, director of the Alliance for Microbicide Development (AMD), a Silver Spring-based consortium of businesses, research institutions, and advocacy groups dedicated to the development of topical microbicides for the prevention of STDs. "If you were a front-line scientist, this was just not interesting. There [was] no Nobel Prize, no glory in working on vaginal epithelial cells and food

additives like carrageenan" (a seaweed-based compound being investigated for microbicidal potential).

Moench, who was researching the effect of HIV on the nervous system, was one of the exceptions. "What I was doing was worthwhile but at a much later stage of disease than I wanted to work," he says. "At the end of the day, I was happier working to prevent the disease than treating one of its threatening late-stage manifestations."

He began developing animal models to test whether nonoxynol-9, the popular spermicide currently used in condoms and contraceptive foams, could kill HIV. His new interests didn't impress his medical colleagues, he says: "I didn't get a lot of support from the hospital. Prevention is just not what they do. It's foreign to the culture." But he did capture the attention of Hopkins biophysicists Whaley and Cone, who were trying to clone a combination of antibodies that could simultaneously wipe out STDs and sperm.

As it did for Moench, the move into microbicide research represented a dramatic professional swerve for Cone, who spent his early career trying to answer fundamental questions about the human eye's rods and cones. "I was high-flying, publishing, part of a worldwide network," he says, leaning back in the wooden rocking chair in the office of the lab he directs at Hopkins' School of Arts and Sciences. "But when I switched to microbicides, I fell from view. I went from getting invitations to several international conferences a year to nothing. There was no community, no network."

Cone had made that switch even before AIDS loomed large on the medical landscape. In the early '80s, working in the Hopkins lab of the late Dr. Larry Ewing, a pioneer of male reproductive biology, he was struck by the vast numbers of both unintended pregnancies and sexually transmitted diseases. According to the Alan Guttmacher Institute, a research organization associated with Planned Parenthood, the number of abortions worldwide averages out to one per woman, and the American Social Health Association, a national nonprofit fighting the spread of STDs, estimates that one in four Americans will contract a sexually transmitted disease at some point. (Cone maintains that the rate is actually much higher.)

"These are the epidemics that nobody sees--we suffer them in private," Cone says. "Both of these problems are caused by the same human act. But there's nothing out there for women to protect themselves against both pregnancy and disease."

He resolved to find a compound that would fill that gap. He was joined by Whaley, a Hopkins postdoctoral fellow who was beginning to get interested in the herpes epidemic of the late '80s, as well as the emerging pathogen called HIV. Unlike Moench and Cone, he had decided back in his college years to dedicate his career to reproductive technology.

"It wasn't a eureka moment, but rather a long philosophical discourse about life," says Whaley, who also serves as director of antibody discovery for Epicyte, a San Diego firm that is developing plant-based products to boost the human immune system. Those ruminations led him to an interest "in the interactions between human and environmental health." And a period of

study and research in India gave him a big-picture view of the worldwide impact of sexually transmitted disease.

Whaley and Cone decided that their product would utilize a barrier method, as opposed to a hormone or surgical procedure --"something that the end user could see and touch and understand," Cone says. They also favored an approach that improved on the body's own defense mechanisms. Together, they began looking for ways to clone antibodies that would, as Cone puts it, "stick sperm and germs together" and trap them in vaginal mucus so they could not enter the body. A few years later, they teamed up with Moench, who was studying HIV transmission. (Khanna, then a postdoctoral HIV researcher at Hopkins' Bloomberg School of Public Health, came aboard in February 1997.)

To avoid any potentially thorny conflicts down the road (such as who should get money ReProtect raised or own patents it developed), Cone and Moench each took a leave of absence from Hopkins when ReProtect was formed. (Whaley stayed on, but within the university worked only on antibody science.) For scientists who had spent most of their careers in academia, it was an enormous step--and for Moench, one that became irreversible. A year later, he resigned from Hopkins outright. "I wanted to commit myself fully," he says.

Their initial attempts to secure funding were rebuffed by the government and the pharmaceutical industry, but a *Wall Street Journal* report that noted their antibody research caught the attention of Ultrafem, a small New York-based company that was working on a diaphragmlike cap. Ultrafem was developing the cap to serve as a menstrual collector (like a tampon), but believed it could also be combined with a germ-killing spermicide to create a birth-control and anti-STD device. In 1995, Ultrafem and ReProtect signed a \$2.5 million deal to produce a series of products, including both BufferGel and the vaginal cap.

Two years later, however, UltraFem went bankrupt. Suddenly, Cone, Moench, and Whaley found themselves with no institutional backing--and a greater sense of urgency about developing an actual product.

"We had no support, we had no income. We were out in the cold," Cone says. "We had to do something. So we started thinking, *What could we do that would be faster to develop than antibodies?*"

They knew they wanted something gentle that, like antibodies, strengthened the body's own natural defenses. They decided to develop a compound that would boost the vagina's ability to do what it does naturally--maintain a healthy acidic environment that discourages unwanted microbial intruders. That, in a nutshell, is what BufferGel does.

A healthy vagina is moderately acidic, with a pH level of 4, about the same as a tangerine or a glass of red wine--less caustic than stomach acid (pH 2) or a can of cola (pH 3), but acidic enough to kill off many disease-causing pathogens, and even sperm.

Sperm know this. So they arrive encased in semen (pH 8), perhaps the most alkaline (acid-neutralizing) fluid in the entire body. Within seconds of ejaculation, a shot of semen decreases the acidity level of the entire vagina for hours, rendering it no more potent than a bottle of Evian. Sperm and pathogens get the run of the place.

But if the vagina could maintain its normal acidity during and after sex, the ReProtect team reasoned, a woman would be protected from both pregnancy and disease. They had to find a way to cancel out the neutralizing effect of semen.

The concept of reinforcing vaginal acidity is not new. It has been kicking around since the pioneering sexual-health researchers Masters and Johnson discovered the acid-neutralizing property of semen in the 1960s. "I remember Masters holding his press conference and saying we need to buffer semen," Cone says.

To date, no one has been able to find a way do so. Women in the Middle Ages reportedly used lemon juice, vinegar, or acacia bark (a source of lactic acid) in various birth-control potions, but ReProtect's researchers say the medieval approach might have done more harm than good. "You can't just add acid to the vagina . . . because that makes it more toxic," meaning more susceptible to pathogens, Whaley says.

Toxicity is something the researchers wanted to avoid at all costs, especially in light of what Moench calls the "N-9 disaster"--a reference to recent studies showing that nonoxynol-9, a spermicide once thought to have possible microbicidal tendencies, not only fails to protect women from HIV but might actually make them more likely to get it.

"We believe that is because nonoxynol-9 is toxic," Moench says. "It's a detergent so, like a soap, it scrubs everything in the vagina, but in the process it creates what [Cone] calls 'dishpan vagina.' With frequent use, the surfaces of the vagina are simply made raw and are thus more susceptible to infection." A toxic acid could also harm the vagina's lactobacilli bacteria, which create lactic acid, the main source of the vagina's protective acidity.

What ReProtect needed was a mild acid that would act as a buffer to absorb the alkalinity of semen but leave the vaginal environment unharmed. "We wanted to acidify semen, not acidify the vagina," Cone says. It would have to be packaged in a compound made up of fairly large molecules, to keep it from being broken down and absorbed by the body, and one that is safe enough to use frequently and for long periods of time.

To save time, the researchers began looking at compounds already in use. They found Carbopol, a large-moleculed, mildly acidic gel used in hundreds of consumer products, including lipstick, gelatin capsules, hand lotions, and vaginal lubricants. "We got lucky," Cone says, "because we had a very potent buffer, a terrific lubricant, and something that has already been proven to be safe in humans, including the vagina."

Further research indicates that vaginal acidity is effective, in animals at least, against a broad spectrum of STD pathogens. Over the years, BufferGel has been shown to disable sperm and prevent transmission of human papillomavirus in rabbits; herpes, chlamydia, and HIV in mice; and, to some extent, bacterial vaginosis in humans. It has also been shown to kill sperm in humans.

These promising results helped win over the review panel of NIH's HIV Prevention Trials Network, which selected BufferGel for its combined Phase II and III clinical trials overseas. The panel, made up of researchers and scientists from several different academic and nonprofit

institutions, looks at several issues: a compound's track record in animal and human studies; the availability of materials needed to produce it; its possible effectiveness against various STDs and HIV; and its likely acceptance among potential users. "It's not a popularity contest," says panel chairperson Rosenberg. "These products were chosen through a national product-selection process that looks at all the early preclinical data and Phase I safety data. [ReProtect] had the results."

"The strategy of utilizing the body's own defense mechanisms has appeal," AMD chief Harrison says. "But [ReProtect's founders] also combine a solid academic foundation, rooted in Hopkins, with the aura of being a platform company. Their gestalt was that they were entrepreneurial enough to get the funding."

For all its success relative to the rest of the field, though, ReProtect still finds itself in more or less the same position as other microbicide developers--eager for the world to take notice of its work and scrounging for funds so it can stay afloat.

In many respects, microbicide research is more complicated than most drug research. For one, microbicides are a prevention technology, which is harder to test than a treatment technology. To find out if a compound cures a disease, it needs only be given to sick patients, whose progress is generally fast and easy to track. But to learn whether a compound *prevents* a disease, it must be administered to healthy subjects, who may or may not come into contact with that disease for the duration of the study. A microbicide such as BufferGel has to prove that it significantly reduces the number of new HIV infections in healthy women or in the partners of infected women. Thus, prevention trials require large numbers of participants--tens of thousands of women, in this case--who are tracked over long periods of time.

The HIV rate among U.S. women isn't high enough to fill such a study here; therefore, clinical trials for microbicides must take place in the developing world, where education levels and lack of health-care infrastructure make research more difficult and more costly. Working with poor and largely disenfranchised populations also requires an enormous level of attention to ethical details, such as making sure there is informed consent, counseling participants about and providing them with condoms, and treating any STDs free of charge.

The Alliance for Microbicide Development estimates that it takes almost \$57 million (and almost a decade) to usher just one product from initial lab tests all the way to FDA approval. That's more than the entire NIH budget for microbicide development in fiscal year 2001 (\$35 million), and more than the \$50 million donated by the Bill and Melinda Gates Foundation, by far the world's largest private funder of microbicide research. The cost of bringing one product to market represents fully a quarter of the entire \$230 million pie currently committed to microbicide research by private donors and governments around the world. And that \$57 million doesn't include associated business costs: office and lab space, utilities, and other overhead; patent applications and legal representation; manufacturing and distributing.

The approximately \$33 million ReProtect has raised since its inception--most of it from NIH, as either grants or payment for clinical trials--has been barely enough to cover the company's expenses, and it still isn't enough to bring BufferGel to market, should it pass Phase III tests. "If it hadn't been for [NIH], we would never have gotten this far," Moench says. "We've had tremendous problems, we've worked without pay, and we've gone slower than we would have with more funding."

Notably absent from the list of funders is the pharmaceutical industry. "No large pharmaceutical company has indicated a willingness to get engaged in this field in a significant way," Harrison says. In general, the industry has left the burden of microbicide development to government and academia. (The only large pharmaceutical company microbicide developers say has expressed much interest in their work is Johnson & Johnson. Company spokesperson Marc Monseau would not say how much the firm has given for microbicide research, but he says it has contributed to the Global Microbicide Project, a nonprofit research and development effort funded by the Gates Foundation and run by Eastern Virginia Medical School and the U.S. Agency for International Development. The project currently has three compounds in Phase I trials.)

In terms of development costs, microbicides may actually be a bargain: The Pharmaceutical Research and Manufacturers of America, an industry trade association, estimates the price tag for bringing a prescription drug to market at a whopping \$802 million. But the problem may lie less in front-end expenses than back-end concerns. Privately, microbicide advocates say, drug-company officials have raised concerns to them about the limited profit potential of a virtually unknown substance that is aimed at consumers rather than medical professionals, for which by far the largest market is poor women in developing countries--and which could be undercut down the road if an AIDS vaccine is successfully developed. (A spokesperson for the trade group did not return calls for comment.)

"Pharmaceutical companies are oriented towards treatment products, not consumer products," Moench says. "All they have to do to sell drugs is talk to 10,000 ob/gyns, but to sell microbicides they have to talk to 60,000 women in grocery stores. For them, it's just not cost-effective." "[I]f these products are going to be made in the U.S., it will not be by big pharma companies," Stephen Schondelmeyer, professor of pharmaceutical economics at the University of Minnesota, said last May at a media briefing on the issue organized by the Kaiser Family Foundation, a Menlo Park, Calif.-based health-policy philanthropy. "I'm not saying they couldn't or shouldn't. I think they should for all the right moral, ethical, and public-health reasons. But economically, I think it'll be made by . . . a niche-market company."

With the drug companies largely staying on the sidelines, microbicide advocates instead are focusing on governments and private foundations to pick up the slack. While that means they are playing for much less than they would be with industry support, there are promising signs. NIH increased microbicide funding this year from \$35 million to \$41 million. And Morella's bill, which supporters are angling to incorporate into AIDS legislation being drafted in the U.S. Senate, calls for major increases in government funding for microbicides and the creation of a division within NIH devoted to developing them.

ReProtect, however, isn't waiting around for the feds. While the company will continue to seek NIH grants, Khanna says, government funds generally can't be applied to business overhead, patent applications, or other costs associated with launching a commercial product. And bureaucratic funding procedures can add years to development time. "People are at risk for HIV today," she says, "but the academic pace of research is not conducive to getting a product to market quickly."

The company is trying to raise \$8 million in private funds for the four to five years ReProtect figures it will take to get BufferGel and related products to market. That money will help cover operating expenses and launch human trials to test the microbicide on STDs for which it has thus far only been tested on lab animals, such as herpes and chlamydia. It will also help the company develop another product, a disposable diaphragmlike cup that could be used with BufferGel to add even more protection. (Moench and company theorize that the cervix is the most vulnerable point for STD transmission, but that has not been proven.)

The group is currently in talks with one venture capitalist in the Baltimore area and two in New York. "The Baltimore one is very interested," Khanna says, but she declines to elaborate. She does acknowledge that microbicides can be a tough sell. "It is difficult for the field overall to draw private investment," she says, carefully, her words as neatly arranged as the rows of blue file folders in her tidy office. "There is a fair amount of risk involved when the field is so young."

For investors, the field will mature when researchers can tell them more definitively whether microbicides work and--more importantly, from an investment standpoint--whether women will use them.

The upcoming HIV trial will theoretically help answer the first question, testing the science behind BufferGel and its closest competitor, Pro2000. Interneuron's product is formulated to attack the free-floating HIV-virus molecules themselves, whereas BufferGel will probably be more effective against HIV-infected cells than the actual virus.

"If Pro2000 has the edge, it will probably be because HIV is transmitted as a free-agent virus," Cone says. "I don't think that's the mechanism, but right now, no one knows."

However the trial turns out, ReProtect might still have a marketing ace up its sleeve. Unlike most microbicide developers, it plans to test BufferGel as a contraceptive as well as an HIV/STD preventative. Only one other microbicide--a product called Savvy, made by Philadelphia-based BioSyn Inc.--is following a similar strategy. The others are ignoring sperm and concentrating only on HIV and other STDs.

"You have to get your product approved [by the FDA], but it's easier to get it approved as a contraceptive," says Dr. Kurt Barnhart, an ob/gyn and a contraceptive researcher at the Hospital of the University of Pennsylvania in Philadelphia, one of several sites for BufferGel's contraceptive trials. "Almost everything we use in pharmaceuticals are approved for one thing and used for another. That's just common practice."

Along with being a faster route to federal approval than the lengthy, complicated HIV trials overseas, Moench says focusing on contraception will help BufferGel grab market share among U.S. women, who he says underestimate their risk for STDs. "If we didn't have a U.S. and European market, we know that at some point we'd be going out of business,



"Until recently, microbicide science was not considered real science," says Polly Harrison,

because we couldn't make a business out of just the Third World."

The contraception-first approach has drawn some criticism among microbicide advocates, who worry that birth-control testing would divert already-limited resources from HIV work. But ReProtect maintains that its approach will redound to the benefit of STD prevention. In theory, a passing mark in the contraceptive trial could help BufferGel sail through FDA approval and onto store shelves, which would help keep the company afloat and able to keep working on a BufferGel that more effectively attacks STDs and AIDS. Such relatively quick success could also spur investment in microbicide development, leading to successive generations of better and better microbe-killing products--and a genuine dent in the spread of HIV and other STDs.

"The day may come when you put on your microbicide the way you put on your deodorant," Harrison says. But for that to happen, one of these potentially groundbreaking products has to get through testing and move to the marketplace, one way or another. It's clear that the time for microbicides is now," she says. "We just need to convince the rest of the world not just that they're important, but that they're possible."