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Malaria Forum Keynote Address

Seattle, Wash.

Prepared remarks by Bill and Melinda Gates, co-chairs



Melinda Gates: Thank you for that very warm greeting. Bill and I welcome you here to Seattle—and we thank you for dedicating your lives to fighting malaria. You were working on these issues when no one was watching. The fact that so many more people know and care about malaria today is a testament to your vision, your persistence—and to the faith the world has in your work.

In the history of humanity, it's likely that no disease has ever caused more suffering, more sickness, and more death than malaria. Malaria symptoms were described in Chinese medical texts written nearly 5,000 years ago. The disease caused the decline of city-state populations in Ancient Greece, and untold deaths during World War II.

Even now, a century after Nobel prizes were awarded for discoveries relating to malaria and its transmission, malaria is epidemic in many parts of the world. Malaria deaths worldwide peaked in the 1930s at nearly three and a half million and then began to drop with global efforts to fight the disease, reaching a low of about half a million at the end of the 1960s.

But then anti-malaria efforts dropped off, and the disease has been on the rise ever since. Now there are five hundred million cases of malaria every year and more than one million people die from it, mostly children. That's the equivalent of losing every student in the New York City public school system each year.

We wouldn't let it happen here. We shouldn't let it happen anywhere.

But over the course of the last century, malaria changed from a disease that afflicted a broad range of countries to a disease that affected only poor countries. It changed

from a celebrated cause of our scientists and politicians to a source of suffering that the rich world was willing to accept and the poor world was helpless to prevent.

Today, though, the world is coming back to this cause in large and enthusiastic numbers. UNICEF's report, released just yesterday, describes record levels of spending, distributing bednets, and delivering medicine. Global procurement of artemisinin-based combination therapies grew from 4 million doses in 2004 to 100 million doses in 2006. We also have record funding for research, more coordinated control efforts, and greater scientific tools than we've ever had before.

Bill and I believe that these advances in science and medicine, your promising research, and the rising concern of people around the world represent an historic opportunity not just to treat malaria or to control it—but to chart a long-term course to eradicate it.

We know that the word "eradication" is troubling to many people with deep knowledge of malaria. It's an...audacious goal—to reach a day when no human being has malaria, and no mosquito is carrying it.

This is a long-term goal; it will not come soon. But to aspire to anything less is just far too timid a goal for the age we're in. It's a waste of the world's talent and intelligence, and it's wrong and unfair to the people who are suffering from this disease.

The goal of eradicating malaria has the power to create great expectations, grand efforts, and record funding. When you ask people to donate time and money to save lives, they can be very generous. When you ask them to give time and money to eradicate a disease, their generosity can multiply. Those are the benefits. They are also the risks. If high energy and high expectations don't lead to success—it saps money and morale. People give up. Governments, foundations, and corporations cut their funding, malaria surges back—and gains can be quickly wiped out.

In 1955, the WHO vowed to eliminate malaria from the earth.

The U.S. Congress put record sums of money behind the eradication effort—beginning in 1958. President Eisenhower was behind it, as was George Marshall, and Senator John Kennedy.

Armed with DDT, chloroquine, money, and enthusiasm, the world made dramatic advances against the disease.

In Sri Lanka, malaria cases dropped from 1 million in 1955 to 18 cases in 1963. Not 18,000—eighteen. Other countries showed similar gains. Optimism was so high that the young graduate student Andrew Spielman, who would later become an expert at Harvard on mosquitoes and disease, was told by his mentor at Johns Hopkins that he had chosen the wrong field. His mentor said, "By the time you've finished your thesis, all the insect-borne disease problems will be solved."

But the world was not ready for a long fight. As President Eisenhower said in a special message to Congress in 1957: "I propose that the United States join with other nations and organizations which are already spending over \$50 million a year on anti-malaria activities. In five years, these activities are expected to eradicate this disease."

The fight turned out to be more difficult than expected. Mosquitoes developed resistance to DDT and the parasite developed resistance to chloroquine. Gains were made, but eradication seemed remote—and so enthusiasm faded, funding slowed—and then everything unraveled. Control efforts were cut back, and when the disease began spreading again, populations were especially vulnerable—because people in areas where malaria had been made scarce had lost their immunity. Meanwhile, research into malaria had stopped because the world had been so confident of eradicating it—and so there were no new medicines, insecticides or insights. Over the next ten to fifteen years, the number of malaria cases increased by a factor of six in India and by a factor of nine in China.

Based on this history, some might argue that it's better simply to try to control malaria than to try to eradicate it—since trying to eradicate and then failing could be worse than never trying to eradicate at all.

Why should we embrace the goal of eradicating malaria instead of controlling it? Or reducing it?

The first reason to work to eradicate malaria is an ethical reason—the simple human cost. Every life has equal worth. Sickness and death in Africa are just as awful as sickness and death in America. In Africa and other areas of the developing world, malaria keeps adults from going to work, students from going to school, and children from growing up. Any goal short of eradicating malaria is accepting malaria; it's making peace with malaria; it's rich countries saying: "We don't need to eradicate malaria around the world as long as we've eliminated malaria in our own countries." That's just unacceptable.

If the first reason to eradicate malaria is the human cost, the second reason is the financial cost: If we plan only to control malaria, we will never eradicate it. That means we will keep bearing forever the human costs of malaria, even as we keep paying forever the financial costs of trying to treat and control it. To provide even 80 percent control coverage globally, we will need to spend billions more—each year, every year—than we do today. If, on the other hand, we have a plan to eradicate, we can look toward a time when the human cost of malaria and the financial cost of fighting malaria are both gone for good. In the end, the goal of total eradication is the only way to address the classic problem in disease prevention: how do you ensure that prevention remains a funding priority as you get fewer and fewer cases?

The third reason to go for eradication comes from epidemiology: the ability of the parasite to develop resistance to insecticides and medicines tells us that no set of control strategies can control malaria for very long. Malaria is smart—deadly smart.

Fighting it is like playing chess against a computer that changes the rules as soon as it starts losing. This means that without eradication, we will continuously adapt our strategies to the parasite and the parasite will continuously adapt to us—in a back-and-forth battle that will never end.

When I think of what it would mean to eradicate malaria, it brings a memory to mind from a trip I took some years ago to Mozambique. I was visiting a small rural clinic, where I saw a number of children waiting for treatment. One of them, a little girl, was very sick, and the doctors were sending her on to a district hospital, where she could get better care. A physician from our Global Health team was with us. He took a look at the child and said, sadly, that it was a very advanced stage of malaria.

We ended our visit, and I left the clinic. I never learned if that little girl made it to the district hospital, or ever made it home again. It had taken her a long time to get to a doctor. And yet, I couldn't help thinking: she had a better chance than most—because most of the kids with advanced malaria in Africa never even end up in a rural health clinic, much less a district hospital. They die at home with their families—without ever seeing a doctor or getting any treatment.

That is why we have to eradicate malaria. Because little boys and girls in Africa are going to get bitten by mosquitoes. Even if they have bednets, some children will still get bitten when they're out playing at dusk, and some of them are still going to get malaria. And because we can't fix the whole health care system in all of Africa, they're going to die in their village or die on their way to the doctor.

No child should die from malaria. No child. And the only way to end death from malaria is to end malaria.

It's fair to ask how is such a thing possible? Is such a thing possible?

Here's how we see it. To eradicate malaria, you have to end transmission—and there are multiple points where you can intervene. Reduce the number of infected mosquitoes. Keep mosquitoes from biting people. Keep people who are bitten from getting infected. Keep people who are infected from transmitting malaria back to mosquitoes.

Those are the intervention points. If we could find a tool that was one hundred percent effective, and if we could implement it completely at any one of these points, we would break the cycle of transmission and eradicate the disease.

This is just not possible today with the huge numbers of cases and the current tools. But it is possible—using the tools we have today, and addressing all the steps in a multi-pronged approach—to dramatically drive down the number of cases. Then, if we make the cases few enough, and the map of malaria small enough, we could—*theoretically*—with a new vaccine, or a new medicine, or a new insecticide—identify and target one step in this cycle, totally stop transmission, and end the disease.

What will that take? If we're going to eradicate malaria, we have to persist and succeed in three crucial areas.

We have to take on and solve the complexity of this disease. Conquering malaria is one of the most ambitious medical quests of all time. The resistance to insecticides and drugs means the mosquito and the parasites are moving targets. Winning will take intelligence, agility and speed. Above all, it will take relentless research into vaccines, new medicines, and insecticides by some of the top scientific minds in the world.

We will also have to have tremendous coordination—in every aspect of the effort. This means coordinating research, so different laboratories aren't duplicating the same work and can do research with the benefit of each other's insights. It also means coordinating the work in the field so that we use every tool that we have in the most effective combinations, and no area gets neglected.

Finally, eradicating malaria will take commitment. Not a commitment simply to reduce malaria deaths, or eliminate malaria from certain regions. Those are important milestones—but they are only milestones. A commitment to eradication means a commitment to intensifying the effort as fewer and fewer people get infected. It is counter-intuitive, but absolutely essential.

We understand the risks of declaring a goal of eradication. We understand the mistakes of the past and the obstacles of today. But your work gives us confidence and makes us optimistic. Bill will talk about the promising developments we see—and why we are confident that this generation can succeed where past generations have failed.

Bill?

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Bill Gates: It's a privilege for Melinda and me to host this conference and see so many people who are doing brilliant work on so many different aspects of this disease. If the parasite were as ingenious as they say, it would target this hall. There is no greater threat to the future of malaria than the energy and intelligence of the people here today. Thank you for coming to Seattle.

What is the most repeated failure in all of global health? It could well be the commitment to eradicate malaria. So why would anyone want to follow a long line of failures by becoming the umpteenth person to declare the goal of eradicating malaria?

There's one reason. We should declare the goal of eradicating malaria because we can eradicate malaria. Today, I want to make the case that we have a real chance to build the partnerships, generate the political will, and develop the scientific breakthroughs we need to end this disease.

My optimism starts with the rush of new actors who are bringing fresh ideas and new energy to the fight against malaria. The biggest players today were not in the game five years ago. The Global Fund for AIDS, TB, and Malaria had just been created. President Bush had not yet announced his major initiative against malaria. Neither had the World Bank. In the past five years, companies like Novartis, GlaxoSmithKline, Exxon Mobil, and Sumitomo have become very involved in the fight. All these groups are now doing more than they've ever done, all at the same time, with a renewed commitment.

The infusion of new money is allowing countries with high rates of malaria to look for the first time at comprehensive, national programs where they can coordinate a wide

variety of tools and efforts for maximum effect. No single approach will work alone, but several partially effective approaches can have a huge impact.

Zambia is an inspiring example of a nationally-coordinated effort. Three million long-lasting insecticide-treated bednets are being distributed there this year, and the country is close to reaching its national target of 80 percent of households with at least one net—up from 20 percent two years ago. Any pregnant woman can now get preventive medicines as well as nets for herself and children under 5. And pregnant women at ante-natal clinics in Zambia have reached 62 percent coverage for intermittent preventive therapy—one of the highest levels of coverage in Africa.

Earlier this week, representatives from Zambia and three other countries—Ethiopia, Tanzania, and Mozambique—met together here in Seattle, along with major funders of malaria, to discuss how countries can follow Zambia's model of national scale-up. It is a breakthrough that these countries are considering national programs today; a few short years ago there was only enough funding for district efforts.

This kind of coordination is a huge advance. Medicines, bednets, and insecticides are capable of breaking transmission at the intervention points Melinda talked about. When you use a series of partially effective interventions in combination, they can have a very synergistic effect. For example, the more successful prevention is, the fewer people you need to treat—and the fewer people who are infected, the less chance they can spread malaria to others. So prevention increases the reach of treatment; and treatment is a form of prevention. And they're both much more effective when you coordinate them, which more and more countries are doing today.

I'm also very optimistic because of the extraordinary breadth of research underway—in medicines, vaccines, and other control tools.

The transformation in malaria treatment began with the Chinese discovery of plant-based artemisinin and the subsequent developments of artemisinin combination treatments in Southeast Asia, which make it much harder for the parasite to develop resistance. As you know, artemisinin-based combination therapies, or ACTs, are the most effective antimalarial available today. But they're also expensive, supplies are limited, and they require multiple doses over three days. We need to discover new drugs that are not only effective, but also cheap to make and easy to take.

Fortunately, the Medicines for Malaria Venture has the largest and most diverse portfolio of new drug candidates in the history of malaria. One of their most promising projects is an approach to improving on artemisinin with a completely new synthetic peroxide. In early animal studies, a single dose of the synthetic peroxide drug cured malaria—something we've never seen before. This opens the possibility for a single-dose cure of malaria for people. That by itself could transform our fight against the disease.

But that's not all the researchers are up to. MMV and other partners are also making great progress with new plant technology and metabolic fermentation to provide artemisinin at the quantities and savings we need to meet global demand. If you could add those advances to the ability to make the drug synthetically, you could make as much medicine as you need, and far more cheaply and predictably than we do today. These developments could change the world.

Developments in vaccine research today are just as exciting. Researchers with the PATH Malaria Vaccine Initiative are using several different scientific approaches in pursuit of a vaccine. Some are working on a classic approach — which is to pick a few promising antigens and test them. Others are focusing on sporozoites—creating a weakened form of the parasite that would generate a short-lived infection that would then generate immunity. Yet another group is looking at molecular targets using the latest tools. Never in the history of malaria have so many scientific approaches been used in the pursuit of new vaccines.

In addition to vaccines and medicines, researchers with the Innovative Vector Control Consortium are studying a variety of ways of making mosquitoes less capable of transmitting the parasite. They're also working on new pesticides, to make them more effective in preventing mosquito-borne disease in humans.

I'm also optimistic because we're finding ways to stretch the reach of market forces to get the private sector more involved. GlaxoSmithKline is doing fantastic malaria vaccine research in a way that we hope will become a model for big drug companies. Our foundation pays the cost of the clinical trials; GSK bears the opportunity cost. They're pulling top scientists off of work that could lead to more lucrative discoveries. Since they're not in the business of doing break-even R and D, it's the most you can ask a big company to do and still have any expectation that the CEO will keep his job. It's a terrific model, and I hope it sets a precedent for what private drug companies are willing to do in global health. The benefit to humanity is immense.

In a clear and recent example, the Manhica Health Research Center in Mozambique recently finished a small clinical trial of the world's most advanced malaria vaccine, RTS,S, developed by GlaxoSmithKline Biologicals. This was the first study to test the vaccine in young infants.

The trial results—according to a paper published in *The Lancet* today—serve as a proof of concept that the vaccine is safe, is well tolerated, and significantly reduces malaria infection and clinical malaria in infants 10-18 weeks of age.

The study reports that vaccine efficacy for new infections was 65 percent over a three-and-a-half-month follow-up period, and that it reduced episodes of clinical malaria by 35 percent during a six-month follow-up from the initial vaccination.

These are only interim results, but they are encouraging because they represent a significant step toward fighting malaria infections in an age group most vulnerable to severe illness and death from malaria.

There are more Phase 2 studies to be completed, and if all goes well, a large-scale Phase 3 study should begin in 2008 at ten African trial sites.

Melinda and I would like to recognize the many groups that have worked together on this study: the government and people of Mozambique, the hospital clinic at the University of Barcelona, the Spanish Agency for International Cooperation, the PATH Malaria Vaccine Initiative, and GlaxoSmithKline Biologicals.

I want to offer special recognition to Manhica for running the trials. Running a successful trial requires organizing large numbers of trusting people in an infectious area where you know the baseline. When you consider the difficulty, every drug is a miracle drug, just for making it through trials.

More than a decade ago, Pedro Alonso—with a grant from the Spanish government and the help of researchers from Mozambique funded by the government—set up Manhica in one of the most malaria-infested parts of Mozambique. I've visited the Center, and it has the health research facilities of a university in a poor, rural setting—and the value to public health is priceless.

Pedro runs a census so he really knows who the kids are and what the baseline is. And he's got the relationship with the community. So researchers don't just wait until they have the vaccines they want to test and say: "okay, let's find a place where we can go get the trust of the community, and figure out the baseline of malaria." He's already done that. It's an extraordinary asset in the search for a vaccine.

We are now working with other committed investigators to expand this approach. Fred Binka and INDEPTH are crucial to this effort. One of their projects, the Malaria Clinical Trials Alliance, is replicating the Manhica effort by working to strengthen research sites in preparation for what we hope will be Phase 3 trials next year.

These are just some of the reasons why we believe we should declare the goal of eradicating malaria. There is no doubt that if the world dedicates the time and the money, we can develop the tools in the laboratory and coordinate them in the field in a way that will eradicate malaria. The question is—will the citizens and the governments of the world give us that chance?

Right now—in the U.S. government, at the World Bank, we see the approaching end of the funding cycle. Fighting malaria and eradicating malaria is not a short-term job. It's not a four-year or even eight-year event. That can't work in malaria. If you stop halfway, you don't get half the benefit; you could end up with zero percent of the benefit. The progress counts only if we keep it going.

President Bush—by launching the President's Malaria Initiative—has provided a historic level of funding for malaria. If the world is ultimately going to eradicate malaria, then the record funding that began with this president must not end with this presidency.

Melinda and I say to every U.S. presidential candidate: if you win this office, you will inherit a record commitment to fighting malaria. The world needs you to sustain it and enhance it. Malaria will never be eradicated without the full support of the president of the United States.

Likewise—the World Bank, under Paul Wolfowitz, has committed record funding to fighting malaria. We call on the new president, Robert Zoellick, to sustain it and enhance it.

And the leaders of every developed donor country should generously support the work of the Global Fund, to enhance its role in fighting malaria.

We call on heads of state in countries suffering from malaria to implement a well-coordinated, integrated country-wide program, similar to what's being done in Zambia. And we call on donor countries to step in and help fund these efforts.

We call on major donor agencies to work with affected countries to agree on a global plan for malaria—the concrete steps that will make it possible to scale up programs and, ultimately, eradicate the disease. This includes funding, implementation, and monitoring. Then we need those same groups to join together to execute that plan.

In addition, we call on heads of state and heads of foundations and corporations to ensure that as new tools and technologies are developed over the next several years, we can find ways to make them accessible and affordable to those who need them most. Today, we call on world leaders to fund the Affordable Medicines Facility for malaria, a financing mechanism that will provide artemisinin-based combination therapies at reduced prices for those who need them most. ACTs are an incredibly effective treatment for malaria, but their price puts them beyond the reach of most people living in developing countries. If this treatment remains unavailable, people will resort to cheaper, less effective drugs. They may take a form of the drug that will drastically increase the risk of resistance, reducing the effectiveness of this last remaining malaria treatment before the world has time to develop another. We can't let that happen.

We call on the malaria community to press forward with innovation. We have to assess what sets of tools and situations will be necessary to achieve eradication. Then we have to make the investments in innovation necessary to develop the tools and create the situation that makes eradication possible.

Finally—Melinda and I would like to say to the people here in this hall: the hopes of the world rest on you and your colleagues. If you show the world that we can end this disease, you will unleash the energy and the caring and the commitment we

need to meet that goal. So keep on fighting, and never lose heart when things go wrong. If one approach fails, take up another.

We're not done, and we will not stop working, until malaria is eradicated. Thank you very much.

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