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At the TIME Global Health Summit, held in New York Nov. 1-3, TIME magazine convened leaders in medicine, government, business, public policy and the arts to develop actions and solutions to the world's health crises.

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**Jeffrey Kluger:** –Good afternoon. I'm Jeffrey Kluger. I'm a writer with Time Magazine and at this early stage in the conference, I think we're going to set out on something of a high note here addressing the question of treatments and vaccines and protocols that are in the pipeline or at least are getting ready to be introduced into the pipeline and some of the promise and challenge associated with getting them out to the people who need them the most. We have 3 extraordinary people here today. Dr. Adel Mahmoud at the end, who is the Chief Medical Advisor for Vaccines and Infectious Diseases with Merck and Company. Paul Herrling - head of Corporate Research at Novartis and Chairman of the Board of the newly created Novartis Institute for Tropical Diseases based in Singapore and we're going to hear a lot more about that in a moment and Peter Corr, Senior Vice President of Technology at Pfizer and recently

named head of the Pfizer Human Healthcare, which includes global research, pharmaceuticals, and the company's marketing group and we're going to start with Dr. Herrling - forgive me for not knowing this gentlemen, are we doctor all around? Doctor, doctor, doctor? Okay. I just wanted to make sure. I'll go with your Honor if that works. Dr. Herrling, the Novartis Institute is an unusual group in that it can serve as a model for public/private collaboration around the world. Can you describe a little bit about the organization's structure, what it does, and how you came to dream up this wonderful idea?

**Dr. Paul Herrling:** Yes. Thank you very much. Well, the idea came up for discussion with our senior management that ask research what it was that we could do as an additionally unique contribution for success to medicine problem in the developing worlds and through many discussions, they came to the conclusion that one thing we could do is to try to address with exactly the same methods, science, and technology that we use for cancer, Alzheimer's Disease, and diseases we know here to allocate these

resources for diseases that normally would not be addressed by the pharma industry - not because they do not touch many, many people - actually the diseases we chose - TB and Dengue fever both affect millions of people throughout the world but these people are in poor countries and therefore there is no return on investment and we decided we'd allocate this institute specifically to find new therapies for these patients and as I was saying - applying exactly the same modern technology that was never applied to those diseases to the institute. We put it in Singapore because we have a number of criteria where to put research institutes. It's a long-term investment. It's not something you do quickly and stop again and we needed the place in addition to the criteria closeness to scientific networks, access to talent, quality [Inaudible] stability, respect of IT, all of these things. The reason we put it in Singapore is we needed proximity to those patients because if you want to do the appropriate therapies, you have to really understand - not only the scientific problems or the medical problems the patients had but also the cultural environment and, of course, the only place we could combine the

scientific network infrastructure and the closeness to patients was in Singapore so we set it up as a fully dedicated research institute - roughly 100 people. The institute has 2 missions - the discovery of drugs and education of scientists from the developing world in tropical disease drug discovery sciences. The thing that is unique for a pharma company is that the product coming out of this institute will be made available at cost and no profit to the patients in the poor countries that needed them. So that's in a nutshell how we started. The institute started 2 years ago and is now in Biopolous [ph] close proximity to the Singapore academic centers and we have started to build a pipeline to recruit students and we started a series of meeting on [Inaudible] and on TB and we started a number of collaborations - maybe I should mention - the institute will focus on discovery and for the development, we would partner. So we had concrete discussion with the global alliance for TB that is building now a large expertise in clinical studies in TB. In order to band together with them, put our drugs in TB into development in a partnership. That's just an introduction to this institute.

**Jeffrey Kluger:** Terrific. Thank you. Dr. Corr, you've echoed some of the ideas that led to the creation of the Novartis Institute even though you're obviously working with 2 different companies and you've mentioned the collaboration as one of the biggest obstacles to getting affordable drugs out there - collaborations with governments, with NGOs, with locals, and more - can you tell us something about those challenges and also something about what you've described, in some of our conversations, as the 3 A's.

**Dr. Peter B. Corr:** Yeah. Yeah. When I think about the problems that we all face in global health, I really think about it as 3 A's and that's availability, accessibility, and affordability. When I think about availability, it's what can we do across the industry and, particularly, in public/private partnerships. Everything we can do together to actually make new drugs available. That means discovering and developing new drugs. So availability, when I think about it, is what are all the incentives that we can put in place - whether

it's in academic institutions in private companies and particularly with some really great public/private partnerships like the GATB and the Medicines for Malaria Venture. When I think about accessibility, I think what is it that we can do in the infrastructure to deliver those medicines. If you look at the essential medicine lists from the WHO, they're readily available but they're not getting there. Millions of babies are dying just of diarrhea - it's preventable, measles - things that we can prevent. We've got to have the medical infrastructure to both diagnosis, monitor, treat, and change the drugs if the patient's not tolerating them or if it's not doing what we expect it to do. That's accessibility and I'll come back to accessibility in a moment. The other one is affordability. The fact is in many countries in Africa, where the total healthcare spent per individual is \$10 per year - whether the drug is 5 cents or 10 cents, if it's a chronic drug, it can't be afforded. We looked and said in the 50 least developed countries that we would, in fact, give our drugs away for life threatening disease. Now, we've been criticized for that saying it's not

sustainable. I don't know what's sustainable. As long as we're a successful company, we can continue to do that and I think any price is, perhaps, too high a price. We need to have tiered pricing - not only within countries and that includes the U.S., by the way, people who can't afford it - we need to have those drugs at a very low price or free and we have programs to do that. What we have to prevent is the stealing of drugs from countries where they are given free and sold off in other countries. Lets call a spade a spade - that happens so we have to track that. That's the affordability issue. If I think about infrastructure and accessibility, Paul talked about a research institute, which I really commend Novartis for doing this, in Singapore - we, just a year ago, opened up an infectious disease institute in Campala [ph], Uganda and the idea here was to work together with the San Francisco AIDS Foundation with TASO [ph] and with the Infectious Disease Association of America and what we did was we started a clinic there in the Carey [ph] University and they were very helpful and you know what made this work? The president of Uganda was committed to it and the head medical director for

Uganda was also very much ahead of it. If you look at the statistics, no country's doing better with AIDS than Uganda. So it's the commitment at the highest levels of the government. We then went ahead and started the program in which we call "train the trainers" and we treat about 200 to 300 patients a day roughly at the hospital with AIDS. This is a clinic that we built - Pfizer built. We took care of the expenses and the training is about 2 to 300—we have trained about 600 healthcare workers, physicians and they're required to go back to their home country with the materials and train 10 more. So you've got 600, and we're checking on it hoping that they're training 6,000 that would be trained in the treatment of AIDS and other infectious diseases. So those are examples—we couldn't have done that alone. We do it together. Obviously, we have to provide the money, the infrastructure. We learned a lot on that one—more than happy to share our experience but it's working out very well. Thank you, Dr. Mahmoud. However, we get drugs out there. The biggest question is, of course, what those drugs will be. Now, you have described yourself as a vaccine guy and you pointed out that until the mid-

1980s, we were making our vaccines the same way we've been making them since the 1950s or actually for several centuries, which is either to kill the virus with a substance like Cormalin [ph] or attenuate the virus by passaging through an organism. Before we get into the specifics of vaccines, how has that manufacturing process changing and what are we learning about different and better and leaner ways to make our vaccines?

**Dr. Adel A. F. Mahmoud:** Thank you. I think the issue, as you said in the beginning—and the beginning here is approximately 100 years—the idea of vaccination was, although it was very old from the days of the Chinese actually who discovered what virulation is, which is the vaccination method against small pox. The vaccination came in the latter part of the previous century in England and the whole idea of the vaccination was discovered for small pox approximately 100-120 years ago and we really maintained using the organisms as they come—simply, try to culture them or try to attenuate them and maybe kill those organisms and you kill organisms as vaccines. This would have—the easy ones

had been produced and the easy ones are what we use everywhere today. Until the mid-80s, that technology undergone a substantive change when recombinant technology was introduced to produce the first recombinant to actually [inaudible] – the first recombinant vaccine, and that was the Hepatitis B– was produced in this country and in Europe almost simultaneously and now making the proteins, which are repetitive in nature that we use as a vaccine. Now what that means is that you really changed the methodology of manufacturing from being dependent on an organism growing. For example, as you hear from the flu story, you have to put the virus in eggs– so, you are trying to come up with a biological laboratory. Now, you’re coming down to a recombinant technology where you can make substantive amounts of the molecules that is protected and use it for the immunization. In many ways today, this technology is available almost everywhere in the country Merck, in the early 1990s, gave to plans to make the recombinant Hepatitis B vaccine to China, and the major organization program in China today is made through 2 plans that were given by Merck to China. There is Hepatitis B today maybe easier in

Indonesia, in Israel, in Brazil, plus obviously other places in Europe and this country. And that is, in a serious way, not only the discovery of new technology but also transferring the technology to those who really need it most and finally, the price of Hepatitis B today is really becoming a very, very affordable vaccine in many, many ways. Now, that's not the end and over the last 15 years, another technology came into the production of vaccines, which should take the [Inaudible] bacterial pathogens and [Inaudible] them to a backburner of a protein substance, which will then make the immune response of humans able to develop a protective immune response against this organism. That is really what we can contribute in a serious way, which is to provide scientific insights that will make the availability of products for human use an affordable but more importantly, order of magnitude higher in technology and in capabilities. So, those two developments happened between the 80s and the 90s, and we are currently at the verge of another wave of new technology that will come into vaccines. Now, vaccines—not only because I work on vaccines—but vaccines actually—when CDC in the 1990s period,

just as the century was turning, they requested that all the public health authorities in this country and globally think of what public health measures really made difference in human life over the last 100 years—Vaccines were voted number one because the reason we don't have small pox, the reason we don't have polio and many parts of the world, the reasons that we don't have measles, mumps, rubella and chicken pox in this country and many parts of the world are vaccines and they have contributed to public health definitely a lot more than many other—maybe sanitation and pure water was on equal footing—they really contributed—the reason 77 years of lifespan in this country compared to 50 in Sub-Saharan Africa is, in many ways, vaccination and the control of infectious diseases.

**Jeffrey Kluger:** All right. Thank you. Dr. Herrling. The NITD is focusing heavily on Dengue fever and tuberculosis—why those two diseases in particular and what approaches look the most promising?

**Dr. Paul Herrling:** When we selected the diseases, we wanted to make sure—one that our disease would have

a huge impact in the developing world—affect a lot of patients. The medical need was an issue and there is this doubt [ph] that these two diseases have a huge medical need. For instance, Dengue had no treatment [Inaudible] treatment or vaccine whatsoever. And TB, as you know, is a very problematic treatment in the sense we need to treat for very long, resistances are coming up. The bugs can hide and be very difficult to reach, and it was clear at the time that we made the decision that there was not enough people working on TB and certainly not allocated enough of these technologies in modern [ph] sciences I was talking about. For instance, one thing to—you know that the *Journal of TB* has been published four years ago and very quickly, we could find a target in microbacterial tuberculosis that we were working on the commercial part of the organization and found out that it occurs only—not only in those but also in TB bacteria and could, within weeks, use all the science and work and compounds that we had done on the commercial side applied to TB and thereby speed up the process very much. So, the other aspect that we looked at was we didn't want to be redundant so

we didn't do malaria because we already have our new drug coordinator developed with the Chinese and that seemed to work very well. And at least for some amount of time, malaria could be treated with the new drug though it's not the case with TB. AIDS, obviously, was also—continues to be a huge problem but many other people are actually addressing it. So in addition to the medical needs, we wanted to bring our resources to bear on something that really undersourced and neglected. These were some of the most important aspects. Where we are, where we started two years ago, you know that the whole drug discovery cycle is 15 years. We have a number of targets that we're exploring—we're going to lose across levels on the way and most advanced projects, as the one in TB, because as I said, there was some previous work done. We have two—one that is also in collaboration with the global so TB is exploring a compound that is now in phase I with a global line and we are doing backups for these, trying to optimize them and prove them and the second one is the one I was talking about that is reaching now the entry to the pipeline based on this new target, which we call the peptide [Inaudible], which I don't

have time to discuss probably [Inaudible] but it's certainly a new target that was never seen or used so far and would at least be effective if we have antibiotics against that target first against resistant strains. We don't know if it will address the issue that we always want to address is to shorten the time to treatment but we'll have to find out but one other aspect that we are applying is we choose targets that, based again on bioinformatics [ph] and genetics, targets that do not only occur in one pathogenic organism but in several and this—one of the reasons we chose this PDF target is you see it in the leprosy bacterium—another disease that is very unknown—totally neglected, horrible, which is called [Inaudible] occurring in Western Africa and Australia, China, which has no treatment except surgery. It's a disease that eats away your skin. It also contains this target so that we hope one of the ways we want to make the resources that we allocate count is by selecting such targets occurring in more than one pathogen so we work on TB but as soon as we have someone working on this target, we will give these compounds to other people working on the other pathogens and see if they can get starting point

from that and it seems to be the case. In Dengue, we start further back because it was nothing. It's a virus, targets are more difficult but the projects we have is the entry into the host, so the envelope proteins when these attach, then those targets that work in other viruses - polymerases, [Inaudible], and proteases and for instance, one thing I didn't mention is the fact that the Novartis Institute for tropical disease right in Singapore is part of the Novartis research family. We have a lot of the work [Inaudible] ongoing in our other labs throughout them - have excess of 3,000 other countries and one thing that we do so we use the expertise in proteases, for instance, that occurs in Basel and very important—this institute has full access to the entire Novartis compound libraries, which is something that is usually very difficult to access for neglected diseases from outside. So that's in Dengue, we're very early looking at target and leads and TB—we expect to give you numbers and of course, I'm going to be wrong but the goal is again to which our people work, is to have the first two drugs and they would possibly be on the TB field readily for clinical use in 2008 and then one out of the entire

field ready for the patient in 2012 just to give you a few - drug discovery is a long-term project.

**Jeffrey Kluger:** Thank you. Dr. Corr, AIDS seems to be a big part of Pfizer's focus and in our conversations, you stressed a new medication Pfizer is working on based on CCR5 inhibition. Can you explain a little bit about how that drug works and where you stand in its development?

**Dr. Peter B. Corr:** Yeah. This is a target that actually many companies are working on. It's a new approach. It's to prevent entry of the HIV virus into the host cell for replication and it has a lot of implications in terms of even prevention but we're looking at it for treatment at present. We're in the last stage of clinical trials in Phase III of worldwide trial and it's interesting because there were two other companies that were fairly close, and it shows you the risks and those two appeared to have fallen and so you never know which one's going to make it because it isn't that they're not smart and we are. There's a lot of luck involved here in terms of which compound it is and we all know that

working in this business so this is a compound that blocks the CCR5 receptor. We should have, hopefully, the final results on Phase III, at least I'll cross my fingers on Phase III but the Phase II data looked very good. This would be initially used with combination therapy but hopefully as monotherapy as we go forward and it appears to be effective irrespective of the resistant strain. Going forward with the HIV, there happens to be about 127 drugs in development for HIV so there's a huge amount going on. Now that includes co-infections and other diseases but around HIV-127 compounds so across the whole industry in public and private partnerships. We're very grateful that this compound will be a new revolution, hopefully, and then getting it to those patients who need it would be the key and we're now looking at how we go about doing that, anticipating that it will be positive results in phase III. We have other programs—just to give you an example behind that if we go to three or four backups—different stages just in case one of them falls for the CCR 5. There might be a potential problem here. There is another receptor called the CXCR4 that isn't used very often for entry of HIV but we don't

know what's going to happen over time. So we're also looking at how you would block that receptor because we need to do that for that particular hormone.

**Jeffrey Kluger:** All right. Just one follow up question. Perhaps I missed this - the Phase III trials—do you have a target date or anticipated results projection?

**Dr. Peter B. Corr:** No. We actually had planned to see this in '05. Because there were safety concerns with the other CCR5s, the immediate reaction of the regulatory agency was called our data safety monitoring groups, which look at the data unblinded. We can't see that. Everybody looked and said there was no issue and we could go forward. So we had a slight delay but no safety issues at least from their perspective so we moved forward.

**Jeffrey Kluger:** Great. Thank you. Dr. Mahmoud, you've been working with AIDS vaccines as well and in fact, as you mentioned there's a very exciting piece in the Washington Post today about the meaningful progress Merck is making in a topical HIV

gel. You were talking about some of the strategies you're using including clone segments of the virus attached to an adenovirus delivering potentiation vehicle. Can you unpack all that for us?

**Dr. Adel A. F. Mahmoud:** Sure. We have had a program on HIV that started in 1985 with the discovery of the Acquired Immune Deficiency Syndrome and the first product was a protease inhibitor. Merck was the first company that actually was involved in the crystal structure of the protease and we published it to the scientific community immediately when it was resolved because it was an important—this is probably the most important global challenge we all had so we maintained the therapeutic approach for research on HIV through the years with a protease inhibitor and currently, the effort is on an integrase [ph], which is the third enzyme one that really is involved in the life cycle of the virus inside the cell. One of the issues you just referred to actually our CCR5 compound, which Peter was talking about. We gave it royalty free to the National Partnership on Microbicides because there is a paper that will be published in Nature in a

couple of days actually—this week's *Nature* that showed that compound and another compound from Bristol-Myers Squibb—both of them—if delivered—this is Macabe [ph] monkeys experiment—it delivers into the vagina—they prevent infection in approximately 75, 80 percent of the monkeys so it is a very, very tremendous movement. Now, since microbicides is not our main thrust of working on anti-HIV drugs, it was a very appropriate move to license it free of any charges and to commit ourselves that back up compounds that will come from that direction will be available for IPM for the work on microbicides. Microbicides, particularly in Sub-Saharan Africa and in the countries where there is a lot of HIV transmission, will be a very attractive method. It is complementary. There is no one method that will control HIV. Hopefully, the other program that we're working on, which is the HIV vaccine and our investigational vaccine is in proof of concept phase today. We started that late last year and it is an adenovirus delivered 3 pieces of the genome of the virus. For those of us who are familiar with the lingo here, it's the GAGNET [ph] and [Inaudible] genes and the idea here is this construct with

adenovirus delivery raises the host cell mediated immunity in a very significant way and in studies in monkeys, it has been shown that it does protect animals from the disease. It does not prevent the acquisition of the infection. It basically stops the manifestation of disease in these monkeys.

Hopefully, with the studies that we have today as a proof of concept, we will see an impact either on the infection itself or on the set point of the virus in the host or on the manifestation of disease later on. It is a very, very challenging set of studies. I've been in it for 22 years and it is clearly is going to go on for some time, until one day, there will be an HIV vaccine because really, it is the most practical solution for the problem if we can discover it.

**Jeffrey Kluger:** Dr. Herrling, I'm going to go back a little bit to some questions of logistics and facilitating the production of drugs. Some numbers I've read and tell me if I'm misquoting you or the newspapers in which I've read this have misquoted you but the numbers I've read are that a Dengue fever drug alone could cost Novartis between \$500

million and a billion dollars to develop and you have said, at least according to one piece I read that while the NITD will certainly share its research results early, it couldn't be totally open with all of its findings. Novartis is obviously fighting on the side of the angels with the organization you've set up. On the other hand, you still are a profit making company. How do you balance, first of all, your need to recoup some of that potential billion dollars in R&D and second of all, the idea of wanting to roll drugs out as fast as possible and yet needing to maintain some sort of corporate secrecy or confidentiality.

**Dr. Paul Herrling:** That is a very good question and, of course, one we battle a lot with and yet - first you mentioned the cost of 500 to a billion dollars per drug, that is the number that some people have published, which is the average cost per drug that reaches the market but includes all the drugs that failed. Now, obviously we are looking at one particular drug for one disease and that one itself is, of course, much less and, of course, we don't know what the actual costs will be but to come

back to your question - if we're lucky in anti-infective diseases, it may be less expensive, it may be more. We don't know. It's an experiment. I will keep calling this an experiment but I think this balancing act that we do about how much to share or where we do not want to share so I'll explain to you the principle of this. Ideally - and we do share much earlier - I will never talk about the target. I talk to you here in public PDF, at least we're a commercial project alone. Because we want as fast as possible to gain - one of the way the NITD works is by extensive partnerships with academia, for instance, we're part of the Gates Grant [ph] Challenge to find new targets for TB and we share everything we do there with our partners. Now the reason why we don't share quite everything is the following is that of the principle I discussed with you before that our targets are targets that we choose that are [Inaudible] in the sense that are important for more than pathogen and biology in being what it is - let me give you Dengue example just because it illustrates very nice

Dengue is part of the [Inaudible] virus family.

This contains Dengue, West Nile, Japanese

Encephalitis, Tick Born Encephalitis, and also in that family is Hepatitis C. Hepatitis C is the Holy Grail blockbuster of the commercial antiviral research community. The way we set it up is that we work on Dengue and we, through that channel of NITD, make whatever we find on Dengue available, as I said, to the community, but the way it is designed and if any of the drugs we do at NITD that are being picked up by the other people working on, for instance, Hep C on the commercial side, if they turn out to find something useful there, they will sell it and the way it's designed is some of the returns of those sales will come back to refinance NITD. That is first why we patent and before we are not sure that the drug will be only Dengue, if we are sure that that's the case then we can be completely open but before we have explored its potential application with our commercial colleague, obviously we treat it there as a commercial drug so that is the balancing act we do, which contains partly the long - we'd really like to sustain this there for long-term and that's why we build some mechanism in there - at least potentially, could refinance the institute long-

term. It's not a black and white answer. It's a balanced one and that's why. We're much more open than we could be in fully but there are also limits because of this cross-over into the 2 fields. I hope that's clear.

**Jeffrey Kluger:** Right. Terrific. It does. It does. It balances things. Dr. Corr, you've described the big 3 diseases that are either without treatment or without effective and affordable treatment as TB, AIDS, and Malaria. Could you tell us a bit how you're moving in ahead in treating TB and malaria and specifically something about your new combination therapy for malaria.

**Dr. Peter B. Corr:** Yeah. It's the WHO's big 3. What I would say, which is of course HIV, Malaria, and TB and I mentioned about HIV. We've shifted our efforts away from non-nucleoside [Inaudible] transcriptase inhibitors and shifted much more of our effort to very new targets including CCR5 and I mentioned CXCR4. So earlier targets and there were earlier ones back from discovery and, in fact, 4 that we're going after right now but those are

years off. HIV/AIDS - I think there's a lot of effort going on in AIDS broadly - across the industry - partnerships, a lot of research and I hope that we do get to a vaccine. I agree that is the ultimate goal as Adel said. When we look at malaria, there's about 30 drugs in various stages of development right now. The last look was in May that I - it's 30. In TB, there's about 22 but if you take into account attrition that's going to occur in the pipeline, those are the numbers in development not discovery, a lot are going to fall off and that's just part of the business we're in unfortunately. A lot of money and a lot of effort goes into get those few that come out the other end as effective therapeutics. In the case of malaria, we're just finishing phase III trials, the last phase for malaria resistant [Inaudible], for treatment - it's a 3-day course and we should know the results, hopefully, in late 05, early 06. We had very good phase II data, 98% efficacy against [Inaudible] - over 98% in India in the phase II trials. We'll see what the phase III is. In that particular case, one of the combinations - it's a combination drug - one of the combinations is

Zithromax, which is a drug that has brought very good returns to Pfizer. To Paul's point, we can afford to do that and to take on to doing those trials because of that. As long as we're a prosperous company, we'll be able to do that. We have been working - we've decided to put the bill for all of the clinical trials in the development of this and those trials are ongoing in Africa, South America, and Southeast Asia and India. Now, the issue will be there's 300 billion people infected, conservatively - now what do you do and so we have to work through exactly what it is we're going to do with that combination therapy. We actually found this by working together with the army and we did some in vitro experiments and it actually showed a real synergy between Chloroquin [ph] and Zithromax. It was astonishing. Either one alone was 30% effective and the combination is 98. We don't really understand why. Of course Chloroquin [ph] has been around for years - huge resistant problems and still nobody knows really the mechanism of chloroquin [ph]. We know that it interkelates [ph] the DNA and plasmodium but we don't know much more than that.

**Jeffrey Kluger:** One final question for Dr. Mahmoud and then we can open the floor up. A lot of people believe that all you have to do to get big pharma interested in the problem of getting drugs to the Third World or the developing world is create viable markets for them there and you've been quoted as saying the idea that if you dangle money in front of industry, they will come running is not true. The problem is more one of a lack of delivery systems. Can you elaborate on that a little bit?

**Dr. Adel A. F. Mahmoud:** Well, the problem is a lot more than delivery systems, obviously as you just heard from my two colleagues. The first problem is, particularly for the big issues is science. There is no question the reason there is no vaccine for HIV, there is no reasonably good vaccine for TB, and there is no vaccine for malaria is the scientific inability of us all to discover new targets in these 3 organisms to go after and develop a vaccine. People who work with these organisms daily don't like this discussion in a frank way because it says the effort is not getting

us somewhere but we have been talking about the malaria vaccine for the last 20/30 years and we don't yet have a malaria vaccine because the target is a very complex organism. It is really important that all of us appreciate that first, it has to be knowledge - scientific discovery that will lead us to find out targets or opportunities to deal with these organisms and as I was saying to you on the phone the other day, it is very important to realize the power of science today is a lot stronger and a lot more effective than it ever has been. One of the investigations of vaccines that we're working on currently for human papilloma virus infection that causes cervical cancer all over the world - that virus - this is a cancer that is due to a virus infection. That virus infection, to this date, has not been cultured in [Inaudible] free in vitro cultures, yet we have a vaccine that phase III is being finished - 2 companies working on that vaccine that is very, very effective. So what I'm saying is scientific discovery - the virus was discovered - the virus was sequenced in the mid 1990s, the protected antigens were cloned by the late 90s. They were put into delivery systems for

human use and by 2005, we have results that this vaccine is effective 100% in preventing the pathological changes in the uterus - in the cervix of the uterus that is a pre-cancerous condition. This is the might of science. Now, similar situations need to be applied obviously, to HIV, malaria, and TB. There is no escape. That's number one. It is not just simply to say if there is a market, we will just go and spend all the money of Merck to find a target in that market. It has to be scientifically feasible. We don't start a project because there is just somebody out there who will just start a project because - A - it's a global problem. It's a significant health challenge for all of us irrespective of borders and 2, that we scientific feasibility to say we can come up with a difference. We can make a difference here if we put our scientific capabilities behind the problem, we will discover something. Now, of course, the challenge finally will be how to deliver and we are struggling, today, to deliver plenty of vaccines that has been with us for 50 years. We are struggling today to deliver measles vaccine that has been with us for 30 years. I'm not saying that

to be difficult but I'm just saying that as the total global community has to articulate some ideas and some challenges how to deliver the products of science and, for example, GAVI, the Global Alliance of Vaccination and Immunization - when it focused in the last 5 years on delivering hepatitis B vaccine. Today, 2/3 of the birth cohort, globally, this means 90 million out of 130 million kids born every year in this world are immunized against hepatitis B. It is a tremendous achievement. Why? Because all of us - the Gates Foundation, the companies, the international organizations, the countries that are involved gathered together to say we're going to go after this problem so the delivery is equally challenging. There's no question but we have to find, first, some of the solutions because the problems are increasingly more complicated, more significant, and more challenging for all of us. Thank you.

**Jeffrey Kluger:** And we've got about 12 or 13 minutes. I just wanted to open the floor up to anyone who has any questions for any of our guests.

**Justin Golas:** Justin Golas [ph] with the Washington Post Newspaper. Dr. Corr, the gentleman to your left there, his company has just agreed to license an HIV interinhibitor at no charge to the global - to the partnership it's working on that product - working on microbicide. BMS is ready to do the same thing, what about Pfizer?

**Dr. Peter B. Corr:** Okay. We have a CCR5 that's at the last stage of development and we have been actively discussing, with the Gates Foundation, about how we would go forward with a microbicide - I have some concerns about whether in Africa - whether a local versus an oral delivery would be more effective primarily because - not scientifically but in terms of the countries and they don't use condoms to the degree that should be used so would it be better to simply test it based on an oral formulation that should produce the same result. There's no reason to believe it wouldn't. We're actually evaluating that, in fact, we have an internal meeting exactly dealing with microbicides in November in London for exactly that reason but what we do not want to do - there's also regulatory

issues involved here. There are also legal issues. I'm not saying we shouldn't do it but the legal issues are what happens in the 20% of patients who are not protected...

[END RECORDING - TAPE 1]

[START RECORDING - TAPE 2]

**Dr. Peter B. Corr:** ...Things to think about. Does it encourage sex with people who may, in fact, be infected already. Are there legal liabilities associated with the fact that a patient may be infected but actually wasn't compliant with the drug in the first place. Now, we've dealt with all of these with oral contraceptives but nonetheless, having a baby is a different thing than having a death sentence. I think that these are some of the things that ought to be out here. It's not as simple as wiping it on and with a vaginal delivery or with a suppository to solve the problem. I'm not saying that this isn't an important thing to do. I think it could really dramatically alter the spread of AIDS but we want to look very carefully as to whether oral might be a better approach in some areas of the world.

**David Durack:** Thank you. David Durack [ph] from Bacon [ph] Dickinson. Dr. Corr made the point, earlier, that it was not simply a matter of drugs but of screening, diagnosis, therapy and monitoring of the therapy, which is, I think, a sentiment that most of us would very heartily agree with but this really refers to infrastructure on a massive scale and laboratories, people, reagents, quality control, and then follow up so then I wonder if the panel might comment and I think the cost of the - countrywide - not just demonstration projects - but countrywide could be something that would dwarf even the cost of Novartis' next big drug. I just wonder if the panel could comment on how we approach this need for very expensive infrastructure.

**Male Speaker:** Yes. I'll just start off very briefly. This is a huge problem and I think it's going to be utilizing government money appropriately, private foundation money appropriately, and most importantly, the leaders of the countries in the developing world. We went

ahead with a Tricoma initiative 5 years ago and we developed a program in Morocco primarily. We're now in 11 countries to wipe out Tricoma by 2020 worldwide. It's the leading cause of blindness in the developing world and what we learned in that process is working together with Edna McDonnell [ph] Foundation that you've got to have all the pieces and what we came up with was a safe initiative, which was surgeries. So we got ophthalmologists to come in - 75,000 surgeries have been done now across those 11 countries. Antibiotic use - you have to have it there - we've donated that and then face washing - training people how to face wash and also to clean up the water in those areas. We almost have eliminated Tricoma in Morocco by this program. Now, we're going to 11 other countries and we want to expand the program even further. There is a way through this and it doesn't mean a monstrous bureaucracy. It means you start off in certain countries - in this case, Morocco and in a matter of 5 years, we made a huge impact together so - and that's because the government wanted to do it. I mentioned about Uganda before. I think even involving the United Nations, UNICEF,

other groups - I think we can do this. I think someone may want to comment about the millennium goals but some of how that's being done is village by village and I see Alanna Rubenstein here, who's helping with that program and that's a great example of how you do this. I think companies in every sector in the developed world ought to be giving to these things.

**Male Speaker:** Maybe [Inaudible] said before also that science has to make a contribution here. If you imagine, in tuberculosis today the diagnostic method we use is 100 years old and it's very slow and by the time you know somebody's infected with a particular strain, it takes weeks and by that time, you have lost your patients. They have gone back to their villages and so on and here again and one of the reasons why we allocated research capacities to fill that gap and find all the better ways of diagnostic and they do not have modern ways of diagnostic - does not necessarily have to be expensive. The aim is to make them very cheap and a similar case can be made for Dengue where there is no good diagnostic. I think these things, as Peter

was saying, and the advances of science have to go hand-in-hand and without that, it would even be difficult to find out if a new TB drug is actually acting faster or not with some of the methods we have today. We certainly agree with you on some of the solution proposals is what we can come up with.

**Male Speaker:** -Just a quick comment. I think the challenge is really to work with the National and Global Leadership. To convince the National and Global Leadership of these countries that health is as important as many of the other pursuits that most of these countries try to accomplish and as long as health is - the minister of health in most developing countries is the lowest ranking in the cabinet. The minister of the army and the minister of finance run the business. It is about time that all of us raise our voice that health and development is the message and war and wasting the effort on other pursuits is far less impressive. The countries that got their act together - these are [Inaudible] to Uganda - look at what happened in Uganda with HIV prevalence - it decreased - not because they had the most sophisticated methodology

for diagnosis and control. They actually put together a decent control program based on education, condoms, and working with their own people under the national leadership of their President. It really is an important message. Global health is not going to be accomplished by pooling money everywhere in the world. Those solutions have to come from within. Latin America control polio and control measles—not because Latin America is the richest continent in the world because they've got their act together.

**Male Speaker:** Okay. We have time for maybe one more—maybe two.

**Male Speaker:** Thank you very much. Dr. Sam [Inaudible], the Director of Health Services from Uganda. First of all, I want to publicly thank Pfizer for the wonderful work they are doing in Uganda and I want to encourage many more companies to go where the problem is. They have gone there and I'm glad that they have told you the amount of work they are doing. I wish that they could one day just show you what is going on in that Institute.

It is wonderful. Thank you. Thank you very much. Now, [Inaudible] to get some other diseases—so-called neglected diseases. There are very many. I want to thank again Novartis for coming in with Dengue but there are many other disabling diseases not for [Inaudible] in Sub-Saharan Africa that are not being attended to—diseases like sleeping sickness, it's terrible, which was eliminated a long time ago. [Inaudible] has been alluded to so we want to see many more companies tackling those diseases that have [Inaudible] forgotten [Inaudible] that we have never heard about but they are still there. Lastly to malaria—malaria is still our biggest problem. Mahmoud just said you haven't been able to get the target but we in Sub-Saharan Africa believe that it's because you have eliminated malaria in your developed world that you have decided forget all about it. We think if you put in a little more, you could make a dent. We are looking for this vaccine. Malaria is causing gross underdevelopment in the African region and unless something is done, unless Novartis—your drug [Inaudible] gets lower than what it is at the moment, we won't succeed. [Inaudible] you studied



home-based management of fever to make sure that we get to the disease before it causes a problem to children and women. But if you are to use the new SCT combinations, we cannot succeed, it's not sustainable so we need to see you reduce the price of your products. Thank you very much.

**Male Speaker:** Thank you and I think that brings us to the end and my understanding is that we have about a half an hour of breathing room but there's refreshments outside and at 500 in the Rose Theater will be the opening remarks by Jim Kelly and Eileen Naughton and a few other folks. Thank you so much for coming in. Many thanks to our panelists. Thank you very much.

[END RECORDING]