

**XVI International AIDS Conference: August 13-18, 2006**  
**A World Without AIDS:**  
**The Long Road to Effective HIV Vaccines**  
**Toronto, Canada**  
**August 15, 2006**

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**FRANK FARMER:** Well, good afternoon, ladies and gentlemen. My name is Frank Farmer. I'm one of the organizers of this session - "A World Without HIV: The Long Road to HIV Vaccines" - something that we're all dreaming of. I think this is a very exciting session. I'd like to introduce, first of all, the two co-chairs for the session - Dr. Peggy Mitchell from the National Institutes of Health and - Peggy Johnston, sorry - and Warren Mitchell from the AIDS Advocacy Coalition. They'll be introducing the speakers as they come up to the podium.

It's also our great pleasure for us to have with us this afternoon the minister of health for Canada, the Honorable Tony Clement. Tony Clement was elected to the House of Commons in 2006 and became the Minister of Health. He's also the minister for Federal Economic Development Initiatives in Northern Ontario and the chair of the Social Affairs Committee of Canada. He represents the writing of [INAUDIBLE], which is Canada's vacation land, I'm told.

Prior to this, Mr. Clement was a member of Ontario's [INAUDIBLE] legislature from 1995 to 2003 and is - he had several cabinet appointments, his last one being as minister of health, where he oversaw primary health care reform, created a successful tele-health system, oversaw the expansion of the hospital system, and providing a leadership for Ontario and indeed for Canada during our SARS crisis in 2003, also was a

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staunch advocate for AIDS issues. The minister is going to be with us so I think for most of the session and I look forward to his participation and he will want to make a few remarks. Minister Clement?

[APPLAUSE]

**TONY CLEMENT:** Frank, thank you very much and thank you to all of you for being here this afternoon and welcome to this special session on HIV vaccine development. It's certainly an honor to start things off this afternoon and to do so in such excellent company. We've got some distinguished presenters this afternoon and they are merely representative of an accomplished audience so we're all in this together.

As you know, prevention strategies have helped to slow the spread of HIV in parts of the world and effective treatments including antiretroviral drugs such as Prezista, which has been recently approved by Health Canada here in Canada, are benefiting patients with HIV and AIDS. However, these alone will not be sufficiently effective to stop the pandemic and so we do look and we have to look to other solutions such as microbicides and vaccines.

You know, vaccines are one of the most powerful public health interventions for controlling infectious diseases. We've seen this with the eradication of polio and with the dramatic reduction of measles. And the development of safe and effective HIV vaccines is essential if we're to make and to see a major

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breakthrough in reducing HIV infection rates worldwide. But there are many challenges to developing such vaccines and that is the reason for this session.

One of the essential ingredients to achieving success in the development of HIV vaccines is a high degree of international collaboration from basic science through to the production and delivery of the vaccines themselves. This recognition of the need for global collaboration led to a mobilization of scientists from around the world to increase those collaborative efforts in enhancing HIV vaccine development and this resulted in the creation of the Global HIV Vaccine Enterprise, which has been endorsed by the G8. This global alliance has played an outstanding role in advancing much needed collaboration to accelerate HIV vaccine candidates and I'd like to take this opportunity to personally recognize and applaud their efforts.

Now, the global enterprise is modeled after the open science approach of the Human Genome Project, which led to the successful mapping of the human genome and, as you know, this was a very complex scientific hurdle overcome through effective public/private partnerships and collaborative global efforts. And so in the race to develop HIV vaccines, we also face significant scientific, regulatory and policy challenges and in this regard, I do believe we have much to learn from the success story of this collaboration.

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So as we take steps to open and foster a transparent and collaborative research environment, it's also important that we, as nations, do our part to contribute to these global objectives. I want you to know that in Canada, our government is investing in HIV vaccines research as well. Since 2001, the Canadian International Development Agency has contributed \$62 million dollars to the International AIDS Vaccine initiative, \$5 million to the African AIDS vaccine plan, and \$3 million dollars to support Canadian/African partnerships on clinical trials. Here in Canada, \$4.3 million dollars is spent annually on HIV vaccine-related research through our Canadian Institutes of Health Research.

So Canada has long been a player in contributing to global scientific advancement in health and other areas and we recognize that within Canada, a significant cadre of world-renowned researchers contribute towards the global objectives of developing successful HIV vaccine candidates.

I wanted to give you a couple of examples. We have a team led by Dr. Jonathan Angel of the Health Research Institute. Is Jonathan here, by the way? Is he around? I went to school with Jonathan in undergraduate before either of us pursued our careers and I'm glad at least one of us is making some progress on some of the issues. It's great to see that he's involved in the Canadian Research Institute and what Jonathan is doing is conducting the first Canadian-led controlled trial of the

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therapeutic HIV vaccine. This trial combines two products, both of which have been shown in separate tests to induce different aspects of the immune response. The trial is seeking to determine whether the two work effectively together and at what dosages. At the University of Toronto, Dr. Mary Ostrowski [misspelled?] is using state-of-the-art techniques in immunology and virology to design a new, improved version of an HIV vaccine made from the canary pox virus. If this new vaccine is shown to be more effective in mice and monkeys, it will move on to clinical testing in humans.

Now, in addition to supporting these research efforts, I want you to know that the government of Canada is committed to improving access to less expensive medicines that are urgently needed to treat HIV/AIDS, malaria, tuberculosis and other diseases in developing and least developed countries. I want you to know that we recognize that our domestic legislation clearly, currently is flawed and that's why it must be reviewed sooner rather than later. It was due to be reviewed in 2007 but today, I'm announcing that we will undertake an immediate comprehensive, top to bottom review of the legislation. We will do this in consultation with our stakeholders and indeed any others who have good ideas on how to be leaders in the struggle to get inexpensive medications to the people who need them. That's my commitment.

[APPLAUSE]

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Ladies and gentlemen, we need legislation that works and our intention is that all parties will participate in good faith. This is about our humanitarian efforts. We have high-quality drugs that are ready and are available. Let's get them to the people who need them.

In closing, ladies and gentlemen, I'm pleased again to welcome you to this session, which has been organized to bring together leading participants in the quest for HIV vaccines. This ongoing and open dialogue is important to the collective advancement of research and development in this critical area. We will hear some presentations this afternoon on challenges for vaccine development from the scientific, industry, and indeed community perspectives as well as hearing more concerning the experience of the Global HIV Vaccine Enterprise. It promises to be an engaging, an inspiring session and I look forward to the deliberations here this afternoon. Thank you very much.

[APPLAUSE]

**PEGGY JOHNSTON:** Thank you, Minister Clement.

**MITCHELL WARREN:** Thanks, Minister Clement. We want to thank you for your kind words today and it's very kind that your commitment to HIV and AIDS in Canada is great. We just wanted to tell people today that the prime minister is stopping poor Tony from approving the exemption of the Safe Injection Site in Vancouver - Health Canada's study - the Vancouver police

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department, the city of Vancouver, the provincial government - all and it's continuing to save lives. At noon tomorrow, there's going to be an action to try and communicate this basic information to the prime minister because he's kind of new and he - It's hard to catch up with this kind of stuff. But thanks again, Tony, for all your help and for your kind words today.

[APPLAUSE]

**PEGGY JOHNSTON:** I have a couple of more mundane housekeeping announcements to make before we begin. First of all, I would appreciate it, as would the workers here, if you would pick up and carry your trash and dispose of it by the door. Second, there are two reports up here by the front of the podium that I would encourage you to pick up on your way out - one is the IAV [misspelled?] AIDS blueprint - AIDS vaccine blueprint for 2006 and the other is AVACS [misspelled?] - AIDS vaccine new frontier publication and it's important that you distinguish those two instructions here, okay. The trash goes in the garbage and the reports go with you, okay? Please don't mix those up.

Following Minister Clement's remarks, I think it's appropriate for the speaker to be the first speaker. As pointed out in the global enterprise scientific strategic plan, there is a general consensus that the scientific hurdles are among the most important that we have to face. So it's appropriate that our first speaker be someone who is well versed in those

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scientific challenges to review them for us. Dr. Rafick Sekaly is currently the professor in Microbiology and Immunology at the University of Montreal, where he has been since 1998 and he is also the chair of CanVac [misspelled?] so he will present to us his paper on scientific challenges for the development of HIV vaccines. Dr. Seklay.

[APPLAUSE]

**RAFICK-PIERRE SEKALY:** Thank you, and thank you, Minister, for your presence and your kind words. I'll try to, in the next 15 minutes, summarize, I think, what is a big hurdle as Peggy mentioned, which are the challenges for the relevant HIV vaccine and I want to warn you immediately that a lot of what I'm going to cover was already discussed this morning by Francis [INAUDIBLE]. And what I really would focus in my presentation was really on one major hurdle, which is identifying [INAUDIBLE] protection but before getting to this area, I will discuss briefly the major challenges to HIV vaccine development.

So development of vaccines incorporates many different steps all the way from the identification of [INAUDIBLE], identification of an adjuvant, a delivery system, assays that can measure immune responses and then the clinical trials, which are appropriately designed in order to identify efficacious vaccines and all this has to do in fact was inducing an immune system, which for some of you know this

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immune system quite well. It's extremely complex. For those who are less versed in this - it is indeed, a very complex system where, I mean, there's multiple cells that each play a very well-defined role in inducing an efficient immune response. And in order to be able to induce this efficient immune response, it has to be a dry place and a dry place meaning in the context of HIV, to have to be a mucosal interface, which is a place where HIV enters the immune system or enter in the organism and that where it first encounters the immune system and these things are things, which are completely evading us up to now and for which we have very little clues. So not only it's the cells and it's where they are, but also it's how the cells interact together and how the cells interact together is there are major players in the immune response. And I'm focusing here mostly on the T cell response, but it's very similar with the B cell response where you have an antigen, which is being captured by the dendritic cell. This dendritic cell is a cell that is going to digest or fracture the virus and present it now to T cells after receiving appropriate stimuli by either the virus or by other, what we call [INAUDIBLE] and that's going to help elicit - I mean protective CD4 or CD8 responses.

So it's not a system where I mean you have a singular cell system but there's many, many cells that interact together at the right place, at the right time, and we see appropriate

[INAUDIBLE].

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So if one wants to summarize on either the number of challenges that face the scientific community for HIV vaccine development are numerous but I think one has always to keep a strong degree of optimism. And I think these are all things that can be tackled appropriately with - especially with tools that we are having right now. So even for the many vaccines, which we know are successful, we still have a lack of knowledge of defective cells and the molecules, which are involved in vaccine-induced protection. Vaccines work because they induce memory cells because when you encounter a pathogen after you have received a vaccine, 10 years later, your immune system remembers. It has memory and we still don't know how to make those cells generate them and how to make them persist. We don't know how, as I mentioned earlier, at the mucosal interface, how the cells interact together and what they release in terms of effective molecules that will lead to protection and, of course, in the context for HIV infection, generation or [misspelled?] [INAUDIBLE] of neutralizing antibodies [INAUDIBLE] and mucosal interface and also systemically is a major conundrum for which we still are struggling to find real answers.

So in addition to this, and of course you know, to be able to induce an immune response, as I said in my first slide, we need to have appropriate immunogens and we need to have appropriate adjuvants. Appropriate immunogens, we know that the

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more immunogens we have, the more broad immune response we have and broad immune responses have been attributed to protection and adjuvants - there is promise under way because recently, over the past five - a little bit more than five years, the molecules called [INAUDIBLE] receptor ligands, which are very ancient molecules dating all the way to flies can induce protective, strong immune responses. And these molecules have been conserved all throughout speciation [misspelled?] all the way into humans and can also deliver strong immune signals to cells involved in protection.

So in terms of progress that has [INAUDIBLE] already in addressing these challenges, we have - I think - over the past 10 years, a very enhanced knowledge of mechanism of immune responses. We have a novel appreciation of the [INAUDIBLE] dendritic cells and, in particular, the function of [INAUDIBLE] receptor ligands. We have a novel understanding of a mechanism called cross presentation, which allows the design of a new generation of vaccines. We have a novel understanding of cells and molecules, which can attenuate immune responses. A lot of work has been increasingly done on molecules that are called - cells that are called regular T cells, which are involved in dampening immune responses and the way that you can handle those cells might open new doors in terms of generating boosted immune responses. And also the concept of breaking tolerance, which will allow also boosted immune responses and enhancing

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immune responses. In addition, we have developed novel standardized assays to - especially with [INAUDIBLE] and the global enterprise to obtain quantitative and qualitative assessment of immune responses, animal models that can allow in vivo deciphering of protective immune responses and for HIV particularly, the structure of the HIV envelope protein complex [INAUDIBLE] neutralizing antibodies is starting to provide clues how to make neutralizing antibodies and also recently a map of the HIV [INAUDIBLE] organization of [INAUDIBLE] on the [INAUDIBLE] also provides novel ways to address these challenges.

So in the next few minutes, I'll mostly cover one area. I think it's really [INAUDIBLE] to try to cover in the next 10 minutes, all the areas challenges I discussed, but I think the one which is closer to my heart and to my interest is trying to understand what's a protective immune response. And I think if we are able to do this, we are then - we have a benchmark on which now we can design a more efficacious vaccine by trying to mimic these protective immune responses but paramount to this before getting into identifying [INAUDIBLE] of protection, we need measures and we need instrumentations in order to be able to measure these immune responses and already at the strategic plan of the global enterprise.

It was already stated clearly that establishment of standardized pre-clinical and clinical laboratory assessment

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was of major importance and that is a very important clue in trying to be able to decipher those correlates of protection. So in order to reach this objective, it's important to develop novel [INAUDIBLE] that can decipher protective immune responses with the rationale, which I alluded to earlier, first immune response is complex and cannot be equated to one or two parameters. You need to be able to analyze multiple parameters at the same time so we need to develop technologies, which will allow the analysis of multiple parameters in the same time and these technologies will be able to allow the dissection of different effector arms of the immune response [INAUDIBLE] immune responses.

So the kind of measures that we need to be able to do - we need to, in decoding immune response, we need to measure memory, we need to measure effective cells, we need to measure innate immunity and mucosal immunity and, of course, the potency of dendritic cells, which as I said, are the first ones that manipulate antigens and eventually present it to T cells. And of course, we need to have proper assays that need to measure neutralizing antibodies. So along with those assays that we and many others have - are working with and are trying to develop a better understanding of correlative protection, we're working with [INAUDIBLE], which is a technology to [INAUDIBLE], at the single cell level, the definition up to 17 parameters including sensorous markers, which have an

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importance in functions - the cytokine release, cytotoxic [misspelled?] [INAUDIBLE] function and also the differentiation stage of the cells. One technology that we have worked a lot on and I think a lot of other groups, I think should follow on this technology because I think it's extremely powerful of genomics because it's a technology that can be performed on [INAUDIBLE] of cells that will generate a two-prong [INAUDIBLE] analysis, will allow you to measure many, many different factors or many different genes at the same time and will generate an enormous amount of data that can be analyzed by informatics.

So we've learned a lot over the past few years from other [INAUDIBLE] vaccines in terms of a sense of correlative protection. First, it's very clear - there's a very particular role for cellular immunity and particularly memory T cells and effective CD8 cells meaning the cells that can kill infected targets. We've also shown and many others, a role for broad immune responses direct against multiple [INAUDIBLE] protection in a variety of [INAUDIBLE] diseases, a role for [INAUDIBLE] function of T cells including attributing cells, which also have been associated with protection and finally, a role for IL-12 produced by dendritic cells, which also plays a major role in inducing protective immune response.

The one feature of vaccines, which I think really is - makes the vaccine work is the memory cells. These cells are the stem cells of immune response. They can last forever. They can

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last up to 60 years. In the case of smallpox, it's been demonstrated, and they are really the ones that provide and use protection and several vaccines tested to date can induce long-term protection, which can cancel [misspelled?] the protection from one individual to another and that's been done mostly in animal models but also in non-human primate models right now. Why do we think that memory T cells are the ultimate correlative protection? Because first, they are in a variety of context, they're [INAUDIBLE] protection. I think the one closer to our interest is the fact that memory cells, both CD4 and CD8, have actually the protection in long-term, non-progressors. Memory T cells are induced by most efficient vaccines including vaccines to acute viral infection such as flu, yellow fever, smallpox and I think if you read *Science* about two months, there's a recent work by Norm [INAUDIBLE] showing the SIV [misspelled?] model, the critical role of central memory CD4 positive T cells in vaccine-induced protection. So the cells, in fact, those central memory cells are cells, which are recruited very early after immunization and they undergo a series of differentiation [misspelled?] process in order to become those central memory cells. They exhibit a very peculiar set of gene expression profiles that allow them to be covering those cells that can remain forever, as I said, up to 60 years and [INAUDIBLE] protection and continue to seed the immune system with novel cells that can

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mediate eventually, the protection once the [INAUDIBLE] are encountered.

So one example that we have worked and I'll have a couple of slides on data that we're generating now [INAUDIBLE], work on yellow fever vaccination together with Jim Tartaglia and Dirk Keowns [misspelled?] at Sanofi Pasteur, we worked with yellow fever, as I said, yellow fever is a very good vaccine. You get immunized once and you get protection for at least 10 years and we wanted to understand why this yellow fever vaccine is such - why it is able to induce such a good protection. And for that, we used mostly the two technologies, which I alluded to earlier, which are the genomics and the [INAUDIBLE]. And for those of you who are not color blind, okay, you will see very clearly - and I don't ask you to read all the numbers but you have blue and red colors and the blue colors are genes, which are down-related and the red are genes, which are up-related [misspelled?] and then the kinetics is you have a series of time points going all the way from zero to 180 days. And you see, in fact, that where you have the most changes between the baseline and the rest of the time points, it's very early on after immunization at Day 3 and Day 7 and potentially even earlier, that's where the immune system really gets mobilized and starts to induce the [INAUDIBLE] of genes, which are eventually going to induce protection.

And this is, in fact, even better shown in this slide where

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now we show that in a space where the profile of genes induced at Day 3 and Day 7 is clearly distinct from all the other time points that we have analyzed and the genes, in fact, which are induced, in fact, which are genes which are genes important for innate immune responses and for memory T cell responses. And again, stating the importance of memory T cell responses, we can see that those memory responses are induced extremely early on.

If you look at the central memory cells, which are those long-term protective cells, they're induced as early as Day 7 after immunization. They start to colonize the periphery and they go through massive expansion before eventually they regress and they home to lymph nodes. So with these kinds of studies, I think we can learn a lot about what makes a protective immune response.

I think we have some very good elements that we've learned from yellow fever vaccination showing that this vaccine induces very potent innate adaptive immune responses as early as Day 3 with a very [INAUDIBLE] profile and with the induction of survivor genes, which are induced extremely early on.

So we have now, I think, at least tackled that particular challenge - assays that can be in place to identify correlative protection and I think this should be a priority and that will help establish benchmarks. But, also, it will help to provide assays that can be used to screen for adjuvants that can, in

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fact, help induce these responses. Thank you.

[APPLAUSE]

**PEGGY JOHNSTON:** Thank you, Rafick. Since talks are all general, we're going to go through all the talks and then we will have time at the end for questions and discussion from the audience.

As many of you know, Sanofi Pasteur is a partner in the ongoing phase III preventive HIV vaccine trial in Thailand and that trial has been made possible in part because of the dedication and leadership of our next speaker who knows all too well as well as anyone in this room, I think, of the long road we have to vaccine development. Jim Tartaglia is the site vice president of Research and Development of Sanofi Pasteur in Canada and also overseas, the company's global HIV vaccine program. Jim was key in developing the pox vector technology in his prior position at ViroGenetics [misspelled?] and he's since gone on with the company to contribute to the licensure of several products, both in the human and veterinary vaccine fields.

So having been in the private sector now for 16 years, I can't think of a better person to give us an industry perspective of the challenges we face, so without further ado, Dr. Jim Tartaglia. [APPLAUSE]

**JIM TARTAGLIA:** Thank you, Peggy. I'd like to thank the organizers for inviting me to give an industry perspective on

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HIV vaccine development and lastly, I'd very much like to thank Minister Clement for spending his precious time with us this afternoon during this session.

Okay, so I think it's very clear that industry does recognize that HIV vaccine development is an enormous public health priority. Towards that end, industry has been and remains committed to the global efforts to develop an HIV vaccine. Industry is open to evolving public/private partnerships that aim at facilitating R&D efforts internationally. And also, industry is receptive to novel access paradigms that aim to ensure that when we have appropriately effective HIV vaccines available, we're able to deliver them to the people who need it the most in a timely fashion.

As we talk about the specifics of HIV vaccine development and the complexities in that, it's important to discuss this in terms of traditional vaccine development because HIV vaccine development will have to travel through the same processes going from discovery research through licensure and beyond. This appreciation of what it takes to bring other or has brought in - taken to bring other vaccines forward, I think, will help in understanding how some of the complexities around HIV also lead to longer development times and higher costs for development.

There are three major elements to developing a vaccine.

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Obviously, the research - the discovery research pre-clinical development phase, the clinical development phase, and the industrialization phase, and for the sake of this presentation, keeping it simple, this would include access to vaccines. Traditionally, even taking well-established vaccine platforms such as inactivated vaccines, subunit vaccines, or live attenuated vaccines forward has required at least five to 15 years of upstream research.

Now, Rafick has very eloquently highlighted many of the scientific challenges that we face around developing an HIV vaccine and there's a clear need to develop novel technologies in order to address these challenges as he alluded to. And this obviously adds to the complexity and the time required to develop effective HIV vaccines on the global stage. From where the field is with the science, it's clear that we're going to require more complex subunit vaccine candidates possibly brought forward in combination with vector-based approaches in order to achieve the immune response profiles that were highlighted by Rafick. We also might have to look at alternate devices and delivery systems to look at mucosal - inducing appropriate mucosal responses and also ways of potentially augmenting systemic responses in general. Also the - where we are with vaccines to date, we've been very restrictive with respect to the adjuvants that have been brought forward in licensed products. It's very limited with our experience and as

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we think about augmenting potency and breadth of responses for eliciting of broadly effective HIV vaccines, we're going to have to look at developing and bringing forward novel immunoadjuvants that are more active and which have a safer profile.

All of these evolutions and technology mean there are many unknowns both in the development and in the industrialization phase. This schema provides the typical timeframe for vaccine development and it's obviously not specific to HIV. Clearly, it reflects the fact that it takes many years to develop a vaccine even post the research phase. Usually the largest investment in vaccines comes in the first three to four years of clinical development with industrial investment decisions starting to occur around the phase II phase of development. And it's also clear that as we get to the later stages of development, the investment risks increase.

Again, with the advancements in HIV vaccine development, we just covered this timeline. These timelines will be extended significantly. The previous slides highlighted more tangible development risk that we face in industry. However, there are a number of less tangible challenges. The success of vaccines that Minister Clement alluded to with smallpox, polio, et cetera, have increased our expectations around vaccines.

Everyone wants highly effective vaccines with absolutely no side effects. Clearly, the regulatory environment has moved in

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that direction as well. So for all vaccines, we're seeing a longer, more expensive development to ensure the safety and efficacy of vaccines.

The scale of the HIV epidemic has challenged traditional vaccine paradigms in a number of ways. Here we can see how the science has evolved over the last 25 years. Concepts of what is required of a new vaccine have moved faster than our ability to test them. Further, we see that the need to combine new technologies to optimize vaccine performance have, itself, brought forward the requirement for collaborations and partnerships, which were never necessary when we were looking at more conventional vaccine approaches in the past. Further, the process of vaccine development is iterative and typically, several candidates, formulations and regimens are tested before the right one is identified.

For HIV, for all practical purposes, we're going through the research iterations as we speak. Because of the uncertainty of predictability of animal models for HIV, proof of concept in humans remains the critical milestone for decisions on investment, especially when it comes to the larger investments needed for industrialization. To keep things simple for the time being, what we mean by proof of concept is that demonstrable vaccine effect in phase II with respect to either an acquisition endpoint or an endpoint such as a surrogate marker like viral load.

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One can also think about some of the evolutions that we're going to see coming forward, which is around being able to bring candidates forward that elicit broadly neutralizing antibody. Demonstration of that observation in phase I may make industry have more of an appetite for investment at earlier stages of development such as after phase I. Under the traditional vaccine development paradigm, once proof of concept in humans is established, the clinical development process is more streamlined and usually focuses on one population and on one indication at a time. For HIV, we won't have that luxury because there are still many questions to be answered. It will be important to proceed in a way - coordinate - in a manner, coordinated to address these issues to speed development and access.

So to summarize where we are with some of the R&D challenges, science is evolving and dynamic. There's a need to incorporate novel technologies and concepts into vaccine development process. Even after proof of concept in humans is established, significant challenges remain to streamline further clinical development. Finally, this complex landscape has led to increasing partnerships and in moving forward, partnerships need to evolve in order to gain greater coordination and effectiveness. While such partnerships have been fostered for R&D, there needs to now be an increasing emphasis on partnerships that focus on effective access and

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delivery. In the traditional access model for developing countries, industry's responsibilities had stopped when the vaccine went into the vial. At that point, the public sector and donors stepped in to purchase and deliver vaccines.

In this model, large vial purchasing has been the main driver. Everything's done has been done, in sequentially, in that industry licenses and manufactures vaccines in the developed world first, sells them at market value, and then makes them available under a tiered pricing structure for the developing world. The traditional model for the developing world has been a passive or trickle-down system that we need to focus on for HIV - what we need to focus on for HIV is an active system to develop the appropriate infrastructures in parallel to get vaccines to those who need them the most in the transitional and developed countries.

Given the urgency of HIV vaccine development, we need parallel tracks with industry, public sector, NGOs and donors - each working on what they do best - in partnerships so that we can ensure that those who need the vaccines the most have access to them when they're available. As I've mentioned, we've already begun the process of partnerships in the R&D area and now, it's time to have the emphasis of these efforts and partnerships being established for access and delivering. Some things have started. There's been work on demand estimates that are essential for providing the necessary information to plan

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and plan for industrialization and for investment. Regardless of the model, we will need to ensure push and pull mechanisms that are enhanced to facilitate vaccine access. These push-pull mechanisms will have to address key issues around pricing, capacity, and distribution, and effectively turn the traditional access model upside down.

To summarize, access will require a combination from all partners. These might include guarantees of purchase, regulatory harmonization, tax credits, and other incentives for industry and industry can also explore providing greater access to technology or bulk product for eligible countries with capacity. Where appropriate, there is also the possibility of new regional plants that are either owned by industry, by the public sector, or owned and managed through joint ventures. As I've said, partnerships are critical but they need to share both vision and responsibility. We need to recognize that vaccine development will be an iterative process with failures preceding success and different definitions of success in different populations.

It's important to us to identify and discuss everyone's roles and responsibilities now because it would be unthinkable to have an effective vaccine at any useful level and not have created the appropriate infrastructure necessary to get it those who need it most. So no company, government or NGO alone will be able to carry the burden. Governments, academia, NGOs,

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donors and industry must work together to allow for the most effective means for developing and providing access to vaccines. As a global vaccine community, we must do this so that we can deliver a vaccine in a timely and effective manner. Thank you.

[APPLAUSE]

**MITCHELL WARREN:** Thank you. Thank you so much, Jim. That was outstanding and a wonderful transition as we talk about partnerships and what's been clear as we've gone from the political leadership to the scientific challenges to industrial involvement. None of that will deliver a vaccine without effective, meaningful community involvement and it gives me great pleasure then to shift to our next speaker who will address that very issue.

It's also very clear from Jim's presentation is the global nature of our work and while we've had several presentations from the North, it's particularly important that Elise Levendal comes from the South, from South Africa. She's currently the interim director of the South African AIDS Vaccine Initiative, SAAVI, a leading public/private partnership in the development of HIV vaccines. Prior to joining SAVI in 2004, she was a nurse both in clinical practice as well as teaching nursing students in South Africa and for many years, worked in primary healthcare in a leading South African NGO for many years, the National Progressive Primary Healthcare Network. She has

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training in both psychology and sociology and a master's degree in public health and it gives me great pleasure to introduce Elise.

[APPLAUSE]

**ELISE LEVENDAL:** Thank you, Mitchell. You know more about me than I know myself. First of all, I want to thank the organizers for thinking about community involvement within the session as a valuable component of vaccine research and development.

The way that I'm going to structure my talk is based on a model that we are developing and at the same time, implementing and at the same time, evaluating. They've asked me to speak specifically to the challenges in implementing a community involvement model. Just to explain to you that the South African AIDS Vaccine Initiative is a lead program of the Medical Research Council of South Africa and Masikhulisane, which means let's grow together is the community involvement program of the South African AIDS Vaccine Initiative. Masikhulisane is funded by funding, which comes through SAAVI and the MRC from the Department of Health and also largely through the European Union.

Just a little bit of a background, the money from the European Union that came through the MRC was a four-year project that started in 2000 and at that stage, the program was called the South African HIV Vaccine Action Campaign. And I'm

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sure the name of that unit implies that basically this was an advocacy campaign at the time. With management changes in the program, it later on changed and it became the SAAVI Community Preparedness Program. After the first four years, we had to do an intensive evaluation into the program. After strategic planning and the evaluation recommendations, we changed our name to Masikhulisane, which we thought was much more appropriate in the South African environment. This is just to show you how Masikhulisane fits into SAAVI as it is now.

At the bottom, you will see there's a whole group of organizations and institutions. The one at the top [INAUDIBLE] is the HIV and AIDS Vaccine Ethics Group based at the University of [INAUDIBLE]. There's a social behavioral group based at the University of [INAUDIBLE] and then there's the house promotion group based at the Medical Research Council and then Masikhulisane. We obviously are known as the soft sciences but we feel we are the base and the foundation for HIV vaccine research and development because we have to work with the clinical trials group to see this side. But we also have to work with the basic lab sciences and we have to know all of those terms and concepts that we heard in the first presentation because we have to make this understandable to the community. So we work with all of the different role players within the AIDS vaccine initiative.

Just very quickly, the vision of this program is the South

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African Society that works in a mutually beneficial and meaningful partnership with researchers within a vibrant and human and legal rights environment. At that stage, we knew what we had to do. We knew we had to raise awareness about AIDS vaccine research and development but we also know that we had to do our own research and capacity development in related community involvement - ethical, legal and human rights issues. We also knew that we had to be involved in knowledge exchange and collaboration not just inside the country but in the region, on the continent and also internationally. We also realized that we cannot just do awareness-raising. We also had to get involved in policy analysis and policy development. The challenges that we experience at the time and still do as first of all as we've listened and just think back on the first presentation today and even the last one, is the nature and link of HIV vaccine research and development because we have to be careful about raising expectations.

There's also the sustainability of community involvement activities because when I look at the budgets that's sent in by our principle investigators, community involvement is usually a little bit of budgeting only and also the complexity of the HIV vaccine messages, there's much [misspelled?] misconceptions of HIV and AIDS and there's still fears about HIV vaccines in communities. Further challenges, those were the more general challenges, there's specific challenges to community

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involvement and those are community needs. There are other HIV and AIDS needs - there's poverty, there's unemployment but in a democratic society like we have, people are expected to be involved in other issues of governance like, for instance, police forums, housing forms, and then there's the conflict that people still don't have basic HIV and AIDS information and then other preventative research agendas. But then there's also the past experience of research in developing countries where people still feel they are being used as guinea pigs and also that they don't see any sustainable benefits once they become involved and sometimes, it takes years before the medicines actually reach developing countries.

Further challenges at that are specific to community involvement is the relationships and coordinations between community role players. The influence of community leaders support systems in communities are sometimes divided and we also find that people living with HIV and AIDS, they want to be involved in vaccine trials but also in vaccine research and development. Then the community structures that have been formed and other mechanisms that should ensure community involvement in the vaccine research as we find that there are groups called community advisory groups or community advisory boards, they're not sure of their roles and responsibilities. There's poor communication between them. Sometimes there's difficulties in communication between those groups and the

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researchers and then a big issue is the blurring roles and the broad scope of work for community staff at the clinical trial sites. Sometimes, the same person is the community educator, is the recruiter, and also the retention officer and that is how we then came to start developing a community involvement model, as you can see, our own evolution from being activists to becoming proper advocates now for community involvement. And this emerged from our evaluation, from our own learning, but also from earlier documents that we involved.

We first had to look at what do we mean because we knew people were going to ask us - what do you mean by community involvement? We acknowledge that there are terms that can be used interchangeably but in the HIV vaccine development process, we see involvement as an ongoing, long-term process. It includes all those different terms - preparedness, consensus building, engagement, but it must contribute to education and development of people. It's a process where people actually exercise their human rights to fulfill roles in the development of vaccines and other broader issues. For us, community involvement must have a human rights and development approach. Community involvement must mean a means to an end where the end would be a successful and appropriate vaccine but it also must be an end in itself where there's individual and community development and by this - in this way, we ensure meaningful and authentic community involvement. We also knew people were going

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to ask us, now, how do people get involved? There are many forms. People seek information, they form views, they express ideas. They take part in activities and processes, which should include protocol and informed consent development. Peer education, support to other trial participants - so becoming a trial participant for us is just one way of becoming involved. We hope to develop this into a tool by which we can measure community involvement and this is based on a letter from Einstein [misspelled?] and the spectrum that was developed by the International Association of Public Participation. And we must be very careful and I think all of us have been guilty of this where we, first of all, think we involve people by handing out caps and T-shirts and we think we've involved people. We must also be careful of just asking people to do a traditional dance at a function they don't even know why they are dancing and then also, the issue of filling seats in a meeting or asking somebody to open a meeting without them really knowing.

So what we are moving to is community-initiated research, shared decisions with researchers and all of us have been walking up and down this ladder, I am sure. The spectrum in itself at the bottom is where we start involving people - they will protest until we inform, we consult properly and at the end of it, we want collaboration and empowerment. We follow a sectoral approach because we work within the local trial site communities at provincial levels of Africa's nine provinces. We

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work throughout the society but on a regional, international level.

The reason why we follow a sectoral approach is to build accountability amongst the community members and ourselves so that we know if we work within the women and the youth sector that we have spoken to the national leaders before we speak to the local leaders and that's the reason for following a sectoral approach. This is just to show you all the areas that we work in - in South Africa, the different provinces and how do we do it? We raise awareness based on [INAUDIBLE] philosophy and those are the different methods of awareness raising. And I'm sure this is used globally but we also have developed a facilitator's manual where we take people through six different modules, everything from basic HIV and AIDS - we cannot start talking about vaccines if people still don't know about AIDS and HIV.

So we have to take them through this right up to vaccine development, the signs and also ethics and human rights within so what we actually educate people about is clinical research so that everybody knows what clinical research is, what their rights and responsibilities are. Our work is based on real concerns about quality of our education, so what we've done is we've developed unit standards for community education in clinical research. And this was submitted to the South African Quality Patient Authority for approval and we've also developed

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a [INAUDIBLE] learning program. Our two policy documents that we've developed is an adolescent paper and we've also developed care [misspelled?] guidelines, which has been approved by the National Department of Health. That is just to show the supportive role that we play within and outside SAAVI and also internationally.

Solutions are, first of all, international and national commitment and support for community involvement. We believe that every country should have a dedicated national community involvement program. There must be an enabling and supportive environment for all dedicated human resources in community involvement programs. Not just scientists and researchers should have Ph.D.'s, but also the community staff.

Other solutions is to tailor the community involvement programs to solve the complex challenges and lastly, we also believe in utilizing GCP but at this time, it's good community involvement practice, which we follow by the proper community inter-processes and the recognizing and building on to existing skills.

Lastly, I just wish to thank the team at Masikhulisane but also the trial site people who assisted with this presentation [INAUDIBLE] at [INAUDIBLE] research and Drs. Karen [INAUDIBLE] and Linda-Gail Bekker at the Desmond Tutu HIV Center. I want to add that all of the Masikhulisane's staff are busy with their own studies on one condition - that they study an aspect of

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their work community involvement in vaccine research and development. I thank you.

[APPLAUSE]

**MITCHELL WARREN:** Thank you so much, Elise. A really outstanding panel, I must say, sticking very close to time, which is fabulous.

Anyone who works in HIV vaccines knows our next speaker, Jose Esparza - Venezuelan by birth, international by nature. Jose currently resides in Seattle, Washington where he works for a small family operation, the Bill and Melinda Gates Foundation where he serves as their senior advisor on HIV vaccines. Today, he's here in a somewhat different capacity, another hat that he wears, as the interim head of the Secretariat of the Global HIV Vaccine Enterprise. Prior to his shift to Seattle, Jose spent decades at the World Health Organization setting up the HIV vaccine initiative with WHO and UN AIDS and establishing the African AIDS Vaccine Program, and really leading the field not only on scientific levels but on translating that to community. Jose?

**JOSE ESPARZA, MD, Ph.D.:** Many thanks, Mitchell. The rationale for the Global HIV Vaccine Enterprise is the increasing severity of the AIDS pandemic and the realization that current efforts to develop an HIV vaccine are not sufficient. At the same time, we are convinced that every new HIV vaccine effort is needed because new scientific

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opportunities are emerging. New strategies for collaborative partnerships are needed and this will require a more coordinated global effort, a new game plan.

That new game plan, the Global HIV Vaccine Enterprise, was proposed in an article published in *Science* in June 2003, co-authored by 24 leaders in the field of HIV vaccines - some of them are here in this room. The development of the Enterprise has gone through three phases - conceptualization, planning and beginning of implementation. The philosophy of the Enterprise is described in this slide and focuses on the prioritization of key questions, then directing resources to answer those questions and implementing common processes to maximize learning through sharing of materials and data.

The Enterprise model represents a new way of thinking about problems, a new way of acting to solve problems, and a new way of behaving as a global community of problem solvers and the problem that we want to solve is the development of an HIV vaccine.

Soon after we published the paper in *Science*, we developed the original vision of the Enterprise as an alliance of independent organizations - funders and implementers from the public and the private sector, committed to accelerating the development of a preventive vaccine for HIV through the implementation of a shared scientific strategic plan, modernization [misspelled?] of additional resources and greater

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collaboration among HIV vaccine researchers [INAUDIBLE] and this slide represents our vision. The constellation of actors committed to contribute to the implementation of a jointly developed scientific plan.

I need to clarify that the Enterprise is not a new organization but an alliance of independent partners. It is not a global fund. It is not intended to encompass all HIV vaccine research. It does not replace or compete with current research efforts and more importantly, does not replace the creativity of individual investigators but tries to compliment it with the structures and resources needed to harness new knowledge to accelerate the development of a much needed HIV vaccine.

The planning phase of the Enterprise started in 2004 and the main priority was the development of scientific and strategic plan, which was developed through a process of consultation involving more than 140 scientists from 17 countries. And the plan was published in February last year in *PLoS* [misspelled?] *Medicine*. The strategic plan provides a road map on 6 different areas - vaccine discovery, laboratory [INAUDIBLE], product development and manufacturing, clinical trials capacity, regulatory issues, and intellectual property and enterprise partners are committed, morally committed, to align - at least some of their activities with this plan.

To achieve this ambitious plan, we need strong political support and we initially obtain it from the G8 Summit Meeting

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in 2004 and then that support was further endorsed in the G8 Summit in 2005 and 2006. The Enterprise is about signs but we are also developing a small secretariat to vastly take coordination between the partners of the Enterprise alliance and this slide shows some of the proposed activities of the secretariat.

But the Enterprise, really, what the partners are doing to implement the scientific plan and these activities started in 2005. The first major activity was launched by DOS National Institute of Health and it is the center for HIV/AIDS Vaccine Immunology or HAVI, which was launched last year in 2005 and the second major activity was launched only three weeks ago and it is the collaboration for AIDS vaccine discovery or CAVD supported by the Gates Foundation. Together, these two initiatives represent a major infusion of new funds, approximately, \$600 million dollars but more importantly, these two initiatives represent an exciting network of some 250 investigators in more than 20 countries.

Under the leadership of Bart Hanes [misspelled?], HAVI is focusing on early events of HIV infection, exploring correlates of protection in primates and using that information in the future to develop and test new vaccines but HAVI is not Bart Hanes [misspelled?] alone. It is a network of some 80 investigators in 35 institutions dealing with some of the challenges and activities that are listed in this slide. After

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one year of work, less than one year of work, HAVI has achieved a lot and their work, as I say, is just starting.

The second major initiative is the collaboration for AIDS vaccine discovery or CAVD supported by the Gates Foundation. This highly collaborative network harnesses the creativity of individual investigators working in 11 different vaccine discovery consortia and this individual creativity is complimented with the services provided by central facilities that will conduct comparative immunologic evaluation of the different vaccines as well as comparative statistical analysis. Five of the 11 vaccine discovery centers will explore new ideas to design vaccines to induce neutralizing antibodies that, as you know, is one of the major challenges in HIV vaccine development. And six of the vaccine discovery centers will explore vaccines to induce [INAUDIBLE] mediated immunity supported by central service facilities.

But I want to emphasize that this network is not a compartmentalized cocoon of investigators and in accordance with the philosophy of the Enterprise, we have included strategic links between the CAVD investigators with other research networks including HAVI, IAVI [misspelled?], [INAUDIBLE] and the NIH Vaccine Research Center. So we are creating the global community of scientists that is needed to solve the problem of developing an HIV vaccine.

This slide shows the many collaborative links established

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by CAVD investigators in 20 countries. It represents the collaborative paradigm initially proposed in the vision of the enterprise but in addition to these two major initial enterprise initiatives, other projects are now being aligned with the enterprise scientific plan and philosophy including the IAVI [misspelled?] Neutralizing Antibody Consortium, the announced Swiss Vaccine Institute, a German contribution to CAVD activities, the announced new Russian Center to coordinate regional HIV research in Eastern Europe and Central Russia as well as seven other initiatives to be launched in the near future, some of them hopefully very soon.

In summary, harnessing new opportunities for HIV vaccine development requires an effort with a magnitude, an intensity, and a design without precedence in biomedicine. The Enterprise seeks to accelerate HIV vaccine development through greater strategic focus, researchers, and collaboration. The scientific strategic plan describes major challenges and makes key recommendations. Major activities to support the implementation of the Enterprise scientific plan have already started and finally, all stakeholders are expected to take specific actions to achieve the Enterprise vision, and that vision is to develop a much-needed HIV vaccine. Many thanks for your attention.

[APPLAUSE]

**MITCHELL WARREN:** Thank you, Jose, and more important than the Vaccine Enterprise is the fact that he saved us three

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minutes and 27 seconds and that is - I think that's probably unprecedented in the 16<sup>th</sup> International AIDS Conference - leaving all the more time for people to please make their ways to microphones, I believe 1, 2, and 3 and if you would identify yourself, although we did save some time with Jose, please be as brief as possible so we can get to the questions. Number 3, please.

**DAMIAN:** Hi, my name is Damian. I'm from the United States. I have a question about vaccine technology. So, and maybe this can be answered by the speakers, particularly Dr. Tartaglia and the right Honorable Minister.

All of these technologies that Bill and Melinda Gates have been funding utilize the immune system and fundamentally, vaccine utilize the immune system to assault the virus that we're trying to defeat, HIV in particular. I wonder if there's any investment happening in technologies that do not require the immune system itself to fight HIV since HIV is targeting the immune system and where those technologies stand - I mean outside of antiretroviral therapy.

**PEGGY JOHNSTON:** So your question is - are there any technologies being developed that don't target the immune system?

**DAMIAN:** So my question is, for example, pox virus models that utilize HIV genes in vaccines work on the premise that you're going to prepare the immune system for an eventual

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exposure to HIV and so presumably since - well, most of the pox virus models involve mucosal activity, you're going to have an influx of immune cells to the site of infection, which could be the vagina in a woman's case and, if that were to happen, some of those cells were not capable of withstanding the assault of HIV then you would perhaps be promoting an infection. So I guess my question is, are there technologies that do not require the immune system itself to combat HIV in development?

**PEGGY JOHNSTON:** Well, while Jim's thinking that one over because I know he wants to comment, I think, first of all, your point is well taken that in fact, we do have to be sure that immunization in activating immune cells is not going to make one more susceptible to infection. And we do that through very thorough evaluation both pre-clinically as well as in early clinical studies.

And, in fact, there have been some - one candidate vaccine I know that did, in fact, through selectively stimulating only CD4 cells, probably made that infection worse in an animal model. So the goal here is to balance that activation of the target CD4s with activation of CD8s. And I'll see if Jim wants to comment further on other approaches.

**JIM TARTAGLIA:** Well, I'm sure that there are ways and - eliciting non-specific immune responses that may act to neutralize virus but it would be in a very transient fashion.

As Rafick very clearly stated, the value of vaccines relies on

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immunological memory and so that memory is imparted by whatever the vaccine technology is delivering HIV components in order to do that.

And your question is also interesting that maybe some of these other technologies could be used in concert with vaccines. But with respect to vaccine development, as we sit here today, we're still trying to find out how to best induce significant immunological memory against HIV.

**MITCHELL WARREN:** Microphone number 2, please.

**FEMALE SPEAKER:** My question is regarding HIV controllers or nonprogressors. I know Dr. Sekaly mentioned them but I'm wondering what we know about this group of people and how we can use that in vaccine development.

**JOSE ESPARZA, MD, Ph.D:** There was some echo. So your question was, how do people control HIV?

**FEMALE SPEAKER:** Yes, and how we can use this knowledge for the rare population of people how do control HIV without medications. How can we use our understanding of them to aid us in vaccine development?

**JOSE ESPARZA, MD, Ph.D:** I think that's a very, very important question and in fact, I kind of alluded to in my talk, I think long-term on progressors, which are those individuals that have been infected and I would control infection without any other intervention so mostly throughout their immune system. They are really providing us with,

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hopefully, answers and that we can then use them to benchmark our potential vaccines.

And I think what we know already is that those individuals have very broad immune responses. They have very good CD4 responses, very good CD4 memory. They have also very strong CD8 effector cells. But to come back now to a vaccine and be able to mimic this, this is really the challenge. There is - I think a lot of indications that you need the autoimmune response, you need strong memory, you need strong effector cells, and I think the challenge is [INAUDIBLE] really try to mimic this.

**MITCHELL WARREN:** Number 3.

**MALE SPEAKER:** I'd like to speak about [INAUDIBLE] of our [INAUDIBLE] knowledge about HIV. We are very interested by antibodies by T cell immunity and we have completely forgotten the most important point in HIV. It is the variability - no data on HIV variability has been done except one and this is the data I would like to inform you.

In the Pasteur Institute in France, they completely succeed to reduce HIV intervariability. It is a very important breakthrough because if you reduce HIV intervariability, you have not to make a vaccine against millions and millions of [INAUDIBLE] but only a less numerous number of types. The researcher is from the Pasteur Institute from Paris, I repeat. It is not [INAUDIBLE], it is [INAUDIBLE] GP and from Simone [INAUDIBLE]. You know them probably if you work at the Pasteur

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Institute. They published in 1999 that they put magnesium in the cell culture of HIV and surprisingly, the HIV variability completely decreased tenfold. It is the first time in my knowledge that a person succeeded to decrease intervariability. So I saw the [INAUDIBLE] for your [INAUDIBLE] there is no work, no team, no scientific team searching to develop this point of attack.

**MITCHELL WARREN:** Thanks so much. I don't know if anyone would like a - thanks very much again. Does anyone on the panel like to respond to that comment?

**RAFICK-PIERRE SEKLAY:** I think the point you make, that you have to control the HIV variability and to [misspelled?] be able to induce a good efficient vaccine, I think is a point that we all have to grapple with. And I think it's again, one of the challenges that we have to deal with.

But I think that whenever you have a pathogen and you have an immune response, you're always going to be reducing your variability because there is a selection and at one point, what the virus does is always try to escape the selection and selects [misspelled?] for mutants so I think - except if you try to reengineer HIV but in a vaccine, I think there always will be this Catch-22 where HIV will always try to escape the immune response.

So I don't see how you can limit absolutely HIV variability but we know very well that it's a challenge that we have to

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face, and one way to face it is by inducing as broad an immune response as possible against many, many different epitopes so that this way - HIV is not able to escape all the effector cells of immune response.

**MITCHELL WARREN:** Thanks, Rafick. Microphone 2, please.

**DINA LAUMAN [misspelled?]:** Hi, Dina Lauman [misspelled?] from the United States. I've been very encouraged by some of the passive studies using monoclonal antibodies that have shown protection or at least modification from disease over the last few years but the amount of antibody in terms of milligrams per kilogram that have been required for protection are somewhat concerning. And I was wondering if you might be able to speak to any of our other viral models that we have in terms of how the level of antibody protection needed for HIV compares with, for instance, yellow fever or influenza.

**MITCHELL WARREN:** It's such an excellent question that we are getting there.

**PEGGY JOHNSTON:** Your point is well taken. Whether or not one needs that same level of antibody on board - remember those experiments were all done with systemic administration of antibody and protected against both systemic and mucosal challenge so whether that level of antibody actually needs to be on board when the initial exposure occurs or whether we can rely on memory to then get up to that level, I think is still an open question.

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However, I will also amend that by saying that none of us are yet pleased with - completely pleased with the current immunogens and the level of antibody that we're seeing and the quality of antibody as well.

**JIM TARTAGLIA:** And the durability.

**PEGGY JOHNSTON:** And the durability. Thanks.

**MITCHELL WARREN:** Microphone 3, please.

**DAVID MATOBU [misspelled?]:** Thank you very much. My name is David Matobu [misspelled?] from Uganda. The AIDS Support Organization. My concern or my comment is about the community involvement in the whole process. I think one thing we have to emphasize is the political leadership right from the national level to the village level because this is where we are going to have the volunteers who are going to take part in the trials.

So I think - I don't know how to go about it, I'm a former member of Parliament so I'm talking about the political leadership - that has got to be mobilized if we are going to have any success in vaccine research because it involves people. They've got to be mobilized and they've got to be led. I don't know how to go about it, from you, the experts, but I suggest this is something that we have to consider very, very seriously. Thank you very much.

**MALE SPEAKER:** Yeah. I'm going to jump into the fray here. I felt like that guy that was just in the DVC studio and was put

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on the air because he thought he was an expert on the Internet or something so I didn't want to jump in on any of the other discussions for fear of being way outside my league but politics - I know a little bit about and I think my - the only comment that I'd like to make on your comment, sir, was that it really is incumbent upon - In a democratic society or in any civil society, to keep the - you've got to keep the pressure on the political decision makers. Because the fact of the matter is there are so many pressures on a health care budget, on a public health budget, that there's - and all of it involves people whose lives might be in danger that it's so important to - If you want to have success on something that's obviously long-term in terms of getting to a better place on this, you've got to keep it on the agenda, and it has to be a civil debate because I'm here at this conference, next week - might [INAUDIBLE] Mental Health Conference. And although none of you might be at the Mental Health Conference, there are people just as passionate as you and just as committed as you who are demanding that society face the mental health crisis and this could be true in any civil society, by the way.

So I guess my point is that you have to recognize that - that the pressure's on any political decision maker are [INAUDIBLE] and just as intense and involve people who say if you don't sign on the bottom line in terms of your commitment and your dollars and mobilization, people are going to die and

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that is true in this terrible disease. It's true on a thousand other terrible diseases and what we have to do as a civil society is to make sure that we have the proper balance and the proper perspective and the proper mobilization, if you will, to keep this as a priority. So I'm not sure I've solved the question raised, but I wanted to put it in a, perhaps, a bit of a different spin and in a different context because these are the issues that public policy decision makers, ultimately, have to grapple with.

**PEGGY JOHNSTON:** We'll take two more questions and then we have to clear the room for the next session. Number 2.

**NICOLE LONDON:** My name is Nicole London from Canada. I just had a question about whether or not you could comment on prophylactic vaccines and whether there is any in development.

**MALE SPEAKER:** We look at where the field is today, we have a phase III proof of concept in [INAUDIBLE] with canary pox and the Vaxgen and the Prime Boost. We have phase IIB ongoing, the Merck Adeno and also the VRC is moving towards a phase IIB with a DNA prime adeno boost.

And then there's a number of different vaccine candidates or regimens that are either in phase I or completing phase I to look at safety and immunogenicity whether it be with adeno, DNA, pox, proteins, and combinations thereof. So there's a number of things in the pipeline.

I will say that there's a lot of things that are repetitive

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and that also provides the need as Jose said, for greater coordination and interaction so that we can learn together and we don't necessarily duplicate things in the future.

**PEGGY JOHNSTON:** I would refer you to pick up a copy of the HAVI report, which has a very nice table of what is ongoing in vaccine development right now. Thank you. One last question.

**MALE SPEAKER:** Actually, it's a comment. I think the point that was made about the monoclonal antibodies protecting monkeys, I think, is one of the most fundamental ones that we have to face in vaccine development and the reason is because all licensed vaccines that we know that are effective in men are based on the production or regeneration of neutralizing antibodies. I believe also that one of the most important findings that I hear in this conference is the fact that it seems that now two groups have shown that the virus that is transmitted seems to be the one that has less glycosylation [misspelled?] on the envelope.

So when experiments for neutralization with monoclonal antibodies are conducted with a strain that have high glycosylation [misspelled?] and so on, it's not surprising that using protective studies, which are based on those response curves, you have to use high levels of antibodies. That may not be the case in the natural [INAUDIBLE] where the virus does not have this protection as seems to be demonstrated by these two groups and furthermore, those were challenges like Dr. Rupert

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spoke this morning about that were inordinate in terms of the amount that was put in those animals. Most people don't get exposed to that kind of volume so there is a quantification factor and there is a specificity factor that has led an enormous value to this work [INAUDIBLE] antibodies because indeed, bringing forth the fact that a vaccine is truly possible because neutralizing antibodies are capable of inducing protection and that's the comment.

**PEGGY JOHNSTON:** Thank you for that comment and thank you for your attention and I would remind you to pick up copies of the reports to take with you. Pick up your trash for the bins. It will help them turn the room over much more quickly for the next session. Thank you very much.

[END RECORDING]