

# Center for American Progress



## **SPECIAL PRESENTATION:**

### **“PREVENTING HPV, EASY AS 1, 2, 3 SHOTS? ENSURING ACCESS TO THE NEW ANTI-CANCER VACCINES”**

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SHIRA SAPERSTEIN: We're a few minutes late so I'd like to get started. I want to, first of all, welcome you to the Center for American Progress. Probably most of you know this already, but it's a two-and-one-half-year-old, progressive think-tank, and we address a wide-range of critical policy issues, both international and domestic. Among those: public health, women's rights, bioethics, and science in society, which is obviously a reason to have this briefing this morning.

As those of you in the room undoubtedly know, Merck and GlaxoSmithKline have recently announced a huge medical breakthrough. Two new vaccines to prevent infection with human papillomavirus – or the strains of human papillomavirus, I should say, that are the leading cause of cervical cancer. Cervical cancer is a leading killer of women worldwide, and in this country almost 4,000 women die every year from cervical cancer, disproportionately those who are poor and women of color. The development of these vaccines is obviously something to celebrate and it could save hundreds of thousands of lives, but the medical breakthrough is really only part of the story, and there are a number of hurdles still to jump before we can realize the benefits of the vaccines.

Ensuring access to the vaccines will be an enormous challenge. There are issues of cost, health, health infrastructure, and politics that have yet to be addressed, and these issues are even more significant overseas than they are here at home.

Fortunately, we have some wonderful public health professionals who are leading the way and we have asked four of them to address us today to begin exploring these issues. I think in your packets you have short bios for the speakers, but let me just briefly introduce them. Our first speaker will be Deborah Arrindell, who will give us – she'll start us off and give us some of the political and social context into which these new vaccines will be introduced. Deborah is the vice president of health policy for the American Social Health Association and the head of Washington's D.C. office. She has more than 25 years of experience in social policy, including work for women's economic justice, reproductive and sexual health, and employment and training.

Our next speaker will help us look at some of the scientific and funding challenges of the vaccines, and that is Professor Neal Halsey, who is the director for the Institute for Vaccine Safety, and professor of the Department of International Health, Disease Prevention and Control Program in the Johns Hopkins Bloomberg School of Public Health. He also has a joint appointment in the Department of Pediatrics in the Johns Hopkins University School of Medicine, and his research interests have focused on vaccine preventable diseases.

And then our third speaker, Greg Zimet, is a professor of pediatrics and clinical psychology in the section of Adolescent Medicine at Indiana University School of Medicine. He will be helping us look at issues around the acceptability of these new vaccines among pediatricians, parents, and the public.

And then, finally, to make sure that we have an international context and some sense of the international challenges we have Dr. Tom Broker, who is the president of the International Papillomavirus Society, which is sponsoring or cosponsoring a major series of regional clinical training and scientific workshops in countries around the world to further HPV education, advocacy, and public health activities in advance of the anticipated availability's of these new vaccines.

So I'm supposed to ask you all to make sure you turn off all pagers, cell phones, other kinds of interruptions, and without further adieu I'm going to turn it over to Deborah. I'm going to be a ruthless timekeeper. We've asked people who really have hours and hours of information to give to us to limit themselves to 12 minutes because I want to make sure that we have time for questions and answers, so Deborah we're ready for you.

DEBORAH ARRINDELL: Well, my cell phone's refusing to go off, so I can't help that. (Laughter.) Anyway, thank you so much. I want to first thank the Center for pulling this briefing together. This is a wonderful thing, an important thing, and I think that we can't really hear too much about it. We need to be – all of us – constantly learning, gathering as much information as we possibly can. I think that those of us who are working on these issues regularly find that every time we go to one of these meetings and learn a lot, we leave with a whole other set of questions that we hope that the next briefing will answer for us, so I am certainly very, very much looking forward to listening to my colleagues and learning and calling them all next week with all the questions that I leave here with today.

I've been asked to talk about a couple of things. One, to just kind of give you a thumbnail sketch of the disease, talk a little bit about the politics of the issue, and remind us of some of the issues that are going to be coming down the pike that are as yet unresolved, that are going to be kind of ongoing questions for us, and things that we really might not know until the FDA has approved the vaccine and the ACIP, which Neal will be talking about, has issued its recommendations.

How many of you feel that you have more than a cocktail party knowledge of HPV? How many of you have actually ever been to a cocktail party where people wanted to talk about HPV? (Laughter.) I think I should probably rethink that question. If anybody talks to me about HPV at a cocktail party, I'm planning to leave so it can't be a party. (Laughter.)

HPV is the name of many, many types of viruses, viruses that affect the skin. They infect the skin. There are more than 100 types – probably more than 100 types, depending on who's counting, but there are more than 100 types of these, and these are viruses that, as I said, infect the skin, and they're the viruses that cause warts on your hands and feet. Those are pretty harmless viruses. About 30 of those viruses are genital papillomaviruses, and those are viruses that are the ones that we will be concerning ourselves with and talking about today.

Of those 30 types, those are divided into viruses that are considered low risk and viruses that are high risk, and two of the viruses that are high risk and two that cause genital warts, are the ones for which the vaccines are being – are being in development – or have been developed – have been developed and for which we are waiting for approval, and Neal will be talking about those in a couple of minutes.

Probably one of the most important things to know about HPV is that it's the most commonly – the genital HPV is the most commonly sexually transmitted disease in the country, if we're just talking about the U.S. It is very common. If you take a snapshot of the United States at any given time, you would find probably about 20 million people infected. About six million people will become infected each year, and it's estimated that most of us – somewhere between 50 to 80 percent of sexually active people – will be infected with HPV at some point in our lives.

For most of us, these are transient infections. Some of us never even know we have them. You have them, if you have a healthy immune system, your immune system will clear the disease – clear the infection within – probably about 90 percent of infections will be cleared within a matter of months. Where we get concerned about it is where it is persistent, where these – where the infection is persistent, chronic, your body does not clear it, and you don't get the kind of treatment and follow-up that you need to ensure that it does not progress to cervical cancer. Left untreated, these high-risk types can progress – can cause cervical abnormalities, and these cervical abnormalities cause – can cause cervical cancer.

Cervical cancer actually is already – we know that cervical cancer is preventable, it's treatable, and it's curable. Women who receive regular Pap smears, DNA testing for HPV, and the appropriate follow-up care don't develop cervical cancer, which is why, as Shira mentioned, it is much more a concern for women who don't have access to good healthcare, women who are not being regularly Papped, and women who are not receiving follow-up and treatment. Those women, unfortunately, disproportionately tend to be women of color, low-income women. So while HPV affects all of us, cervical cancer, as it turns out, is much more likely to be a disease of poverty, which is why the access issues raised by this vaccine are of great concern.

The other issue I've been asked to talk about is the politics around HPV and I apologize – I have – I'm suffering this morning from every speaker's nightmare – all of my notes – all of my carefully long worked out notes, all of my fabulous quotes to read to you, are sitting on my desk at 13<sup>th</sup> and K – (laughter) – so I wasn't even going to confess to that, but as I'm feeling increasingly stupid, I thought I would go and play the sympathy card. (Laughter.)

The politics of HPV have been very interesting. Those of you who've been working on the politics around HPV for quite a while have as much an understanding, if not a better understanding, than I do of the real complexities around it. HPV made its political debut in probably 2000 – 1999/2000, and it debuted not out of a concern for

what do we do about cervical cancer and what do we do about keeping women healthy, but it really entered the political arena as part of a larger debate about sexual health and abstinence and marriage programs and monogamy, and lots of things that were really pretty unrelated to cervical cancer. Because of that, there was an awful lot of – there was a lot of negative press around it. There were punitive political – political maneuvering around it, and there actually some very punitive legislative initiatives that grew out of that era.

HPV emerged as kind of the bad-boy of STDs. It was the one disease for which prevention messages were much more complicated than there were for other diseases. You couldn't quite – you couldn't say quite simply, "Use a condom and you're protected," because of the skin-to-skin transmission. The messages around condoms and HPV were very complex, and are still a little complex, though I think that with research they're getting clearer. As a result, there was a lot of kind of negative politics going around, a lot of partisan politics, and a lot of kinds of politics of sexual health – politics of sex and monogamy and abstinence.

That continued into the very early stages of the – the early information that we began to get about the vaccine, so when the vaccines – when we first started hearing about the information coming out of the clinical trials, the messages that we were hearing around HPV were still very highly politicized. And there was a time – and some of you have heard me do it – when I had a laundry list of some scary and some amusing quotes from organizations like the Family Research Council and the Medical Institute for Sexual Health, and some other organizations about the vaccine. And a lot of those comments really had to do with whether or not it would encourage promiscuity, would it discourage abstinence, would it send mixed signals to kids, would it cause psychological harm, would it cause emotional harm? It was quite a list of quotes from these organizations and it was very chilling and caused an awful lot of concern.

My favorite moment was that in researching those, I found a woman whose title is Director of Life. (Laughter). I've always wanted to call her up. (Laughter) Could you do my closet? (Laughter.) Could you help organize my life? But I can say that although I think although I think that it is not helpful to pretend that none of that happened, because it's so much on our minds and so many of us are kind of locked there, I think that there's been an awful lot of progress in that arena in the last few months. You've heard a lot less of it. There's been a lot less negative stuff in the press about HPV, and about the vaccines and, in fact, some of the more onerous statements have been removed from the websites of some of those organizations. And actually some other – some of the organizations have issued statements that I don't have to read to you today, but have issued statements that are much more supportive of the HPV vaccine, and that is actually really good news. And I think that what that says is that this is – in the face of science, in the face of what we know to be a sound public health intervention, that the political – those kinds of political messages have not been able to survive in this environment. This is just not an environment that nurtures that kind of politics.

The Family Research Council, from whom the quote that we saw most often about it leading – vaccines leading to promiscuity now has issued a statement pretty much saying that they support the development of vaccines. There is a caveat in that statement, or in their press release that accompanied the statement, that said something along the lines of “and these are decisions that should be made by adults for themselves and their children, and they should be free to make these decisions,” which, of course, gets to the issue of whether or not these vaccines will be mandatory, which Neal will be talking about a little bit more.

And the other kind of issues that I hope that we’ll be talking about that this discussion will raise for us, and we can spend a little bit of time on it at the end, are a lot of kind of unanswered questions. I mean, what we know is that this vaccine will deal with the strains that cause 70 percent of cervical cancer. That leaves the remaining 30 percent. It means that women will continue to have to be Papped. Those messages will have to be loud and clear. Abnormal Paps will need to be followed up with DNA testing so that we can see whether or not women have HPV, and what kind of strains they have. So those messages are going to have to be things that we kind of keep front and center.

In addition, I think that the issues of access for low-income women, for women who receive their services from clinics – will those women have access to vaccines? There is going to be a lot of catch-up vaccine issues. Will those women have access or will the women that have access to the vaccines, women who are least likely to die of cervical cancer anyway, who are already receiving the kind of interventions that are keeping them safer?

So with that, I will stop and turn it over to Neal.

MS. SAPERSTEIN: Thank you, Deborah. Neal?

NEAL A. HALSEY: Well, thank you very much. I have the privilege to talking about the vaccines themselves. Just to emphasize a couple of points that Deborah made, cervical cancer is very common. We’re fortunate that in the United States we have a relatively low incidence of cervical cancer as shown by the white in these colors. Colors in green, and increasingly dark green, have higher incidence rates of cervical cancer, so globally this is an enormous problem. In spite of the screening with Pap smears – and it’s recommended for all women – we still have 14,000 women every year in the United States who develop cervical cancer caused by the human papillomavirus, which you have heard a lot about already.

The vaccines to protect against this infection are made in brewers yeast, taking advantage of technology that was developed for the manufacture of Hepatitis B vaccines. They induce the yeast to produce the L1 protein from the outer surface of the HPV, and then they’re manufactured in large quantities. And the unique characteristic of these particles from the outer surface of the virus is that they self-assemble into a small sphere that looks like the virus, but it’s not a complete virus. There’s no complete virus; there’s no risk of getting the infection from the vaccine. It stimulates an immune response that

protects against the viruses without actually causing the infection – some of the magic of the immune system.

The types – Deborah’s already mentioned that Types 16 and 18 – 16 is shown here in pink, and 18 is in the orange – protect – they cause about 70 percent of the cancer in the United States and the rest of North America. A smaller proportion in Latin America, and in some of the other areas of the world, but the majority of cancers in every place in the world where it’s been looked at to date. Therefore, both manufacturers – the GlaxoSmithKline Cervarix, and the Merck Gardasil – both have Type 16 and 18. Merck has chosen to add Type 6 and 11 to their vaccine because those two types also cause about 90 percent of genital warts, which are an important problem in their own.

Both vaccines are administered in a three dose series over a six-month period of time, similar to the original Hepatitis B recommendations when it first became available for adults and adolescents. The vaccine – once they’re manufactured, these virus-like particles – they form these little spheres that you can see here on an electron micrograph that look very much like a virus. The goal, of course, is to protect the cervix against the effects of the infection and the every progressing changes that occur to – after infection for some time to a low-grade cervical neoplasia here that progresses to high-grade and then progresses to cancer, so that’s what we’re trying to prevent.

This is a schematic showing what Deborah said: that a large number of people actually clear each of the HPV infections, but some don’t. They go on to persistent infection and then this epithelial neoplasia, a long complex word but CIN, and it’s the high grade CIN that then moves on into cancer. So our goal here is to protect against persistent infection, and protect against the high-grade infection.

So far the efficacy studies show – most of them show close to 100 percent protection against persistent infection, but because of the study design, some women weren’t studied long enough to know whether they cleared it or not, and so some of the studies as low as 70, but usually close to 100 percent. And almost 100 percent in all studies against the high-grade CIN that predisposes to cancer – so very, very effective vaccine; as effective, or more effective, than our other vaccines against other diseases.

Merck is going to be filing – excuse me, Merck did file in December with the FDA for licensure of this vaccine. They’ve asked for an expedited review, which is then completed in six months. The usual process is an 11- to 12-month process and FDA hasn’t decided whether they’re going to grant that expedited review or not. We’ll find out soon. GSK is filing this year in Europe and several other countries. They haven’t announced their U.S. filing date. It won’t be this year; it’ll be at least another year before they file in the U.S. But both products may be available in some countries this year, and I think there’s a good probability that Merck will be successful in getting licensure this year, but it’s impossible to predict because the FDA doesn’t say anything until they make their decision, and that’s appropriate.

The efficacy studies that have been done were in women 16 to 23 years of age, and these little white dots with the bar show the height of the antibody response that they develop to the viruses, and these types of antibodies protect against the viruses. Now, Merck has done what they call bridging studies to look at the immune response in younger children – younger – both males and females, and you get an even better antibody response in younger people. I like to say that by the time we grant people the right to drive cars with driver's licenses, we're already over the hill with regard to our immune response to several things, so the best immune response is in people under 16 years of age.

Also the antibody titers are much higher than what you see. This is with natural infection. These are the antibody titers after natural infection, and this is a logarithmic scale, so this goes up tenfold, another tenfold here, so it's 1,000 times, so you get much higher response to these viruses with the vaccines using these unique viral-like particles. And they persist. They persist for at least four years now – 48 months – that they've been followed, and the efficacy has been shown to persist for at least three and one half years in the follow up studies.

So this is the U.S. immunization schedule. And as Deborah said, once the vaccine is licensed we'll hear from the advisory committees as to when the vaccine should be used, and who it should be used for. There's no doubt in my mind that this should be another one of the universal vaccinations.

Now, if FDA grants the data from those bridging studies, it may be licensed down to as low as nine years of age in the data that I've seen, but 11 to 12 years is the right target for the giving vaccines to protect against sexually transmitted diseases. And you certainly can do this maybe a year or two earlier and, as I've come to learn, there's a lot more – a lot of women who are being exposed at even by 12 years of age, but this is a good – we used to call it an early adolescent visit, but some people objected.

The schedule is made by the Advisory Committee on Immunization Practices for CDC, the American Academy of Pediatrics, and the American Academy of Family Physicians, and they all agree upon this schedule every year. They're already having meetings and deliberating as to how the vaccine should be used. I'm pretty confident this is the target, plus older individuals who've not yet been vaccinated. But we'll wait to hear from them later this year.

The cost of the vaccines have not been announced, but it's likely that this will be a fairly expensive vaccine, and perhaps more expensive than any of our other vaccines. The CDC has put together data on what the actual costs are through the federal program of all the vaccines that are given to children and adolescents. The figure at the far right, the 2006 figure, is a projected figure with what they are estimating might be the cost of HPV, and then there's another rotavirus vaccine coming along. Over \$1,000 by the end of this year to potentially immunize a child in the public sector, and in the private sector the prices will actually be higher.



We have a problem, though, in that we don't have adequate insurance coverage for immunizations for adults. These are data for 18- to 64-year-olds. We have private insurance that covers immunizations for about 40.9 percent public. That takes you up to about 50 percent, but 50 percent of adults are either underinsured for immunizations or totally uninsured, so that means half of the adult population will not have access to some third-party payer who will provide them with this vaccine. This is a major problem with implementation.

With regard to the public immunization funding, most of the vaccines are, of course, given to children. We have a vaccines for children program which is highly effective, but additional funds are needed through Section 317 funds, which are monies given to the states every year to run immunization programs as well as to buy some of the vaccine for people who are not eligible under the VFC program, and then Medicare and Medicaid. The problem with 317 funds is that they've been declining in recent years in real purchase power. Because we've added vaccines, the total number of people who could be immunized each year with these vaccines is shown here, and it's declining, and it's going to decline even further with the availability of these additional vaccines. Something needs to be done to help move toward more stable funding through 317 funds so that the states can have programs that can provide immunizations to adolescents and young adults. Action is needed here, and this is where I think we should target efforts to help improve bringing these vaccines to women throughout the entire population.

Hopefully, we'll do a little better than happened for Hepatitis B vaccine. This is coverage rates in children. It took nine years to get high rates – over 90 percent – of children immunized against Hepatitis B, but look at the problem in developing countries, as shown in the yellow line at the bottom. It's a bigger problem in developing countries than it is in the U.S., but yet we're not doing a very good job of getting Hepatitis B vaccine to all children in the world.

In addition, the total number of antigens that we immunize against in the U.S. and Europe are much higher than they are in developing countries, and that gap is widening because of the increased availability of vaccines in recent times. The Gates Foundation and the WHO and the Global Alliance Vaccine Initiative are trying to target this and trying narrow that gap, but it's unlikely to happen quickly.

There's no doubt about the power of vaccines to protect children and adults against disease, as evidenced by the impact on all of these diseases. Soon after the vaccines are introduced and widely used we see dramatic declines, and sometimes total disappearance of the diseases that are there, and I hope someday soon we'll be able to say that we've done the same thing for HPV and cervical cancer.

In conclusion, these vaccines offer the potential for preventing most, but not all, cases of cervical cancer. The vaccines are going to be expensive. We need increased public support for programs to deliver these key vaccines to older children and adults.

Thank you.

MS. SAPERSTEIN: Thank you. Greg?

GREGORY ZIMET: Can we get the –

DR. HALSEY: Oh, yes. We can try.

MS. SAPERSTEIN: Oh, sorry.

MR. ZIMET: Okay, my focus is really going to be on some of the attitudinal research about how healthcare providers, parents, and individuals – adolescents and young people – feel about, and their attitudes about, the potential for these vaccines.

We've heard about – the vaccines are – have been shown so far to be very safe. There haven't been any major problems identified with safety. They appear to be extremely effective, particularly against those specific types that are included in the vaccine obviously and clearly have the potential to substantially reduce rates of cervical cancer when they're used.

However, despite the obvious benefits of HPV vaccination, which are very clear, availability of the vaccine may not automatically translate into vaccine acceptance and use. Again, in order to be used, it has to be acceptable to healthcare providers. They have to be willing to recommend the vaccine, parents have to be willing to accept the vaccine for their children, and adolescents and young adults also have to be interested in getting vaccinated for optimal effectiveness of the vaccination programs. We've also heard about some of the logistic issues and I'm going to reemphasize some of those and bring up some others.

We really haven't had a broad, standardized preadolescent or adolescent healthcare visit. There's been a lot of efforts to establish such a visit, but that hasn't happened yet in any broad sense. I think the hope is that, in fact, this vaccine and some of the other adolescent or preadolescent vaccines will help to leverage that kind of a visit. This vaccine is going to require for optimal efficacy a return for the second and third doses, and that may be a challenge. You know, how do you get these young adolescents, preadolescents, back for a second and third dose? And that certainly was a challenge with Hepatitis B vaccine, particularly before mandates.

We're going to be seeing – we already have multiple adolescent focused vaccines, and this will add yet another one to the mix. How are people going to respond to the idea of multiple vaccines being administered during a single visit? The cost issues that Neal brought up are enormous issues that will have to be dealt with.

The other thing that we don't know about – there's been a tremendous amount of media attention already. That's only going to increase over the next several months, and we really don't know what effect pharmaceutical advertising, as well media attention on either side of the issue, may have ultimately on acceptance.

So let's look first at healthcare providers and see what we know about their attitudes about this HPV vaccination. We have research that's looked at nurse practitioners, Ob/Gyn's, pediatricians, and family physicians – and in general across these groups there's really positive attitudes about the idea of HPV or other STI – sexually transmitted infection – vaccinations.

In summary, the important thing for healthcare providers is that there's approval and recommendations from their professional organizations, like the American Academy of Pediatrics. In general, there's a relative preference for vaccinating older adolescent patients, and young women as opposed to young men. There are still questions about whether the vaccine is efficacious in young men, so the whole issue of who should be vaccinated is still up in the air, and conversely, a relative reluctance to vaccinate 11- to 13-year-old young women and some preference for a vaccine that covers both warts and cervical cancer.

Moving on to parents, quickly, some of the issues that people have brought up and wondered about is how will parents feel about the sexually transmitted infection issue of HPV vaccine? Will parents be worried that approving or wanting their kids to be vaccinated against HPV will be interpreted as approval of sex? Will vaccination then lead to early initiation of sex or reduce condom use or risky sexual behavior, and how would parents describe the vaccine to adolescents or pre-adolescent children? So these are the concerns that have been raised, but in fact the research suggests that parents are really, really interested, by in large, in this vaccine, and in sexually transmitted infection vaccines in general.

What the studies so far indicate is that what parents seem to be focusing on is not so much how the infection is transmitted, but how effective the vaccine is, and how severe the disease is that the vaccine is designed to prevent. It's very important to parents that a vaccine be supported, recommended by their healthcare provider. In general, parents seem more comfortable with the idea of vaccinating older teens, but not by a huge amount. There's limited opposition to these vaccines, but in my own research and in other research it seems to be associated with concerns about the vaccine leading to increased practices of unsafe sex.

This is a small study I wanted to show because it shows – it's a brief – they used a very brief behavioral intervention – and in this study before the intervention, there were 55 percent of the parents wanted the vaccine for their kids, which is already encouraging. But after the intervention, which again was a very brief intervention just really providing information, education, that increased to 75 percent, mostly from those who had been undecided. So most of the increase in the pro-vaccine parents here came from the undecided group.

So some of the questions that have been raised, you know, should be sexual transmissibility issue be avoided when talking about this vaccine? I think there are several points to be made. One is that, to date anyway, the research does not support the

need to avoid this issue. Parents are focused on efficacy, again, and focused on the severity of the disease that the vaccine prevents. They are less focused it seems on whether the infection is transmitted sexually. Avoidance of the STI issue is not realistic in my sense. Media attention has already highlighted this issue, and I think it is – it would be a mistake to presume that somehow it can be avoided. Any vaccine that includes types related to genital warts, already the cat's out of the bag essentially, so it seems like a bad idea to try to actively avoid this. Certainly it makes sense to talk about this vaccine as an anti-cancer vaccine, and I would completely support that approach to talking about it, but I think actively avoiding the STI issue is a mistake.

We need to think about why we encourage preventive behaviors in general, and I'd thank Susan Rosenthal, one of my colleagues and friends, for thinking of these analogies. You know why do we cover electric sockets for infants? It's not because we are worried – it's not because we expect that they're going to electrocute themselves, but we want to prevent an uncommon behavior, a rare behavior, that's risky. We're not trying to encourage them then by putting covers over sockets, to play with sockets. Same thing with seatbelts, we don't have kids wear seatbelts because we want them to become reckless drivers. I think it's important to realize that a lot of preventive behaviors are to prevent rare but serious outcomes. We don't put fluoride in water because we want people to stop brushing their teeth. So, I mean, there are a million of these kinds of analogies.

When we look at individuals' attitudes, one of the things that's very striking – this isn't just individuals, parents, healthcare providers as well, particularly pediatricians – there's a lot of confusion regarding HPV. What is HPV? What is it's – you know – what is the relationship with genital warts, cervical dysplasia, abnormal Pap tests? People don't understand these things. The link of HPV to Pap testing is not well understood, and there's really a poor understanding of the meaning of Pap test results.

Nonetheless, there's a high level of interest among adolescents and young adults in getting HPV vaccines and other STI vaccines. Key determinates: it's important that they know what HPV is and what it can cause. People look to physician recommendations as being very important in terms of their own acceptance of the vaccine. If people have positive beliefs about vaccines in general, they're more likely to feel positive about this kind of vaccine. People are also relatively accurate assessors of their own risk behaviors, so people who understand their own behaviors place them at risk for sexually transmitted infections are more interested in prevention. For adolescents the parent's attitude about vaccination is very important, so I'd like to think of it as sort of a reverse food chain. Adolescents look to their parents, and parents look to the providers, in terms – and providers look to their professional organizations in terms of interest in this vaccine.

So summarizing, again, there seems to be a lot of interest among providers, parents, and adolescents in vaccinating young people against HPV. There are no major problems identified as of yet with the whole STI issue. Parents – and I really want to emphasize this – parents want to protect their children, and parents are mostly motivated

by that desire – to protect their children – rather than as a desire to withhold treatment or prevention. Parents and providers show a relative reluctance to vaccinate younger versus older adolescents, but this – in at least one research study I did, this held true for both STI vaccines and non-STI vaccines. It's clearly an issue that going to need to be addressed because, as we've heard, ideally you would want to target 11- and 12-year-olds for this kind of vaccine.

Some of the strategies to facilitate uptake: people have discussed different strategies and some of the things that have come up are, is it possible to use existing visits like sports physicals as an avenue at least to start vaccination? The vaccines, as I mentioned, could be used as leverage to create and normalize a regular preadolescent visit. It would be worth looking into school-based vaccination, although there may be some issues with this. It certainly makes scheduling easier and follow-up easier, reduces time and transportation demands, and may decrease cultural barriers as well.

The message I think – the take home message, in a sense – we know that risk-based strategies for vaccinations do not work. We tried it with Hepatitis B vaccine and it largely did not work. What works are universal recommendations, so – based on age. So when we're thinking about HPV, we want to universally recommend vaccination at age 11 or 12 because that protects the most vulnerable youth. The vast majority of adolescents – of individuals do not start engaging in sex until older ages. They don't start at age 13, but the most vulnerable children we want to be able to protect – and I think that's the idea is we want to protect all children, by vaccinating at 11 or 12 or protecting them as they are vulnerable, but we're protecting all of them as they go through adolescence and into young adulthood. This is really not just an adolescent vaccine, this is a vaccine for adults as well, for – you vaccinate as children, but it protects them into adulthood.

And again, I want to thank Susan Rosenthal and Jessica Kahn who are friends, colleagues, and collaborators of mine, and have shared some of their slides as well.

Thanks.

MS. SAPERSTEIN: Thank you. And last we're going to turn to Tom to talk about the international context.

THOMAS R. BROKER: Thank you, very much. I really appreciate that the Center has pulled together this forum. It's very timely. I'd like to represent some of the international perspective on what we're trying to do with the subjects that have been discussed by the other panelists, but now extending it to the worldwide. (I've?) seen a picture from Neal very similar to this.

HPV is primarily a problem of poverty, of the underdeveloped portions of the world. You can see – in my case it's red, not green – the red areas are the most severe with the incidence of cervical cancer, but I want to emphasize that major parts of the world, for instance the Soviet Union, the Islamic world, have not even been surveyed, so

in many cases we don't know how severe it is. China used to have a – has a light color right now, but I think that color, in fact, is going to be tinting toward the red when more extensive studies are done.

Basically, while there are about 14,000 new cases of cervical cancer in the U.S., worldwide it's about half a million. Approximately a third of a million women die each year. The analogy I like to use is that it's similar to about four airplane crashes a day, every single day, of lost life. This rather overwhelming diagram are all the human papillomaviruses that are now known. In fact it's about 120 types and, as Deborah mentioned, some of them are involved in the mucosal area – the mucosal surfaces – the anogenital tract and also the head and neck region.

All of the viruses in that top arch, so-called alpha papillomaviruses, are capable of infecting the genital tract. What I wanted to point out is that just through the similarity in DNA sequences, these have been grouped into what we're now calling species, and this Species 9 includes HPV 16 that you've heard about as responsible for about half of all cervical cancer. But I want to point out that there's another six types very, very similar to HPV 16 that are not covered by the vaccine, and why that's important I'll get to in a moment.

The next group with HPV 18, the so-called Species 7 marked in blue, has five other viruses very, very similar to HPV 18 capable of causing cancer, but not included in the vaccine. Another group in Species 6 has four viruses capable of causing cancer not included in the vaccine. This group also has four viruses capable of causing cancer and not in the vaccine. And just for perspective, HPV 6 and 11 that cause genital warts and laryngeal papillomas are low-risk and that's where they reside in the (taxonomic?) tree.

The point I want to make is that while there is a good start in the formulation of the vaccines to target probably the four most common viruses, there's very similar viruses that are not yet covered, and that is illustrated in this figure. Each successive bar shows the amount of cancer that could be prevented by including yet one more virus in the vaccine program. On the left is the experience in North America, mainly the U.S. and Canada and Europe, and then on the right is Central and South America. What's not shown is Asia and Africa. So HPV 16 is the top bar and it accounts for about 50 to 65 percent of cancers. The next bar shows the gain of adding HPV 18 to the cocktail. That takes us up to about two-thirds of the cancers. Everything below that is disease that would not be prevented or covered by the current formulation of vaccines. If we were to look closer at Asia, we'd find that HPV 52, which is a close relative of HPV 16, and which does cause cancer, as you can see from the chart down toward the bottom, is actually a very significant cause of cancer in other parts of the world. So as we think about global vaccination, as well as domestic here, we have to be in the long run thinking about expanding the coverage to include perhaps 10 to 14 high-risk virus types.

Now, I'm going to in a sense play devil's advocate. I want to first say that I'm a strong proponent of the vaccination program. It's truly enabling us to see the light at the end of what's been a very long and grim tunnel, but I want to also add some cautions as

to – so that our enthusiasm doesn't totally run away with ourselves. The first I've already mentioned: that only either two or four of the types of 46 that can infect mucosa are even included. We don't know, but I frankly do strongly suspect that when we do eradicate or minimize the HPV 16 and 18, that their very, very close relatives will fill in. Nature abhors the vacuum and these ecological niches are going to be vacant when HPV 16 and 18 and 6 and 11 are minimized, and I'm deeply concerned that there'll be backfill of those ecologic niches by these very, very similar types. I think it's imperative to expand the coverage in the vaccines.

We don't know, however, because the studies have never been done, whether a cocktail with 14 types would be equally effective against all 14 or whether they might actually conflict with each other. We simply don't know. We don't suspect that there's much cross protection of one type to any other even similar type. So far the evidence doesn't suggest that. We also do not know if these vaccines would be effective in the context of immunodeficient diseases. Certainly HIV/AIDS stands out, but other parasitic diseases, even malnutrition or chronic illness. In a study I did, people with end-stage renal failure were reactivating their latent HPV in middle-age years, so immune capacity and capability makes a big difference.

Now some of the logistic challenges. The reason these vaccines are so expensive is they're really hard to make. They're very, very unstable particles. Those virus spheres that you saw have to be kept cold from the moment of manufacture to the moment of injection. This raises an extraordinary challenge for vaccination in underdeveloped nations and remote villages where electricity is not even available. I mean, even today we hear that Iraq, for example, has electricity maybe a few hours a day if they're lucky, so keeping a vaccine cold would be a big challenge.

Another huge logistic problem in the underdeveloped world is the need for three shots spaced over a six-month period. In many cases people would have to walk miles just to get to a village where there might be a clinic and then have to do it two more times over a six-month period. That's a big challenge, and weather even becomes a challenge because so much of the world is dependent on the rainy season versus the dry season issues.

We do know that serologic titers declined steadily following the third shot, as you saw from Neal's presentation. The response is extraordinarily robust to these particles, but we simply don't have a timeline on what amount of serologic capability will be left after, say, 10 years or 15 years. We don't know how long protective immunity will persist and whether it would be restimulated quickly through memory cells upon exposure to an actual infecting agent. But it may become necessary to have booster shots somewhere down the line, especially if 10- or 12-year-old children are being vaccinated, and maybe somewhere in their 20s or 30s and maybe there's going to be a divorce and a second marriage where there's a reexposure to other sources may require booster shots later in life. We simply don't know.

Now a little about males. Obviously with any sexually-transmitted infection, males are part of – a very integral part of the equation. And I think we could say this is, like many diseases, a ping pong situation. Men give it to women, women give it to other men. We don't know yet if males will receive adequate protection from this particular vaccine. The studies in males are only just beginning in the past year or so. We don't have a timeline to know whether they'll work, but I do want to point out the problem with the herpes virus vaccine. They work pretty well in females, and they don't work very well at all in males. And the big issue is that the – in the female, the vagina and the cervix are mucosal epithelium. In the man, the shaft of the penis is a cutaneous epithelium with a very different local immunity, so we don't even know if it will work.

Now just for talking points, is it ethical to give one section of your population a medical procedure to protect a different section of your population? Do you give men a vaccine to prevent cervical cancer in women? It's a fairly interesting bioethical question. But maybe of a more practical nature, is it economically reasonable to give vaccines to males to protect women when in fact you could for the same price vaccinate twice as many females and get the coverage directly where it is most needed? We clearly are going to be having to address limited resources.

Now the footnote to all of that, of course, is that men do get mucosal infections with HPV. Well, it's almost never discussed, but 100,000 men a year get penile cancer from HPV; primarily HPV 16. Many to most of them die. It's also a significant problem with gay men and, frankly, it also affects women having anal intercourse. Anal papilloma and anal cancer is of epidemic proportions now. These vaccines would protect against those sites of infection and disease, as well as cervical.

Now, a potential and inadvertent consequence that we're a bit concerned about: of all of the medical procedures and tests and services available that I'm aware of, the Pap smear is one of the great success stories of all time. After its implementation and expansion to universal availability in, let's say, Europe and Canada and the U.S., there's been an 80 percent decline in high-grade cervical dysplasia and cervical cancer deaths – an extraordinary achievement. If we had the same achievement in ovarian cancer, prostate, or breast or lung, with an 80 percent reduction, I mean, we'd be hanging out the banners of success. The Pap smear is an extraordinary success story. If somehow the message gets out that because of this vaccine it's less necessary to go in for an annual Pap, women may be missing the opportunity for other general physical exams, update on reproductive services, and sexual health and mammography, so we hope that this is not an inadvertent outcome. Greg had just mentioned the value of the vaccination program to bring adolescents in for health visits, and I think the same pertains to women.

The family values issue has come up. Deborah mentioned it. Cervical cancer is a family value issue. In Latin America – I just got back from a long trip there promoting HPV meetings – the average age of cervical cancer is about 30 years old. These are young women with young families, children, and they're dying at age 30 or thereabouts. It's a value to keep those moms alive and the families together.



The second thing is recurrent respiratory papillomatosis. Infections of the larynx is typically – not always, but typically a transmitted infection from a mom to her baby. It affects about 7,000 American babies each year and to protect those newborn kids and young kids from this disease, which is caused by HPV 6 and 11, is an extraordinarily positive possibility.

But one of the most astounding and unexpected statistics is that about 30 percent of the children who have laryngeal papillomatosis, which can cause respiratory obstruction and death, occurs in adopted children. So those people who, for example, favor adoption over other decisions, this is a family value to help these kids lead a better life and the adoptive family have a healthy child. We have the battle to – we have the opportunity to win one battle against cancer as well as STDs and to provide kids a healthy future.

So what are some of the other worldwide challenges? Lack of awareness, the great range of political systems and whether or not they're committed to preventive healthcare, diversity of religious and social standards and expectations, screen costs in the face of economic disparities. In certain African countries, as an example, the average budget available for healthcare is \$1.00 a year per person. That means that 300 people would have to forego treatment to get one round of vaccination. And in many cases, women especially and their children have minimal access to healthcare.

We have competing issues with other extremely serious diseases: HIV, malaria, tuberculosis, other childhood infections, even basic malnutrition, availability of vitamins – huge problems. We have societal issues that are challenging us economically: environmental deterioration, pollution, and certainly population growth. In major parts of the world the sex trade is a fact of life. It's unfortunate, but a reality. Condom acceptance, which Deborah mentioned, is part of the discussion. Most of the world has little or no screening. You talk to people in most countries about Pap smear, they don't know what you're talking about. HPV is not a reportable sexually transmitted infection. I'm glad for that, but the fact is there's very little statistics. Extreme shortages of trained healthcare workers. I was talking with a colleague about – who's from Zambia, two days ago, and the capital of Zambia has 12 doctors for about a million and a half people. There's not enough people to go around to provide health.

There's a logistic problem in manufacturing the vaccine. It's hard to make. We're seeing in the news every day how hard it is to make a flu vaccine when we know it's coming and we know how to make it and we know how to distribute it. There's not the manufacturing capacity for papilloma vaccine today. One of the opportunities is the production of both the vaccines and the diagnostic screening tests to be outsourced to the developing nations – local manufacture, stimulate local economy. This is going to take companies like Glaxo and Merck and others to perhaps provide these subsidies for outsourcing.

And some final thoughts. Papillomaviruses are part of the human condition. They are ubiquitous. Over 85 percent of the women in studies I've done, at some point in

life are HPV positive, especially evident when they're immunosuppressed. Another thing that has not been totally talked about is this is a prophylactic vaccine. It is not a therapeutic vaccine. Anybody who has HPV today is not going to directly benefit from the vaccine. We still need to do the research to develop therapeutic vaccines and certainly in the meantime to improve screening tests for these and any other papillomaviruses. We need to develop a comprehensive network of clinics, especially in the third world.

And I thank you very much for coming today, and I look forward to continuing the discussion.

MS. SAPERSTEIN: Thank you very much to all of you. A lot of information, and I probably personally have enough questions to fill up the rest of the time, but I guess I won't do that. So let me see from the audience if any of you have questions, and if there's someone you want to direct it to, please say that as well. Questions? Or comments, I should say? Yes, and please introduce yourself as you speak. Thanks.

Q: Hi, I'm Maura Burke Weiner. I'm a board member of the Recurrent Respiratory Papillomatosis Foundation. Our daughter has RRP, which is the disease that Tom was referring to.

Merck has its own series of issues that it's been going through recently, as do a lot of the large pharmaceutical companies. How much oomph is there going to be for them to – how much are they going to put up with in terms of pressure around this? And are they going to take advantage of the positive side of this to kind of wipe their nose a little bit?

MS. ARRINDELL: Can I take a shot at that?

Q: Yeah.

MS. ARRINDELL: Is there anybody here from Merck who would like to take that on?

MS. : (Off mike.)

MS. ARRINDELL: Okay. I had – I went to Merck and had meetings with a lot of their staff in December. I think Tom went in November. We just kind of have both had these meetings, and it appears that they are very, very excited about this vaccine – very optimistic. And in fact I think that they are responsible for a lot of the change in the political environment around it. They have been systematically meeting with those organizations that were – responsible is not the word I'm looking for, but were – we were seeing repeatedly quoted making very negative comments about it, and they have been meeting with those organizations regularly. I think that they've kind of turned around a lot of this dialogue. And because of the things that you were talking about, because of

concerns with some other issues, I think they're probably even more likely to energize around this, and Tom might have a –

MR. BROKER: Yeah.

MS. ARRINDELL: – another perspective.

MR. BROKER: No, I completely agree. In several positive features, they've – they're phenomenal, frankly, at their market research and understanding, both in the U.S., but I can say all around the world. They are doing solid research as to attitudes, the challenges, some of which I mentioned, about distribution or the different types that may be more prevalent in Southeast Asia, for example. They are very much a player and have been for at least a decade in that sense.

From a purely business point of view, they've been facing some real interesting challenges over the Vioxx issue and they are looking at this as the foundation and the savior of the company. Believe me, they have a huge stake in this, just as we all do.

MR. HALSEY: Can I just add one point in that I think the respiratory papillomavirus problem in infants and young children is really hidden. It's not known. There's not much out there. And with other vaccines that have been introduced in recent years – the meningococcal vaccine – the voices of parents of children who had been affected, many of whom had died, really helped play a role to push the national programs towards universal immunization with that. And I would encourage your group to be more vocal and to get that message out. I have seen children who do have this problem. I have seen children walking around with tracheostomies in developing countries where it's an even bigger problem, so there as a need for that information to be out there.

Q: I'm Vijaya Melnick. I'm from the Immunologist Center at Georgetown, as well as the University of the District of Columbia. My question is that how willing will Merck be to work with the vaccine-producing companies in Brazil and India and so forth if the vaccine is found to be very efficacious and to be used in those countries? That's one question.

The other question that I have is that once we have the vaccine and the cost is going to be prohibitive for the developing countries, so unless we have a mechanism to produce this vaccine at lower cost, such as in Brazil and India and so forth where the generics have been produced, we're not going to see it distributed around the world where it is very badly needed.

MS. SAPERSTEIN: Neal?

MR. HALSEY: Let me start the response. I can't speak for either company, but I am well aware that GlaxoSmithKline appears to be taking the tact of going after the international market fairly aggressively and early. Both companies studied their vaccines in many different countries. Merck's was in 13 different countries. I'm trying to – it's a

similar number for the GSK vaccines. And GSK is going aggressively for licensure and approval in Latin America in particular, and so I know they will do that. I would be surprised if Merck didn't take a similar stance.

You're right, if the vaccine is to be produced at lower cost, people need to work toward transfer of the technology to developing country manufacturing plants where they can make the vaccines cheaper; Brazil, India, are two prime examples. Those steps come later usually, and they first have to get themselves established by having licensure in some countries and getting some markets so that they have some income and then can move forward. But voices from – I hope that there are voices from developing countries to speak up about the need. Everyone who has been involved in human papillomavirus disease from an academic standpoint is well aware of the burden of disease in developing countries. And I hope that WHO and the Global Alliance Vaccine Initiative that's helping with other vaccines will pick up on this very quickly.

MS. SAPERSTEIN: Thank you. There's a question over here?

Q: Hi, I'm Janet Riessman with the Association of Reproductive Health Professionals, and I want to thank the panel. It's been terrific, and it's a really great collaboration of talks.

Speaking just domestically, I know that whether or not this vaccine becomes one of the required vaccines for children will make an enormous difference in terms of how many children are vaccinated. And it seems to me that if it isn't a required vaccine, and I know it's complicated and it's state by state, et cetera, but it will simply increase the disparity between the poor and the non-poor with respect to HPV and then cervical cancer. If only the people who can afford it and for whose insurance covers HPV vaccines, then – do you see where I'm going with that? So what – if someone could speak a little bit to the process of it becoming a required vaccine for children and the likelihood of that in the near future or whatever.

MS. SAPERSTEIN: Can I ask you, Neal, first to just address how in general vaccines are made mandatory at the state level and –

(Cross talk.)

MR. HALSEY: The speaker mentioned this is information that the states have to have. The states make a decision. There's variability from state to state with regard to the timing of when vaccines are added, which vaccines are added, and so it will be individual state legislatures that have to implement or add to the existing laws, and there's good reason for that. We shouldn't just have one national program that insists that everything be the same in every state so that no one can predict exactly how that will take place. But the steps that are necessary are first of all the availability of the vaccine and we don't have it yet, so nobody is taking any action.

Almost always, for all of the other vaccines that have become mandatory, there's some time gap where people – there is widespread use, there is increased comfort after we've given it to many millions of people that there isn't going to be something that we hadn't detected earlier, and then individuals such as yourselves working within the states – every state that I know of, it's been activist groups and a lot of physicians involved in making this process happen.

What's different about this vaccine than all of the others is that this vaccine is initially going to be approved for basically adolescents and adults. The other vaccines that have become mandatory are vaccines that are given in very early childhood. And so certainly this could happen, but it would be the first vaccine that would be giving – and assuming Merck is successful in getting the FDA to accept the comparability of the immune response as a measure of protection, it's not going to be licensed for young children, I mean, under 9 years of age now. The initial licensure might just be for 16 and above. By the time you're 16, you don't have to attend school in many places, so all of this gets confounding. So I think we first need to get the licensure for a younger age group and then looking to see the practicalities of getting the vaccine delivered to them and widespread availability and enough supply, because you can't mandate something when there isn't enough of it made, and we have had shortages of a number of vaccines.

MS. SAPERSTEIN: I'm going to ask Deborah to follow up a little bit to that and then anyone else who wants to regarding the politics of pushing for mandatory access, even if it's a couple years down the line.

MS. ARRINDELL: Well, I think that's a hard question because I don't – I'm learning about vaccines in this process, and I think – and I was going to ask Neal this before I move on to that – I think that, isn't there a way in which these recommendations come from the ACIP that makes them more likely that people will give them or that states would pick them up? Aren't there levels of recommendations –

MR. HALSEY: Yes.

MS. ARRINDELL: – different ways that ACIP recommends them?

MR. HALSEY: Right. And you're right, it's usually – it's a strong recommendation that all children should receive, which leads to the picking up by the states in the mandatory immunization process. So I – my guess is there will be a very strong recommendation for a universal use of this vaccine. All the science points in that direction. But those decisions haven't been made yet. So –

MS. ARRINDELL: All right, well I think that for the – some of the kind of issues that the audience has raised, especially those relating to poor children that – and I don't know enough about how these vaccine processes work to know what kind of case you would even make to be able to make or how you would make the case for a mandatory – so that you would pick up 16-year-olds, and to – I think that a lot of these things really depend on how they're licensed, Shira. I can't think it through really quite beyond that.

I think one of the things that we worry about, and I don't know how these recommendations affect what happens to catch-up vaccines for all of those adult – you know, for adult women that are low-income women and likely to – less likely to receive Paps and those kinds of things either, so I think there's a lot we don't know until we get – hear from the FDA and the ACIP. Is that accurate?

MS. SAPERSTEIN: Greg. Go ahead.

MR. ZIMET: There's just one thing I was going to add that I think is maybe a little bit encouraging is that there are at least, I don't know how many states, but quite a few states that require Hepatitis – for those children that didn't get it at school entries, they have catch-up mandatory hepatitis B vaccination for transition to middle school, and if this vaccine was approved for the 11-to-12-year-old group, then that would at least fit in to that pattern for those states that have mandated transition vaccination.

MS. SAPERSTEIN: And wait for the speaker. Thanks.

Q: Hi, I'm Cynthia Dillard, Guttmacher Institute. I also thought it was a fantastic panel. One thing I'm a little bit unclear about is the utility of this for older women. And what I mean older, I mean women who are ready, sexually active, since there's a pretty good chance that you're sexually active, at some point you're going to have HPV. I thought I read that studies were underway – that Merck was doing studies on this age group, like a post-infection prophylaxis, but I wasn't sure from your comment. And I've heard other people question whether in fact these studies are really underway.

MR. BROKER: I can answer some of it, but –

MR. : (Off mike.)

MR. HALSEY: Tom's already answered it in part. The studies are underway. I'm not as optimistic as some people have been in the past that the vaccine will have an effect in helping clear the virus. So far the data don't look strongly that that will happen. But any woman who is not yet infected with any particular type of either the 16 or 18 would have some benefit. If she is already infected with one of them, then she'll have less potential benefit. And that's going to create a potential problem down the road in that there will be women who do develop cervical cancer after receiving the vaccine where they were hoping that it was going to protect them. That's a credibility issue that has to be faced.

MR. BROKER: What I would like to add is that this is a moving sense of research. We have today the availability of a quadrivalent vaccine from Merck, for example, but that can easily be expanded to include other types of the same general nature, but a tremendous amount of work is underway to develop therapeutic vaccines for existing infections. The worldwide effort against HPV diseases is truly extraordinary. It's – we've kept a fairly low profile because we didn't want to be talking about this

subject when we couldn't offer something – when I say “we,” it's the whole field – either in terms of better diagnostic capabilities, better Pap smear reading, better DNA testing, and also vaccines. But the part we haven't really been able to talk about is all the work underway to develop therapeutic vaccines, which I have little doubt that they will occur. It's just a question of time.

It's a very tricky virus. To put it in some perspective, the virus family is 100 million years old. Papillomavirus is in, effectively, all the vertebrates: snakes, amphibians, birds, and almost all the mammals. This virus coevolved with the vertebrate kingdom, and it's just part of what it is to be alive. It's a virus that's extraordinarily successful at persisting and passing itself down to the next generation not just in people, but in any animal you've ever seen. So it's something we just have to deal with.

MR. ZIMET: Related to that, the persistence issue, we often talk about in most cases women clear the virus, and it's actually not at all clear that it's cleared entirely but becomes more latent and undetectable by our current diagnostic techniques. There is some evidence, for instance, that people who are immunosuppressed, like people with AIDS, people who are post-transplant, that there's a reemergence of what was thought – what was apparently a “cleared” infection, so –

MS. SAPERSTEIN: Go ahead.

Q: I'm Kathryn Guccione with Women in Government and I wanted to go back for a moment, if we could, to the whole implementation questions and whether are not any of you could address the Vaccines for Children Program which may help to eliminate some of the economic and other disparities that exist for access to this vaccine and how the Vaccines for Children Program may – if it's recommended from the ACIP that the vaccine be included in that program or what the process is?

MS. SAPERSTEIN: Neal?

MR. HALSEY: Yeah, you've actually touched on the key elements of the process. First, the ACIP must vote to recommend the vaccine and it's a separate decision as to what it is covered under the Vaccines for Children Program. If the – let's take some hypothetical situations. Assume the vaccine is licensed for down to nine to 10 years of age. Then the ACIP has to decide if they're going to recommend it universally. And if they do, then – and they recommend that universally at a particular time, then they may specify under a separate vote that the Vaccines for Children Program should cover all eligible children at those ages. And I can tell you they sometimes take half an hour to get through a vote to try to get it nailed down exactly right because those votes do carry with it the power to provide the vaccines to a large number of children in this country. That will help immensely.

It is a vaccines for children program. It is not a vaccines for adult program and it will not – and it's unlikely that first time around that it's going to cover adults, but there has been some effort to try to expand this. And there have been some congressional bills

introduced that talk about broadening the coverage for adults under a similar program. So far they have been gone very far because the cost would be very large and in this day there's a lot of resistance to larger such programs. So I think if we can get it licensed for children and get those votes, then it will get started at least.

Q: Thank you. Yeah.

Q: Dana Weckesser with the Pan American Health and Education Foundation. We're supporting a project in Latin America for low-level screening for cervical cancer. Hearing that these vaccines require the cold chain and that they're quite vulnerable is a concern to me. Are there any pharmaceutical companies out there that are actually looking into developing vaccines that are more stable, that can be actually taken out into the field?

MR. BROKER: Yeah, just as efforts are under way to develop therapeutic vaccines, other efforts are to develop vaccines that can withstand room temperature, even elevated temperature. Obviously it's an economic benefit to the company as much as to the public. If they can make them and they're more stable, transportable, they'll have a much wider ability for distribution, so there are indeed efforts to bypass that serious problem.

MS. SAPERSTEIN: Yeah. Go ahead.

Q: Thank you. Good morning. Good morning to the panel. My name is Robin Lewis. I'm with JHPIEGO, which is an affiliate of Johns Hopkins. I manage the cervical cancer prevention program at JHPIEGO. We work internationally on developing simple, effective screening and treatment approaches for cervical pre-cancer. We're also a member of the Alliance for Cervical Cancer Prevention, which is – of which PAHO is a member as well.

My comment really is regarding the likelihood of successful vaccine introduction in developing countries because we know that cervical cancer really is a disease of poor women in low-resource settings. And to have a real meaningful impact on the global burden of disease, we really have to intervene among those women who are most at risk and that's in poor countries, which isn't to say that the vaccine wouldn't be important here. But in any case, when it comes to vaccine introduction, the problem has often been that a product is developed, approved, and made available, but it doesn't reach the people who need it because there's no systematic approach to integrate it and to make it available to the population at risk.

My question is whether or not there would be support for a global initiative – a coordinated initiative to link vaccine introduction with existing screening programs and whether or not this – or what comments or observations this panel might have in that regard.

MS. SAPERSTEIN: Tom, do you want to start?



MR. BROKER: Greg.

MS. SAPERSTEIN: Greg?

MR. ZIMET: Well, I think much of the issues brought up are of course extraordinarily challenging, and one of the great ironies when any of us submit a grant to NIH is that we talk about the burden of whatever disease we happen to work on. It could be diabetes, it could be heart disease, it could be papilloma. And we also cite the big worldwide numbers as justification for what we do. But as you point out, right now we maybe have the capability to develop to rich nations and all of those people that in fact are why we're doing the work remain beyond the reach of the capability or practical and unfortunate economic reasons.

I wanted to show one thing if it's still here. We're trying to tackle this through information and awareness, and I know PAHO and JHPIEGO and the Gates Coalition and so forth are doing incredible things to understand how to reach people who have been somewhat beyond the reach up until now. So what we've been doing, as an example, we recently had a big international meeting in Florianopolis, Brazil. Is that up on the screen?

MR. ZIMET: Okay. I just got back from Buenos Aires and Montevideo. They'll be organizing a big meeting covering their entire countries next year; Santiago, Chile, as well; Bogota, Colombia for the Andean nations in the northern part of South America. That level of awareness will spread through ministers of health and health networks at the governmental level, the medical societies, and rank and file physicians and nurses and other healthcare providers. Each of those meetings would have about 500 people, and then they in turn would spawn other meetings. If we look in Africa, we're looking at meetings now in Cape Town, Zambia, Senegal, probably Egypt, certainly in Turkey, as a starting point. And if we look in Asia, Japan – the big papillomavirus meeting next year is in Beijing. We just had a meeting in Malaysia, sponsored by Ajin (ph). Their next meeting is in the Philippines. We've just had one in Korea from their gynecologic society. We're working on one in Bangkok, one in Taipei, one in Mumbai.

So it's through these kinds of efforts that they're we're trying to have as much outreach, and in that sense, the partnership with all the other nongovernmental organizations is critical. And we're trying to work together as a coalition to share our resources and spread the message even more widely. I think it's the demand from the public as much as the capability from the top that will make the difference.

MS. SAPERSTEIN: Unfortunately, we're close to out of time. I want to give the panelists a chance to make some closing remarks and perhaps drawing on where we just landed to say what each of you think the most important next steps are from the public education and public advocacy point of view if we want to move access forward. Final comments?

MS. ARRINDELL: Well –

MS. SAPERSTEIN: Deborah?

MS. ARRINDELL: I think you really summarized it a lot for the communities that many of us in this room work in and certainly that I work in, that it is going to be very important that we do a lot of public education on this issue, that we do advocacy on this issue, that we try to keep our politicians honest if we see some slippage in that area, and that we work to ensure that there's some success around this vaccine in many, many ways, not the least of which is making sure that we don't overpromise and that we ensure that women continue to get Pap smears and protect themselves in traditional ways.

MS. SAPERSTEIN: Thank you. Neal?

MR. HALSEY: With every vaccine that's been introduced, there have been concerns raised about not just the issues that have been talked about here today and sexuality and so forth, but rumors about vaccine safety issues. None have come up from the clinical trial so far, as Tom mentioned. There are no safety issues from a scientific standpoint. Of course, this will require a careful monitoring as the vaccine is introduced. But with every vaccine that's been introduced, there have been false rumors that have started. I will anticipate that there will be some here, and we just need to respond to those as quickly as possible. We need to maintain the public confidence in the systems that we have in place to evaluate the safety of vaccines after licensure. That's really what I'm – that's what I do. I direct an Institute for Vaccine Safety at Johns Hopkins, and I just expect there will be even more problems here than with the others. So expect them, but don't believe the rumors when they first come out. (Laughter.)

MS. SAPERSTEIN: Thank you. Greg?

MR. ZIMET: I think in the research that I've done and some of my colleagues have done, what's striking to me is that parents really are interested in these vaccines. I don't think – you know, this has been raised as a potential concern. I think for the most part parents are eager for these kinds of – for this kind of vaccine to protect their children and also that it would seem that the more they get accurate information about HPV, about the vaccine, the more interested they are. So it's a situation where more education, more information, if it's accurate and not rumors, really just increases interest and willingness to get children vaccinated.

MS. SAPERSTEIN: Thank you. Tom?

MR. BROKER: I had two comments. The first is that the research field as well as the clinical providers are extraordinarily energized by the vaccines. The best evidence – when we began the papillomavirus meeting in 1982, the international meeting, we had 128 people at the first meeting. We went to a steady state of about 600 people every single year at some part of the world and that was very gratifying. But in the meeting we've just had in Vancouver, 1,400 people showed up – more than double. The awareness of HPV, the sense of capability and progress is absolutely palpable.

Now, ironically there's been one strange downside to this, and that is some people at the government – NIH – think HPV is a done deal. The available research funding for the ongoing needs for HPV research is crashing. Significant numbers of us can no longer even get a grant. So the last message I would like to take is we can see the light at the end of the tunnel, but we're not there yet. These issues that have been brought up about vaccine stability, making it cheaper, making therapeutic vaccines, and making very, very inexpensive diagnostic tests remain goals that we need to work toward and that will require ongoing funding for these issues as well as for the understanding of how to distribute what we can already do.

Thank you.

MS. SAPERSTEIN: I would like just to add that as we can see there's enormous potential and enormous challenges, but in meeting or beginning to address some of the challenges for the HPV vaccine, we will have to be addressing broader public health challenges of vaccination programs and funding and general access to medical care, particularly for adolescents and the divide between the richer and poorer world. So I hope that we will keep all of that in mind; that this is an opportunity, as difficult as these challenges are to address, that in addressing them we'll be coping with and grappling with some bigger problems as well.

I want to thank the panelists. I learned an enormous amount and I thank you all. I hope this will be beginning of ongoing work in this area. I also want to just thank the Center for American Progress, and particularly Sam Berger and Rhian O'Rourke who did so much to get this panel together. So thank you all for coming and have a good weekend and rest of the day.

(Applause.)

(END)