



## **Zika Virus: Control, Monitoring, & Prevention**

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MARILYN SERAFINI: Okay, we're going to go ahead and get started. I'm Marilyn Serafini with the Alliance for Health Reform. On behalf of our honorary co-chairs, Senator Cardin and Senator Blunt, I'd like to welcome you today's briefing. We're going to be talking about the Zika virus.

For twenty-five years, the Alliance for Health Reform has been a balanced source of healthcare policy information for policymakers and the media in Washington DC and beyond. We'd like to thank the Jayne Koskinas and Ted Giovanis Foundation for their partnership and support for today's briefing. I'd also like to recognize *Health Affairs* for their partnership in today's briefly and also, for this series of briefings. And in particular, my co-moderator today, Rob Lott, who's Deputy Editor at *Health Affairs*.

Dr. Anthony Fauci is the world's doctor when it comes to the most challenging emerging infectious diseases of our time – HIV/AIDS, Ebola, and now Zika. He's the Director of the National Institute of Allergy and Infectious Diseases at NIH. Dr. Fauci will be giving us an update on the Zika virus today. After Dr. Fauci's remarks, he's going to take questions and then he is going to have to leave us. After he is finished, we're going to turn to the second part of today's program, which will be a panel that will focus on the federal response and the challenge of actually controlling the mosquitoes, monitoring, and diagnosing cases and educating patients and medical providers on the ground. At that time, we'll have a panel that consists of Rick Bright of BARDA – the Biomedical Advancement Research and Development Authority in the Office of the Assistant Secretary for Preparedness and Response, which is part of the Department of Health and Human Services; Kelly Murphy of the National Governors Association; and LaMar Hasbrouck of the National Association of County and City Health Officials.

And now, I'd like to turn over our program to Dr. Fauci.

ANTHONY FAUCI: Thank you very much. It's a real pleasure to be here with you this afternoon. As you heard, I'm going to give an update on Zika and I hope it will answer a lot of your questions but even more importantly, will trigger an agenda – additional questions that you might have, which I will leave as much time as we need after the presentation to hopefully answer them for you.

So let's see if this works. There you go, it does, thank you. So I've entitled this presentation "A Pandemic in Process" because I think it's obvious to all of you that in fact, that is what we are seeing because literally every day, week, or month, things evolve and we get new important information.

Now, in December of 2015, I wrote an article for the *New England Journal of Medicine* and I show it to you here because of the second part of the title, *Yet Another Arbovirus Threat*, when we first recognized that Zika was indeed a problem with us. And the reason I say that is this is not a new phenomenon. I mean, if you look historically at what we have seen in the Americas over the years and literally over the most recent years, we have seen arboviruses appear. And by arboviruses, that's short for arthropod-borne virus and in this case, the arthropod is the mosquito. And what we have seen is West Nile in 1999, we have Chikungunya in 2013, we have Dengue appearing at various waves over the years, and most recently, we now have Zika.

So having said that, I'm going to tell you a bit about Zika, divide it up into four parts of the talk, the first being Zika background. And I know at this point in the attention that has been paid to Zika, probably most if not all of you are very familiar with it so I'll go through it very rapidly because there are some points that I want to underscore that maybe have not been underscored in the past.

So Zika is a single-stranded envelope RNA and the important one is the second bullet. The family is Flaviviridae and the genus is Flavivirus. Why is that important? It's important because we have considerable experience over the years with very closely related viruses of the same family and genus such as Dengue, Yellow Fever, Japanese Encephalitis, and West Nile Viruses. And in fact, we have successfully developed vaccines to more than one of these. So the issue of a vaccine for a Flavivirus is not completely new territory to us. The other issue is that it's transmitted primarily by the Aedes mosquito – Aedes genus mosquito.

So let's take a little bit of the history. You're aware of it. It was first recognized in 1947 in the Zika Forest of Uganda. First recognized doesn't mean that it evolved at that point. It didn't all of a sudden start Zika. Zika was probably around for a really long time before that. It was only recognized then. The first human cases were reported in Nigeria in 1952 and as you well know, the mystery that still has not completely unfolded is what happened to Zika in the decades in Africa and Southeast Asia? It certainly was there. We did not have any recognized outbreaks. We'll get into in the question period about how you can go back and look at stored sera and find out if maybe there were serious amount of infection. It's going to be compounded by the cross-reactivity that we have with other diseases in the area but that's another story.

Now, things changed dramatically. As I've spoken to many, many times, diseases that smolder may have aspects to it that are unrecognized until you have an outbreak. And the reason is you need a certain critical number of cases before you see the things that are uncommon or perhaps rare. So what happened is in 2007 there was an outbreak in the Islands of Yap. In 2013, there was an outbreak in French Polynesia, and then a very interesting epidemiological issue unfolded – I mean, if you want to write a textbook on epidemiology, it's right here on the slide – as it's worked its way across the Pacific until, as we talk about in Infectious Disease and Immunology, the perfect storm. And what was the perfect storm? The perfect storm was an immunologically naïve population in Brazil – a really big country that has densely populated people, not just in little villages throughout a country, in which you have a healthcare system that can recognize things that happen and you have copious mosquitoes. That was the perfect storm in that area.

Now, before we go on, let me tell you a little bit about Zika and sometimes and often compounds and confounds the issue. About 80% of the people are without symptoms, 20% have symptoms. They're usually mild – skin rash, aches and pains in the joints and muscles, fever and conjunctivitis or red eye. Rarely, you'll hear about – and we'll get into that later – that somebody gets really very serious disease but that's really rare. We'll get into the other things that have unfolded over the months in a second. But if you take Zika in a vacuum as a disease excluding pregnancy, it is a disease that's relatively mild, often unnoticed.

Okay, the modes of transmission are shown here. Let's briefly go through them. Mosquito bites are overwhelmingly the most important and most predominant modality of transmission. And I happen to have a comment about mosquitoes that I think looking at the audience, I've seen you all here in times when I've mentioned this before. But mosquitoes are really bad actors. The two types of mosquitoes that we have that are capable of transmitting, at least two, are the Aedes aegypti and the Aedes albopictus. Don't get confused at that because whenever we have overlapping mosquito populations of Aedes aegypti and Aedes albopictus, almost invariably – I say “almost” because I don't want to be wrong when somebody comes up with it a month from now – but invariably, the Aedes aegypti predominates as the major one and out-bites, as it were, the other mosquito. So even though albopictus can do it, it's the Aedes aegyptis that are doing it.

Which leads us to one of the countermeasures that needs to be implemented, and we can get back to that, I'm sure, in the questions. You do mosquito control by a variety of ways. They're shown on the slide. Importantly, clean up the environment – standing water, larvicides, insecticides, you've heard me say many times with the media, to the extent possible, stay indoors with air conditioning, make sure screens on doors and windows are intact, proper clothing when you go out, even though it might be uncomfortable in the heat, and insect repellent with 30% DEET, use it liberally.

Intrauterine and perinatal transmission. We're all now very well aware of the complication of microcephaly. We will get back to that when I talk a little bit in more detail about microcephaly and other complications. Sexual transmission, another complicating issue. So not only is this the first mosquito-borne infection that can be resulting in a congenital abnormality in a woman who's infected during pregnancy but it is also now sexually transmitted. The efficiency of sexual transmission is unclear. We know it happens. We also know that every time another report comes out, the virus is sequestered in the semen first 62 days, then 80, then 90, the latest report was 180-something. That just literally came out from Italy just today. The sexual transmission is predominantly from men to women. No sooner did we say that, there was a case report of one that looked like it was from a woman to a man.

So that's what we mean when we say things evolve. They may be outliers but you pay attention to outliers but you don't let the outlier dominate the picture. You've still got to look at what's the most usual thing that happens. But you can't ignore the outliers.

Similarly, blood transfusion, we know clearly that it could be transmitted through blood, which is the reason why there was a scramble successfully to develop a screening test for the blood in those areas in which there's local transmission.

And then there's the "other." And I say "other" because this gets back to what I said a moment ago about don't let the outlier dominate your thinking. There was the case of a lab worker in Pittsburgh who accidentally was infected with Zika. That happens all the time with laboratory accidents. Luckily, it was a mild disease. But there was a patient in Utah, as you know, who was a gravely ill man who had the highest level of viremia that has ever been noticed or even recorded with Zika who was taken care of by his son and the son got infected. Was it a particularly voracious virus? No, because the son had a mild disease. So there's something there about a very high level of viremia in a man who had somewhat of an underlying illness. That, in fact, is something you need to keep an eye on.

Okay, quickly, the current outbreak in the Caribbean and Latin America. You know now that there are a number of countries, at least 55, countries or territories, 46 are in the Americas or the Caribbean where there is active transmission as of this month – August, 2016. What this slide shows you, if you look at the dark orange, is people who are in the Americas who live in areas that are environmentally suitable for Zika transmission. And "environmentally suitable" means the right weather and the right mosquitoes. So if you look at that, living in those areas that are darkened out are around 300,000,000 people and within those 300,000,000 people, there are over 5,000,000 births per year. Those are just numbers. Don't make anything out of that that it isn't. That's just what the denominator of susceptibility is.

Now, moving onto more details about microcephaly. Clearly, there was now unquestionable documentation of the relationship between infection during pregnancy and microcephaly. Obviously,

there are going to be some that were over-called; namely areas where there was microcephaly for another reason. But the change in the rate of and incidence of microcephaly is very clearly shown on this slide.

Now, it's a very tragic situation. I mean, the pictures in the newspapers and on television are really, you know, very sad to see how babies' fetuses are, in many cases, very terribly involved with this particular infection. This is a typical picture of an imaging of the differences in size. Notice the black area above the brain on the right hand side. That should've been tissue, that's not tissue.

So microcephaly involves a couple things. It involves the interference by destruction of neural tissue of the developing brain. But also, we know that there's a situation where you have a fetal syndrome where you have development of the brain and then they get infected a little later and the brain actually collapses. And that's where you see the skin folds.

The risk, again, still needs to be completely nailed down but it looks like we're circling it and getting there – somewhere between 1% and 13% of women infected in the first trimester will have a microcephalic risk – 1% to 13%. Be careful because we know from other studies that you can have problems if you're infected in the second, and even up to the third, trimester.

Now, we're only talking about microcephaly. We know from our experience with Rubella that a baby can be born with Rubella syndrome that looks perfectly normal but may have things like calcifications of the brain, may have blindness, may have deafness, may have intellectual impairment. So the full spectrum is going to depend on following cohorts of babies for years following birth, and that's one of the things we and the CDC will be doing.

It isn't only microcephaly. I don't have time to go through each and every single one of these manifestations. They're very uncommon, because, as you can see, several of them you will not be able to pronounce. But one you can pronounce because you're going to hear a lot more about it is arthrogryposis. And arthrogryposis is when you have a deformity of the joints – and we're just starting to appreciate what the mechanisms of that might be. There was a recent study that came out a couple of days ago from Brazil in which seven children with documented Zika infection of the mother during pregnancy had arthrogryposis. And here's a picture of it. As you can see, the curling up of the hands and of the legs, starting to think that may be due to aberrant neurological signals that require contractions as opposed to a primary disease of the joint.

Guillain-Barré – again, we know it's associated. We don't yet know the precise incidence of it. There was a study from French Polynesia which showed that it was about twenty-four hundred thousand population – infections.

Zika in the United States. Remember, Puerto Rico is a territory of the United States and Puerto Rico is having a very terrible problem. They have 3.55 million people there and they are in the middle of a very serious outbreak. The reason it was predicted accurately by the CDC that it would be a serious outbreak is that it's the same pattern as we've seen with Chikungunya. In 2014, this is the evolution. May 5 to June 4 to July 4 to August 12, you see the red culling in of people who are infected with Chikungunya. It's the same mosquito so there's no reason to believe exactly the same thing is not going to happen. In fact, what is happening in Puerto Rico is that 1% of the population is being infected every week, 4% every month. So right now, we're in a crisis situation there where you have a considerable amount of

infection and over 1,500 pregnant women are already infected. That is a very serious issue in Puerto Rico.

Now, if you look at the potential for imported cases, this is a flight map – more than just a flight map, a travel map – showing that in any given year, there are a couple of hundred million passenger journeys to the United States from areas that already have local transmission. Why is that important? It's important because with the mosquitoes – and again, and I show *Aedes albopictus* and *Aedes aegypti* – focus on *Aedes aegypti* for the time being. What we're having now in the United States – Continental United States – is over 1,800 cases of travel-related Zika. Now, the US territories, the 5,548 at the bottom, is mostly Puerto Rico. But focus on the 1,800 cases. Many of them are in Florida – over 400 of them are in Florida. So when you have a situation of infected people in the area with mosquitoes that are capable of transmitting, what you're going to have is a situation which we'll get into in a second. Of note, there are 479 – and probably more – pregnancies in the Continental United States of women who were infected. Now of that group, it's interesting data that, again, you've got to be careful with confidentiality so we don't have really solid data. But these data are real, that there have been 15 live born babies with birth defects and six pregnancy losses with birth defects. So already, you have 21 out of that 471 that's telling you that there really is this connection that we're talking about.

Now, as was predicted – and unfortunately happened – you know, we talk about the perfect storm that I mentioned in Brazil. You have travel-related cases, you have the right mosquitoes, and sooner or later, we said there would be a local transmission and it likely would occur in the Gulf Coast states. And in fact, it did. Florida has a semitropical climate right now in August of 2016. They have a considerable number of travel-related cases and they have the mosquitoes. And right now, as of last count, there were 22 cases in Florida that are locally transmitted.

This is just to give you a perspective of the location and the restricted locality of it. If you go down by that red dot towards the tip of Florida, it's an area just north of Miami in which most of the cases are originating within that one-mile radius, which is the red lines. That green box is where the cluster of case – not every single one because those cases aren't all connected. There are some singletons that occurred and then there are some that are associated with each other. Not unexpected. That's not anything that people are surprised at. And as I mentioned, most recently, there are cases now – or a case in Palm Beach County. This was just a few days ago on August 8 noticed. Importantly, that person likely traveled into the Miami-Dade area.

So let me close up with the role of Research and Development. I can't go over all of it because I want to stay within my timeframe. But what we've done is what we did exactly with Ebola, what we do with other outbreaks, is try and understand the disease, work closely with the CDC who's involved in the public health issues and the surveillance. And by the knowledge we get, determine whether or not – and in this case we can – develop countermeasures. And countermeasures are diagnostics, therapeutics, and vaccines. And in this regard, this is now a well-shown slide. We've shown it many times – of various candidates lined up in their temporal appearance into human studies. This doesn't mean that the one on the top is the best vaccine or will be the best vaccine. We don't know what the best vaccine is going to be. But the one that's on the top is a DNA candidate that we started a Phase I clinical trial on August the 2<sup>nd</sup> at the NIH Clinical Center. The other sites will be Emory and the other sites will be the University of Maryland. There will be 80 individuals in the trial. It should end by the end of 2016. If it is safe and induces the response you would predict would be protective, which is the only question you ask of a Phase I trial. A, is it safe? And B, does it induce the response that you hope it would? If it does, you move on to the second phase, and the second phase will start in early 2017.

Right behind them are other candidates, such as the one that's second – the Walter Reed, NIAID, BARDA, Sanofi. That will almost certainly go into a Phase I trial in October of this year with the same sort of thing of going on, getting the information that you need. And there are multiple other candidates.

This is just a picture of the first patient, which I had the opportunity of being in the room and watching them give the first injection. And as I mentioned, there'll be 80 volunteers in that.

I'm going to end with this last slide to remind you about what I said in the first slide is that we're not dealing with a phenomenon that's unheard of. Emerging infectious diseases have always been around. They're around now and we will continue to see them. And it's up to us to be able to be prepared to move as quickly as we possibly can to address it in an appropriate manner.

So I'll stop there. I'll be happy to answer questions, thank you.

MARILYN SERAFINI: Fantastic. So let's start with our questions. I'd like to ask that if you're asking a question you wait for the microphone and please identify yourself. And we'll start in the back here.

ALI DUKAKIS: Hi, Dr. Fauci. Ali Dukakis with *ABC News*. And I'm just wondering from what you said, this isn't something new. But what, if anything, does differentiate Zika and its spread thus far that causes worry? And what keeps you up at night about Zika?

ANTHONY FAUCI: Well, that's assuming I go to sleep at night [laughter]. So the thing about this that's really disturbing – and we've said it many, many times – is that it's the dichotomy of the disease. If you were to put aside pregnant women, it is really a relatively mild disease – 80% don't get symptoms, 20% get symptoms that are mild. The virus lasts in the body and the blood for seven days, it's gone. It lasts in the semen of men for variable periods of time.

The issue of pregnant women – on the one hand, you have a relatively mild disease that when a woman gets infected during pregnancy, it could be absolutely devastating to her and her fetus. That is an unusual situation, particularly when you're dealing with a mosquito-borne infection. In some respects, apart from the mosquito part of it, it's very similar to what we were seeing in the 1960s with Rubella. Rubella as a disease is a relatively mild disease. If children get infected before the vaccine – I got infected with Rubella before the vaccine – if children get infected, you would hope that all the young women – babies – are going to get infected. Because then when they get older, they're protected. But what happened is that some of them didn't and then they got infected during pregnancy. And although everybody else was getting a mild disease, we had the congenital Rubella syndrome, which was devastating – 20,000 babies per year in the United States had the congenital Rubella syndrome.

So that's the thing that, you know, keeps me up at night if you want to use that metaphor, is the concern about protecting pregnant women.

JENNIFER VASQUEZ: Hi, there. Jennifer Vasquez, Producer of *NBC Washington*. Dr. Fauci, in your presentation, while you mentioned mosquito control, you talked about removing standing water. Our investigative team has found an increased amount of cases here locally where local health departments and agencies have received complaints about standing water in backyards and city fountains. How

critical is it for local government to address this and what should they be doing? How should they be responding?

ANTHONY FAUCI: That's a very good question. It is not an easy thing to accomplish. I mean, for me to say, "Clean up the environment, you know, pots, pans, tires, even bottle caps," it's easy to say. And even with the most vigorous effort, it often is not adequate not because of a lack of trying on the part of authorities but because water gets in some places that are just not accessible. I mean, if you just go out – you know, I live in Washington, DC. I go out in my backyard, I have these plants and I see these plants that these little pools of water on them so I spend my morning, instead of doing what I should be doing, exercise, I'm knocking water out from my plants [laughter]. Just kidding, right?

So the answer to your question is authorities are trying very hard to do that. And you know, there's a balance between being intrusive upon an individual's home by authorities versus trying to get the population to realize that they need to do that themselves. Because you can't go into every yard of someone's home and do that. But you know, that's where the mosquitoes breed.

JENNIFER VASQUEZ: [Off mic] ...city-owned fountains or even public pools?

ANTHONY FAUCI: Yeah. You know, again, I don't want to be making statements that will certainly get taken out of context about someone who isn't doing something so I won't do that.

MARILYN SERAFINI: Okay, right here on the front?

JAMES ROSEN: Hi, thank you for doing this, Doctor. Without asking you to dive into the political realm – okay, my name is James Rosen. I report for McClatchy and the *Miami Herald*. Obviously, the *Miami Herald* is all over this, reporting there. But I think what's a little bit confusing is on one hand, health officials like yourself and then some of the members of Congress have said that the extra money is urgently needed. It's an emergency. President Obama asked for 1.9 billion, the amount's been lower than that. And yet on the other hand, we see you guys developing vaccines, doing aggressive mosquito control and so forth. In other words, acting very aggressively. And so how do you reconcile for the lay reader – how do you reconcile the fact that you're acting very aggressively in all kinds of directions and yet you say you need a lot more money?

ANTHONY FAUCI: Okay, that's a very good question. And I will give as a prototypic example of what I had to do at NIH and the CDC had to do very similar things in their own arena and their own realm. So when Zika first came and I mobilized my team in December, 2015; there was no designated Zika money. So I got my vaccine people and I got my people who had been working historically on Flaviviruses and I said, "What we've got to do is we've got to take your attention now and you're going to pay it on trying to develop a vaccine," I'm doing all these things. There was no additional money to do that. So what I did is I moved money from other accounts of money that I would've spent four, five months from then. So remember, we're in December-January. So money that I might've spent on malaria or tuberculosis or universal flu vaccine that I was planning to spend in August and September of the same year, which the malaria people weren't spending it because I was going to spend it later.

So I borrowed money from myself to get it started. Then when I sort of ran out of money that I could borrow from myself, the department – HHS with the Secretary and the approval of the White House – allowed us to move money that was in other accounts outside of the NIH and gave us a certain amount of money to spend. I got through NIH \$47,000,000 from unexpended money that was from the Ebola



accounts. Now, NIH had already spent all of our Ebola money but it was Ebola that was in other accounts that we still need. I don't want to give the impression that we don't need that Ebola money. We need it. But it was moved from another account to allow me to do the things I'm doing now.

Right now, we're reaching the point – I've told you I started the Phase I trial. I paid for that with the resources that I've just described. The Phase I trial is in no danger, it's paid for. However, once you start a Phase I trial, you need to prepare the sites – and there'll be at least 20 or more sites – in which we will do the Phase II trial. And that will be in areas where there is active infection – South America, Central America, Puerto Rico, and even some sites in the United States. So in order to have the smooth transition from the Phase I that ends in November-December to the Phase II, which I hope to start in January, I need money to prepare those sites. I need to hire people, renovate clinics, get nurses and other staff hired, get the reagents ready to go. We've reached the point now in August of 2016 that if I don't get some additional money, because we've already used up the money I borrowed from myself, using up the money that the Secretary allowed me to spend from other accounts. If I don't get additional money literally within the next days to weeks, then what's going to happen is that the transition into the Phase II trial will get dramatically delayed and may not even be able to go forward.

Is that clear?

JAMES ROSEN: So basically, the vaccine, the most promising vaccine development will be stopped in its tracks, is that it?

ANTHONY FAUCI: Well, I will not be able to transition. What people get [interruption] – well, let me just explain it again slowly. You have a Phase I trial. It starts in August – August the 2<sup>nd</sup>. It takes several months to finish. It finishes in November and December. When you start the Phase I trial, if you want to – and I'll use that word – transition smoothly to go from Phase I to Phase II, namely, don't delay, go right in and start testing if it works. In order to do that, you have to start preparing the sites now.

So what I'm saying, if I don't get that extra money now, I will not be able to prepare the sites to do a Phase II trial. If that happens, there will be a gap that's unnecessary. I will finish the Phase I and I will not be able to go into Phase II. Is that clear?

QUESTIONER: [Inaudible]

ANTHONY FAUCI: How much do I need? I need \$33,000,000 for that.

MARILYN SERAFINI: Okay. Over here and then we'll come to this side.

PAIGE WINFIELD CUNNINGHAM: Paige Winfield Cunningham with the *Washington Examiner*. Of the 1,800 or so cases in the US, I was just wondering why are so many pregnant women – you said 400 or so – is that because they're getting routinely [interruption] tested?

ANTHONY FAUCI: Yeah, that's a good question. What's happening is that when you're dealing with a disease that has a devastating impact on pregnant women, the pregnant women are the ones that go to get tested and go to their physicians and say, "You know, I think I had a rash when I was down there." Whereas if you had a man who didn't even notice it, he wouldn't care. So it is a bias in the numbers that is generated by the concern for the people who have the most devastating consequences.

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QUESTIONER: [Inaudible] ...physicians testing for this, is this a routine thing for pregnant women?

ANTHONY FAUCI: Right.

QUESTIONER: Or are you recommending it?

ANTHONY FAUCI: No, that's what – I'm not, the CDC is. So the CDC has come out with a very important recommendation. What the CDC is saying, that in the United States – all over the United States – when pregnant women go for their antenatal visits, they should be assessed – not necessarily tested – but assessed for the possibility that they may have inadvertently been exposed to Zika.

So how does that work? I'm an OB/GYN person in my office. Somebody comes in for their routine. They say, "By the way, I may not have asked you this before but have you done any traveling in the following areas?" If the answer is no, the next question is, "Your husband and/or sexual partner, has he traveled to that area?" Because he may have been inadvertently infected – 80% of them are without symptoms – and come back. Then, if that triggers a red flag, then you get tested.

MARILYN SERAFINI: Okay, over here.

TOM HOWELL: Hi, Tom Howell with the *Washington Times*. You mentioned that you need 33,000,000 to make sure this Phase II goes smoothly.

ANTHONY FAUCI: Correct.

Question: With Congress deadlocked, are you able to kind of scrounge around the couch cushions anywhere in your agency? Able to get that 33,000,000? And what would you have to take from?

ANTHONY FAUCI: Yeah. Secretary Burwell, in her capacity as Secretary of HHS, has the authority to transfer money within accounts. In other words, what she can do is to say, "I'm going to transfer some money from other things that are going on at NIH to give to you to do your \$33,000,000 trial." And that's something that is under very serious consideration right now. In fact, there's movement in that direction as we speak.

QUESTIONER: You said you're moving in that direction as you speak. What are you looking at to target and swipe from?

ANTHONY FAUCI: Well, you know, I don't want to say that if I want to continue to have my parking space at NIH [laughter]. But what's going to happen is that the Secretary will allow the Director of NIH to tap the other institutes a certain amount, it's a 1% transfer authority to come up with the – you wouldn't have to use it. I mean, 1%, we have a \$33 billion dollar budget. But we can tap the NIH's budget to give to a particular area in an emergency, and that's called the Transfer Authority. And the Secretary has the legal authority to do that and she has been discussing with us – and it very well may have already happened for all I know so maybe you could check that out when you get out of here.

MARILYN SERAFINI: And hopefully, we'll maybe hear a little bit more about that on our next panel. Maybe?

ANTHONY FAUCI: Not any more than I told you, I can assure you that.

MARILYN SERAFINI: Okay, alright, darn. Okay, yes, let's – we have a couple questions on this side and then we'll move back to the other side of the room.

NICK FORKER: Hi, Nick Forker [PH] with *Inside Health Policy*. So FDA recently released their finding of no significant impact on genetically engineered mosquitoes. Looking at that, the Florida Mosquito Control Board has agreed not to move forward with the trial until they hold the referendum in November. The manufacturer of those mosquitoes has said the same thing. I'm wondering if you can comment on how that will impact the use of genetically engineered mosquitoes to control Zika and if you think it's a wise decision given the current situation we're in.

ANTHONY FAUCI: Well, remember, the go-ahead that the FDA gave was not for widespread usage of this particular technology of genetically modified mosquito. It gave the go-ahead to do a clinical trial to see if, in fact, it works in a defined area. The only comment that I could make is that that is certainly something that needs to be pursued. As I'm sure you're aware, there always is – understandable but we'll see what the science tells us – concern about anything that might be a permanent modification of the environment, including modification of the mosquito population that might have what we call unintended consequences. You have to balance the concern of unintended consequences with the potential benefit of that approach, which is the reason why you actually do a trial as opposed to an all-or-none phenomenon. Yeah.

QUESTIONER: Hi, Dr. Fauci.

ANTHONY FAUCI: Hi.

QUESTIONER: Hi. With GSK and Sanofi making their commitment, and then a couple of other companies out there, that they're working on Zika vaccines, are you still afraid that the companies will back out if this funding doesn't come through from Congress? And what more can industry be doing right now to be moving forward with this? Are they moving as rapidly as you'd like to see them move?

ANTHONY FAUCI: Well, you know, we're very pleased with the collaborations that we've now had with industry, with Sanofi, with GSK and others. What you'll probably hear from Rick Bright is it isn't that the companies are backing out. It's that the companies in many respects are dependent on that kind of partnership that they have with the federal government, with BARDA, which provides them with things that de-risk what they do. But you'll hear more about that from Rick.

JOYCE FRIEDEN: Hi, Joyce Frieden from *MedPage Today*. I wondered if you could talk about any gaps that you feel are remaining and the knowledge of disease, the pathogenesis, how the disease works, the attack rates, any of that that you're...

ANTHONY FAUCI: Well, there are a lot of gaps. There are epidemiological gaps and there are fundamental scientific gaps. And what is the precise mechanism whereby the virus can get through and interaction with the placenta to get the baby? That's one.

The other scientific gap that's very, very important is the fact that we still don't have a highly specific antibody test for Zika. We have really good specific and sensitive PCR molecular tests to determine are you infected or are you not. Where we get into trouble, particularly in regions where there are other

Flavivirus infections that are going around, is if you ask the question, “Was I infected three months ago or two months ago,” the cross-reactivity we’re working on, the more specific you make it, the less sensitive it is. So that’s a very important scientific issue.

The epidemiological issues are still open. Like what is the exact percentage of Guillain-Barré? What is the exact incidence in various periods of pregnancy – first trimester, second trimester, third trimester – with regard to the incidence of congenital abnormalities. Importantly for the babies, what happens to babies when they’re born from an infected mother but they look physiologically normal? What about their developmental landmarks? What about intellectual capacity? What about vision? What about hearing? Those are the things that we really don’t know a lot about.

So that falls under the epidemiological gaps and the other falls under the scientific gaps.

LAUREN NEERGAARD: Lauran Neergaard with AP. Can you talk a little bit about what might be the plans for testing vaccines in pregnant women or women who are thinking about conceiving? And can you talk a little bit about the rationale behind going forward first with the DNA vaccines, since that’s kind of a new technology?

ANTHONY FAUCI: Yeah, sure, good questions. Well, generally, when you’re dealing with pregnant women, as is always the case, the safety issues of pregnant women are paramount. The safety issues with anyone and a vaccine. So when you talk about a vaccine, we’re aiming a vaccine not for pregnant women; we’re aiming a vaccine for women of childbearing age to protect them before they get pregnant. Because if you look at what happens, so if a woman gets pregnant, by the time she knows she’s pregnant, she’s well into her first trimester. So she’s been exposed, it’s already too late.

So the real target ultimately is going to be women of childbearing age and their sexual partner. That’s why you can’t forget the men here. If we didn’t have a sexual transmission issue, we’d only be worrying about women of childbearing age. But their sexual partners could inadvertently, you know, wind up giving them an issue with regard to transmissibility.

The idea of the DNA vaccine is that the fact that we went into it first is that it was ready first. And we are right now in a race of time to get the best vaccine. That’s the reason why people will ask – I’m surprised they haven’t asked – “Why do you have so many candidates? You know, are you duplicating?” No, no. Whenever you develop a vaccine, you almost always need multiple candidates and multiple platforms.

So we have DNA – it’s a very promising platform. It’s promising because it is so easy to scale up if you really need it.

Then we have the purified inactivated, which is, you know, as the whole virus intuitively would say it might give a more powerful response. The only trouble is it’s much more difficult to make, which is the reason why we’re going to start it later and we likely will not go into Phase II later.

So there was nothing special about the DNA that said go first except that it was first.

TONI CLARKE: Hi, Toni Clarke from *Reuters*. I wonder if you could talk a little bit more about the budget transfer. You mentioned that’s 1%. Is that 1% a year? And then, how do the decisions get made within NIH as to which other programs get cut? And then thirdly, do you have any concern that you

will never get that money back from Congress and that this could set a precedent for future funding discussions if people say, “Well, you could just transfer money around within NIH?”

ANTHONY FAUCI: So you’ve asked three bad news questions, haven’t you? [Laughter] Okay, so the Secretary has the authority to make a 1% transfer within an agency. In other words, she has authority on a given year to transfer money. The NIH, it’ll be up to the Director of NIH, Dr. Collins. He will decide what he will do. Would he just go – and what usually happens, to be fair, he’ll probably do a prorated the same amount across based on the percentage of what your budget is. So the Cancer Institute has a five-plus billion dollar budget. You’re not going to take the same amount from the Cancer Institute as you’re going to take from a smaller institute. So it’ll be done in as fair a way as possible.

The fact that it is being done so late in the fiscal year is going to make it very difficult to pay back them except in the next budget cycle, attention will be paid to pay back to the institutes that got tapped in the previous year. The authority is a year-by-year basis, it isn’t a one-shot deal. You’re allowed a 1% transfer per year out of that. And that’s just an emergency type of authority.

ANDREW SIDDONS: Dr. Fauci, Andrew Siddons of *CQ*. While you were speaking, the administration announced that Secretary Burwell had transferred thirty...

ANTHONY FAUCI: Right. I knew that but I didn’t want to be the one to announce it [laughter].

ANDREW SIDDONS: So with this action today, why wasn’t that done sooner? And it was for 34 or \$33,000,000, which you suggest is for the Phase II trial. Are there other areas that you will similarly have to reprogram or do a similar transfer for?

ANTHONY FAUCI: No. Actually, what I need now until the end of the year, money was mostly for the vaccine Phase II. There was a small amount of – a little bit over a million for the ZIP trial, the Zika in Infancy and Pregnancy trial that the Child Health Institute is doing. Now, you asked the question why did we wait so long, was that? We were hoping – continually hoping – that the Congress was going to appropriate the money for us. And we are in – when I say “constant contact,” I mean daily contact with either the Secretary herself or people very, very close to the Secretary at a high level of leadership in the Department. And we were continually being asked, “What do you need, what do you need?” And we had a recent meeting in which we confirmed – and this is taken very seriously by the Secretary to make sure the right thing was done – is what is the latest that you can wait before we start getting into trouble? And we had different answers depending on different agencies but my answer to the Secretary was, “I will run out of money this month if we do not have the money for me to smoothly go into a Phase II.” And she took that under advisement and I think wisely, she made a courageous decision of saying, “We’re going to have to tap in a 1% transfer other components of the NIH.”

QUESTIONER: [Inaudible] ...similar transfer for?

ANTHONY FAUCI: When you say – no, it’s other things with Zika that will have to do it? No, I’m actually good now until, you know, November-December. We’re going to start getting into trouble because I do need – remember, and I want to make sure this is clear so I’ll say it slowly – that we asked for \$277,000,000 for the comprehensive NIH approach to Zika. The money that the Secretary is allowing us to get by transfer is paying for the preparing the sites for Phase II for one candidate. If you remember the slide I showed, we have three other candidates. We have a ZIP trial – the Zika in Infancy

and Pregnancy. So we still need, in addition to the original 47 that the Secretary allowed us to spend to the \$34,000,000 that she is now using through the Transfer Authority, we need about \$196,000,000 more. If you do all the adding up, you take 277, you do all the subtraction, it comes up to that we need about \$196,000,000 more. Otherwise, the second, third, and fourth candidate will get not only slowed down, we wouldn't even be able to start them.

MARILYN SERAFINI: So I was about to say this is our last question but is everybody clear on the numbers?

QUESTIONER: Not really.

ANTHONY FAUCI: Alright, so what's unclear? I'll try to help. Okay, we asked for \$277 [interruption] – yeah, yeah, yeah.

MARILYN SERAFINI: Okay, wait for the mike, please.

QUESTIONER: Okay. So I mean, just to play the devil's advocate here, it seems that what you're doing is exactly what the opponents of the 1.9 billion or the 1.1 billion so you could – have been saying for a long time that you could do, which is you could find previously appropriated money and use it. I think what we're trying to kind of put a finger on is when do you get to the point where whether it's Ebola or malaria or other critical needs where you simply can't do that anymore.

ANTHONY FAUCI: Okay, yeah, it's a good question but let me answer it in a way that I'm very convinced of. I'm talking to you in a way that seems not casual but I'm saying, you know, I took money from this account and money from that account and then we're going to have a... All of that is extremely damaging to the biomedical research enterprise. So even though you say, "Well, you know, you took \$47,000,000 from this and you moved it over. You took this amount and you did that. And by the way, you're going to do a 1% Transfer Authority." That's really bad. That's bad for the biomedical research enterprise because we're taking money away from cancer, diabetes, all those kinds of things. So just because you can do it, what the Secretary did, and that's why I said she made a courageous decision to do something that she really did not want to do, is take money away from other areas.

So I don't see how that plays into that it's okay to do that. It isn't okay. And if I gave the impression that it's okay to do those transfers, it's not. It's damaging to the biomedical research enterprise.

MARILYN SERAFINI: Okay. We're going to take two more questions. We have one in the back here. Okay, he's good. So we've got a desperate question in the back there. We're going to take that one and one here and then we're going to need to wrap it up and let Dr. Fauci go back to work because it's a desperate situation.

SUE DARCY: Hi, Sue Darcy from *Medtech Insight*. I'm curious about next year, 2017. Do you see enough funding? What if all the stars align? What if all the Democrats take over the Senate, Hillary Clinton gets elected? Because this seems to be a very political battle. How much money would you need next year and do you think you can get it?

ANTHONY FAUCI: Well, the money that I will need through 2017, when we were asked by the President and by the Secretary how much money we'd need to go through the effort, at least get us on the road to what we would need to adequately address, that's when I put in the \$277,000,000. So

\$277,000,000 would take me through what I need to do, but the landscape changes. You never know what's going to happen with the outbreak.

So right now, I'm okay for 2017 but as is happens whenever you're dealing with an outbreak, depending upon how things shift, it may turn out that in the middle of 2017, I may say, "You know, we really need more money." I don't know what that's going to be. That could be a supplement that could go into the next year's budget.

So the 277 is the number you need to latch onto. That's what I need to do what I need to do.

QUESTIONER: [Inaudible] ...*Pharmaceutical Executive* magazine. For the Phase II study that you're contemplating, are the subjects mostly going to be young men and women because that's who you want to test it on? And are there other therapeutics or medical diagnostics that you need besides the vaccine to treat people now?

ANTHONY FAUCI: Yeah. Yeah, let me answer the second part of the question because that gets to what other – I think the gentleman from *GQ*? *CQ*? I don't know. I don't have time to read that stuff. That was a very good question. There were other things. I mean, we're focusing on vaccines but there are other things. There's diagnostics, there's screening for therapeutics, there's a whole variety of other cohort studies that need to be done.

So yes, that's what we mean by "other." So there will be need for that – for resources for that. I'm sorry, and the first part of your question was?

QUESTIONER: [Inaudible]

ANTHONY FAUCI: Yeah. You know, that, again, we're going to roll mostly – not mostly – non-pregnant healthy young men and women. When you get into a trial, depending upon the incidence of the trial and – excuse me – the incidence in a country, you may need to expand. So the trial is designed for 2,400 up to 5,000 people. The price of that will vary depending upon the number. So if it's 2,400, it's going to be X amount of number. If it's 5,000, it's going to be that. And you could change by amending the protocol. You start off with generally healthy young people of a certain age group. You then can extend it to children, you could extend it to the elderly. You might recall we did the same thing when we were doing trials for influenza. Remember during the pandemic influenza we started off by just a certain group and then we extended it to pregnant women, to children, to the elderly? We can do the same thing with Zika if necessary.

ROB LOTT: Thank you very much, Dr. Fauci. We appreciate your time.

ANTHONY FAUCI: Thank you.

ROB LOTT: I just want to ask folks to respect Dr. Fauci on his way out. He won't have time for any more questions. Thank you.

Good afternoon. I'm *Health Affairs* Deputy Editor, Rob Lott, and it's my pleasure to introduce our next set of speakers. We just heard about the scope and method of Zika spread and its potential impact on people's health. Now we turn to folks on the front lines developing medical diagnostics and

countermeasures, supporting prevention and preparing to respond street by street, neighborhood by neighborhood.

With us today we have Dr. Rick Bright, Acting Director of the Influenza Division in the Biomedical Advancement Research and Development Authority. Dr. Bright's division is leading BARDA's Zika Medical Products Development program. Dr. Bright has served as an advisor to the World Health Organization and the US Department of Defense and has spent many years working on influenza vaccine and therapeutics development at the CDC.

Kelly Murphy serves as Program Director for the National Governors Association Center for Best Practices Health Division with a focus on maternal and child health, opioid abuse, and childhood obesity. Previously, Kelly served as Policy Advisor for the Alliance for a Healthier Generation.

Dr. LaMar Hasbrouck, Executive Director for the National Association of County & City Health Officials, which represents 2,800 local health departments across the United States. Previously, Dr. Hasbrouck was the top doc in Illinois managing the state's public health agency. He has also spent, again, many years at CDC serving as the Senator's Guyana Country Director focusing largely on polio eradication and PEPFAR.

Let's start with Dr. Rick Bright.

RICK BRIGHT: Great, thank you, and thank you all for inviting us to participate in this afternoon's briefing and I'm really grateful for Dr. Fauci for giving such an elegant and comprehensive overview of the Zika virus outbreak and the situation we're facing on the ground currently. As he mentioned, I'm from the Biomedical Advanced Research and Development Authority, which I'll call BARDA, which is an office in the Assistant Secretary for Preparedness Response, which I'll call ASPR. ASPR's close coordination with local and state officials has been critical in the last ten years and we were created in responding to a number of public health emergencies including the 2009 H1N1 pandemic outbreak, the Ebola outbreak in 2014, and even the recent situation with the lead in the water in Flint earlier this year.

The response to Zika is no different. It will take all of us at the state, the local, federal, international level to be able to coordinate and protect the best that we can, public health response. We do this by working carefully together with healthcare coalitions nationwide and we develop resources to inform and guide the response at all levels. To help ensure that local and state public health responders have the resources that they need, ASPR has a Hospital Preparedness Program. The Hospital Preparedness Program is carefully collaborating with the Centers for Disease Control to develop a checklist for hospitals to help them be prepared for the Zika outbreak once it meets their doors. We're also working very carefully to prepare Primary Care, Emergency Care, and Urgent Care providers and give them the resources and information that they need including carefully written CDC-issued guidance to help them prepare and respond to the Zika outbreak.

We've also created a number of resources that are currently available including the Zika Resources at Your Fingertips guide that was developed by our Hospital Preparedness Program and is available online at our TRACIE site. The TRACIE site is the Technical Resources, Assistance Center and Information Exchange at [ASPRTRACIE.hhs.gov](http://ASPRTRACIE.hhs.gov) for more information.

We also work very closely with our partners like NACCHO to provide these resources to their membership, as well, and is very glad to be on the panel with our collaborators today.

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We are also very instrumental in leading the advanced development and medical countermeasures and other medical products that our country needs to respond to Zika.

BARDA, or ASPR-BARDA, was created with an important mission in mind to accelerate and support advanced development and medical countermeasures for chemical, biological, radiological, and nuclear threats, as well as emerging infectious diseases and other things such as pandemic influenza. As part of our mandate, we have a critical mission to accelerate the development of medical countermeasures that include vaccines, diagnostics, therapeutics, platform technologies, pathogen reduction technologies, and other medical countermeasures needed to combat the Zika outbreak.

BARDA is focusing on three main areas for the Zika outbreak. Number one, to be able to detect who is, or who has recently been, infected with the Zika virus. That means supporting the advanced development of diagnostics that can be used for the current outbreak.

Number two, to prevent people from getting infected. That means supporting the advanced development of vaccines that can be used safely in people before they are exposed to the Zika virus.

And number three, to ensure the safety of the blood supply. That means by supporting the advanced development and rapid screening diagnostic assays that can detect Zika virus in donated blood and also, in pathogen reduction technologies that can be used to inactivate Zika and other pathogens in donated blood so it can be used.

It's very, very important to know that developing a vaccine for any disease is extremely difficult. It takes a significant amount of resources, including time and money, to develop a safe and effective vaccine. It also must be guided carefully through development including manufacturing, scale-up, and clinical evaluation that's guided by our regulatory authority, the FDA in the United States. BARDA works very closely with industry to bridge the gap and bridge the valley of death the industry falls in very quickly when they develop a new vaccine candidate for any disease. This is usually that valley of death that occurs after a Phase I clinical evaluation, before Phase II clinical evaluation, because of the difficulty and the excessive cost involved in developing vaccines through development.

For Zika, we're working very closely with our industry partners to understand the landscape of technologies and platforms and approaches being used to develop a Zika vaccine candidate. There are over 30 different technologies and companies right now working very hard and very quickly to develop a Zika vaccine candidate. It's important to know that we are leveraging everything we've learned in the past from other Flavivirus vaccine development strategies, everything that we have learned in developing vaccines for Japanese Encephalitis, Yellow Fever, Dengue vaccines, and other vaccine approaches that we can use to accelerate the development of a Zika vaccine candidate. This information allows us to leverage that knowledge, to leverage the clinical experience with those technologies and vaccines, and to leverage the regulatory experience and knowledge that our regulators have with those different approaches and vaccines and adjuvants being considered for Zika vaccine development.

We anticipate right now with sufficient resources that three or four vaccine candidates will enter clinical development in 2016. With adequate funding and additional resources, we anticipate several more vaccine candidates entering clinical development in early 2017. BARDA is supporting a number of approaches to accelerate vaccine development, including supporting platform-based technologies.

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These are technologies that leverage platforms that have been used successfully to develop and license other vaccines, meaning they have vaccines that have experience in the clinic, they have a sufficient safety database that have been used in a number of people in clinical trials, and they've been in front on the regulatory authorities.

So the vaccine for Zika is novel but the platform itself is not so novel so we can use it to respond even more quickly.

We're also collaborating very carefully with our US government colleagues including our colleagues at the NIH, the FDA, the CDC, and the Department of Defense to very quickly bring together all of our experiences and resources in an unprecedented collaboration to develop a Zika vaccine candidate. And that was the whole inactivated virus vaccine candidate that Dr. Fauci mentioned on his landscape slide.

We're also bringing to bear our national medical countermeasure, Emergency Response Infrastructure. This includes infrastructure for rapidly conducting clinical studies, nonclinical studies, manufacturing vaccines, formulating and filling that vaccine into vials so it can be used very quickly, and all the other regulatory experience that we have. In fact, we are activating one of our centers for innovation and advanced manufacturing capabilities that we've established at Emergent BioSolutions. Emergent BioSolutions, one of our CIADMs, is already engaged through BARDA support to begin developing a Zika vaccine candidate. Once that vaccine candidate is developed, we will use our field finish manufacturing network infrastructure to fill that vaccine and quickly go into clinical studies early next year.

We're also developing and supporting the advanced development of rapid diagnostics. So we cannot stress enough the importance of rapid diagnostics and need for diagnostics in the Zika outbreak. It is critical to know who is infected or who has been recently with Zika virus, particularly if you're a pregnant woman or a woman of childbearing age and has a sexual partner who may have traveled or may have been infected with the Zika virus. It is critical to be able to guide your perinatal care and to be able to inform the pregnant woman of her condition.

Right now, we have a lot of diagnostics that are developed using PCR technologies, and those technologies can detect if you're currently infected. However, we don't have sufficiently sensitive assays to detect recent Zika virus infections. So if you're beyond that initial window of infection, you've already cleared the virus, for example, we don't have sensitive assays that can tell you you were recently infected and your fetus might also be infected with the Zika virus.

So BARDA is working very rapidly with industry partners and colleagues to develop these serological-based assays. These are assays that can detect antibodies to the Zika virus in your serum or your plasma or your urine or other body fluids so we can understand if you've been recently infected.

ASPR is also leading the US government's Zika sample sharing working group. So one of the critical needs to develop diagnostics for any outbreak is you have to have clinical specimens that contain that diseased target or specimen so you can validate your assays. It's been very difficult in the Zika outbreak to collect specimens from people who have been infected with Zika to be able to use those serums in that specimen to validate the diagnostic assays. So BARDA and ASPR have formed this international working group to be able to rapidly collect those specimens to validate the assays.

The final area of medical countermeasure development that we're supporting is the pathogen reduction technologies. So as I mentioned before, these are technologies that can be used to inactivate pathogens in donated blood so the blood supply can be used safely in transfusion patients.

So it's also important to know that we are coordinating with other agencies within the Department of Health and Human Services, as well as departments across the US government, to help ensure adequate resources are available to respond to the potential impacts of the Zika virus outbreak. We've hosted a number of international meetings to bring together scientists from around the globe to address the gaps in the science and response to the Zika outbreak, and we're also understanding the response and the global need for a response for the Zika virus is going to require the coordinated efforts of all of our local officials, state officials, our national officials, and our international officials to be able to respond to this current outbreak.

So thank you for the opportunity to be part of this panel today, and I'll be happy to take questions at the end. Thank you.

ROB LOTT: We'll move on to Kelly.

KELLY MURPHY: Thank you. Hi, everybody. Thank you for having me today. My name is Kelly Murphy. I am a Public Health Expert and Program Director at the National Governors Association in the Center for Best Practices. I lead all of our public health work, as was mentioned. I focus a lot right now on maternal and child health, of course Zika, and all of our opioid work.

I have a really quick presentation today and I'm going to skip through some of it. I'm going to talk very quickly about what the National Governors Association is and who we are, state's roles and public health preparedness. Public health implications of Zika virus, Dr. Fauci covered that pretty well so we're going to skip over all of those slides. And then NGA's response and a summary of some state actions that have been going on.

So really quickly, the National Governors Association, we're the oldest organization serving the nation's governors. We have bipartisan leadership. Our Chair this year is Governor Terry McAuliffe from Virginia, our Vice Chair is Governor Brian Sandoval from Nevada. Through NGA, governors share best practices, they speak with a collective voice. And then we also have the NGA Center, which is where I sit. We're a hybrid think tank consultancy. We work to service evidence-based practices and help states innovate around policy challenges. I sit in the Healthcare division.

So a governor's role in public health preparedness, I think coordination has been talked about a bunch today and that will be no different from me. Federal, state, and local governments all play really critically important roles in public health preparedness. Typically, when we're thinking about governors' roles, we see them coordinating among key partners with the federal government, of course; with their local partners; even within state government itself and the private sector; communicating accurate, timely, targeted information; again both internally and externally; and using their executive authorities. All of these have been in action with Zika.

So I have a couple slides on the public health implications of Zika virus. Dr. Fauci talked on all of this and showed, I think, these exact same maps. So this slide, though, I wanted to just briefly touch on because it shows Zika's – Colombia's Zika virus trajectory. It demonstrates how infections can build

over time and accelerate quickly. And a fundamental principle of public health preparedness is prevention and control efforts to avoid getting to that type of tipping point where cases can escalate.

Some key NGA responses to Zika virus, we've been working a lot on this, which I'm sure won't surprise anyone. We started by giving governors an issued bulletin earlier this year to try to get them the information that was breaking as quickly as possible. We also had hosted webinars for governors' communications directors to make sure that they have the right messages and strategies around Zika. And then on May 9, governors did ask for swift action on Zika funding. I believe you all have that statement in your packet. The nation's governors urged the administration and Congress to work together to reach agreement on the appropriate levels of funding needed to prepare for and combat Zika virus.

And then a summary of some state actions on Zika virus. Governors have really been at the forefront of Zika response and preparedness. They've focused on implementing phased jurisdictional risk-based Zika plans that include a variety of strategies – everything from, again, coordinating state agencies and departments, targeting their resources and trying to deploy them effectively, increasing surveillance and vector control, which we've heard a lot about today, certainly launching efforts for healthcare providers and at-risk individuals. Pregnant women come to mind. They have provided educational materials, they have disseminated Zika prevention kits, lots of public education campaigns, so states are really working hard to control Zika virus.

That's actually all I have, so I'm looking forward to taking questions at the end. Thanks.

LAMAR HASBROUCK: Thank you. And good afternoon. So I want to recognize my other panelists and also thank the Alliance for inviting NACCHO to share the voice of local health departments here. So much has been said already. I'm going to focus my comments just on four brief points. The first is – and much of this has been alluded to but I just want to be very clear in terms of from the voice of local health departments – the first is that this is a public health emergency and not a healthcare crisis. So you know, we're really focusing on upstream activities that can prevent that clinical case from happening. So when you're talking about communication or monitoring or surveillance, mosquito control; the other prevention strategies, screening women and if there is a vaccine, actually vaccinating folks in the community, those are all the upstream things and those are all in the domain of public health. It only becomes a clinical issue, a clinical problem, when there's a Zika-infected woman, obviously, that's pregnant and faces the unfortunate outcome of having a child with microcephaly. So the point is, number one, is that this is a preventable birth defect so we need to focus a lot of our efforts and resources on the upstream activities.

Point number two that I'd like to make is really emphasizing the concept of localness. We've kind of taken turns from federal to a state, now to a local perspective. So our public health system, as you all know, is made up of several layers – the federal, the state, and the local. We represent the 2,800 local city and county health officials. And the resources – that is the money, the guidelines, the test kits, the vaccinations, and all that – tends to flow downstream. So you start at the federal level, goes to the states, sometimes it goes directly to some of our large cities. But most often, the ultimate responsibility and the delegated authority to plan, prepare, respond, and mitigate any public health emergency really lies with the local health authority. And we're seeing that play itself out in Miami-Dade County.

So just to remind folks that really, it happens on the local level. So if we're talking about the vaccination clinics that we have in schools and churches related to H1N1, if we're talking about case detection,

quarantine, monitoring clients that have been exposed to Ebola, we're talking about mosquito control, public education around West Nile virus. And now, as we're focusing on mosquito control, public education, screening, and potentially vaccination for Zika, resources must get from the federal level down to the ground where the rubber hits the road at the local level. That's point two.

Point number three, which builds on that, is that the capacity for the local health departments for preparedness has absolutely been decimated over the last five to ten years. So we do not have the capacity there at the local level as much as 40% or 50% over the last five or six years in terms of their capacity, their readiness, their infrastructure, to react not only to Zika but any other public health emergency. What we've noticed is that the decrease in funding has impacted the environmental health divisions of local public health departments, in general, and mosquito control programs, specifically. In fact, you'll note that of our 2,800 members, many of them don't have any mosquito control program or activity going on whatsoever. So as you might imagine, there is a range in terms of preparedness for the Zika virus and any other public health emergency or urgency.

All of our local health departments depend on this federal money coming from CDC or ASPR and others. 55% depend solely on this federal money. That is that no federal money, no emergency preparedness activity whatsoever. So there's a wide range of readiness from those, some of our largest cities and counties that can pivot on the infrastructure for West Nile virus. And then there's those that have absolutely nothing and can do nothing more than inform the general public in terms of some of the things they need to focus on. So point number two is that the concept of localness.

The third point that I will make really focuses on – or that's point number three is capacity. The last point I'll make should be obvious from all the previous speakers but it's very, very simple. And that is that response that we have to any public health emergency – we're dealing with Zika now but there'll be others, there's others before – is directly proportional to the readiness, which is what we call preparedness. So in order for a local health authority, if it's a mosquito control program, the environmental health department or in most cases the local health department, in order for them to be prepared and stay prepared, there must be some level of sustained investment for them to do so. And unfortunately, this seems to be a stubborn lesson that we're learning in terms of Ebola and other things that happen in that if it's a toxic contamination of waters, as we mentioned, if it's infectious disease outbreaks or natural disasters, we're not maintaining the infrastructure, the capacity of readiness to respond to these public health emergencies. I can tell you that our 2,800 members are crying out for additional resources. They have guidance but they don't have the resources, the manpower, the staff to actually implement many of it.

So I will say just in closing, and to make it on the record, that Congress cannot and should not expect local health departments to pull a rabbit out of the hat if there is no funding forthcoming in terms of supplemental funding. The analogy I like to use is that of a firehouse and that the firehouse does not wait for a three-alarm fire to get trucks, to get hoses, to recruit firefighters and train them. They maintain that capacity. So we do well to think about the adage that an ounce of prevention is worth a pound of cure, and I'll leave it there for now. Thank you.

MARILYN SERAFINI: LaMar, I'm actually wondering if you can – when you're talking about capacity and the needs, where specifically is the greatest need right now? Where are we seeing the greatest challenge? Is it in mosquito control? Is it in having the ability to perform diagnostics? Where specifically do you see, if we start to see an expansion here, where are we going to see the hole?

LAMAR HASBROUCK: Right, so I'd say two things. One is there's always going to be, probably one of the tenets of public health is going to be communication, good communication. So we've got to get the lay public involved because as has been mentioned, we can't tip every little, you know, receptacle of water. We have to make sure there's vigilance in terms of the community at large; they know what to look for, they know how to reduce their risk if it's wearing personal protection and clothes, if it's DEET, those types of things. So communication's going to be one.

Then the mosquito control or vector control programs, which include tick-borne Lyme disease and things, West Nile related to mosquitoes and Zika, is going to be key, also. Many health departments don't have any capacity there so we've got to build that capacity, we've got to maintain that capacity. There's a lot that's needed in bringing staff in, training them up, mosquito trapping, mosquito identification, laboratory identification of mosquitoes. And then, some of the other things that need to be done to reduce the mosquito population so we can keep the community at risk.

So those are two big buckets I would say are desperately in need.

ROB LOTT: Kelly, turn it up to questions?

SHEFALI LUTHRA: Hi, Shefali Luthra from *Kaiser Health News*. I wanted to ask Kelly, actually, given what you hear about how local health departments often don't have funding and how it seems like maybe kind of a wash for Congress, what can or are governors doing to try and secure state funding whether it's, I don't know, calling State Leg into special session or other ways to allocate local money?

KELLY MURPHY: Sure, thanks for your question, it's a great question. Governors are trying to coordinate the best that they can. I think I harkened back to that coordination principle. They are looking to their local level folks to find out what their gaps are, what their needs are, how can they reallocate state funds. That's one of the authorities that I mentioned previously, how can they reallocate those and get the local level the resources that they need. So keeping those lines of communication open and trying to identify those gaps, certainly some strategies they're looking for.

SUE DARCY: Thanks. Sue Darcy from *MedTech Insight*. Rick Bright, I had a question for you. You were talking about diagnostics. You said you didn't have sufficient – I'm trying to get at do you mean you don't have enough test kits to go around? Or do you mean that there haven't been enough diagnostics approved by FDA or other government authorities for use, they aren't the precise type of diagnostics you need? And what do you need?

RICK BRIGHT: The FDA's been working very hard to evaluate the data from all the diagnostics and develop as quickly as they can. And they've made a number of emergency use authorization clearances for PCR-based diagnostics who could tell you if you're currently infected with the Zika virus. The challenge that we're facing still is the development, the specificity or sensitivity, the accuracy, in other words, of these serological-based diagnostic assays. With Zika, the challenge that we face is the cross-reactive nature of the antibodies to Zika virus to other Flaviviruses such as Dengue or Yellow Fever. And so if we're trying to develop a diagnostic to detect Zika virus infection in a person and that person's coming from an area where Dengue was already previously circulating, then they're going to have antibodies to Dengue, hopefully. And when they're infected with the Zika virus and we try to use our Zika virus diagnostics, the antibodies to the Dengue, previous exposure to the Dengue are going to cross-react and give us some false information or inaccurate information for those diagnostics.

So it's a scientific challenge then to develop the right reagents and components to put in the diagnostic assay that can clearly distinguish a Zika virus infection from a Dengue virus infection. And so that is where we are at the development for these serological or antibody-based diagnostics now. We have several of them that can tell us you were exposed to a Flavivirus and where the industry, the developers are working now is to improve those and optimize those so we can distinguish to tell you specifically that you have a Zika virus infection. And so that's where we are with the technology.

QUESTIONER: And do you have any candidates right now who could possibly do that?

RICK BRIGHT: There are a number of candidates. There are probably at least a dozen developers right now working very hard on that challenge. And some of them are already collecting data and they're already in communication with the FDA to review those data. This is where the other challenge with diagnostic development comes into play in having sufficient specimens from people who were infected with Zika virus; also, from people who were co-infected or previously infected with the Dengue virus. So you can use the antibodies in those sera from those known infections to be able to validate those assays, to have the confidence that they can reliably and reproducibly detect the Zika virus infection to give you the most accurate information, especially the pregnant women.

QUESTIONER: Thank you so much.

RACHEL ROUBEIN: Rachel Roubain with *National Journal*. I'm wondering – and this question is up for grabs – but I'm wondering where local and state public health departments are pulling money for Zika from. Essentially, what programs are going without funding or with less funding?

LAMAR HASBROUCK: Yeah, so from the local health standpoint, I would say that it's very similar to what Dr. Fauci described. You know, robbing Peter to pay Paul. We have environmental staff at local health departments that may have a myriad of responsibilities from restaurant inspection to, you know, to sewage to vector-borne things. So we're simply shifting them towards this epidemic at this point in time. One of the things that we're seeing is that even the CDC has kind of siphoned off money from the general pot for all preparedness to address Zika is that it's kind of impacting the basic foundation or capacity to do other things. Zika's here but everything else hasn't stopped. So what that means is that we're asking staff to do more with less, but we're hoping to replenish some of the funds so we can keep staff going.

One of the things that we did recently was an impact study with all the local health departments to find out how these funding shifts at the federal level are actually going to impact them on the local level. And we're finding that many of them are going to have to lay off one, one and a half staff. Many of them are going to be impacted in several ways in terms of shifting resources, equipment, and the like.

So we're doing the same shell game at the local level but we're desperately in need of additional shoring up of funding.

KELLY MURPHY: And I guess I don't need to repeat anything he said, just to reiterate that it's very much the same at the state level.

DONNA YOUNG: Hi, Rick. Donna Young from Scrip, how are you. I just wanted you to go into a little more detail about some of the companies other than GSK and Sanofi that are partnering with the

NIH on the Zika vaccine. What are some of the other platforms? You've talked about emergent but what are some of the other types of platforms that companies are pursuing at this time?

RICK BRIGHT: Right, thank you for that question. As I mentioned, there are probably at least 30 – each day it changes a bit – different technologies and companies trying to respond to the Zika outbreak by developing vaccine candidates. A number of different platform approaches are being used. Some of those are more traditional platforms that we're very familiar with such as using an inactivated virus particle vaccine so you grow the virus in cells and treat it with a chemical to kill the virus and then purify that protein. And then in most cases, we're adding an adjuvant with those proteins and then using that as the vaccine.

In other cases, there's live attenuated approaches. So we're using a weakened version of the Zika virus. It's not being inactivated but it's unable to replicate very far or cause any disease. And those types of vaccines have been used successfully for Dengue virus and other vaccines similar.

Another version of a live attenuated is a chimeric vaccine and so you take the Zika virus proteins on the outside of the virus particle and you blend them and merge them with a core particle from other viruses such as Yellow Fever. So Sanofi Pasteur, for example, has a vaccine they call Dengvaxia where they use the Dengue surface proteins on the Yellow Fever core. And so one approach that some companies are using is putting the Zika virus proteins on the core of Yellow Fever or Dengue, for example, and make it chimeric.

Other approaches are nucleic acid-based vaccines so either the plasma DNA vaccine candidate that Dr. Fauci mentioned. There's also a company Inovio and GeneOne that has started the clinical study with another plasma-based DNA vaccine. And an even newer approach with nucleic acid vaccines is called mRNA. And so instead of using DNA as your starting material that you're delivering to the person to make an immune response, you're using RNA. So it's almost the complement reverse mirror of the DNA. The RNA-based vaccines, you're delivering RNA and the RNA then gets into the cell of the person, produces the protein that then elicits the immune response that we're trying to elicit.

Other approaches include recombinant-based protein so a number of companies that have platforms expressing proteins in insect cells and other cell substrates. They're using those same production systems to express the Zika virus protein and then using that as the vaccine approach.

So all of these platforms and production systems or other live virus vector approaches to deliver the payload of the Zika virus are in play right now for Zika vaccine candidates.

QUESTIONER: Are all 30 of those companies and technologies, are they getting government funding at this point? Every one of them? Or just some of them?

RICK BRIGHT: Actually, hardly any of them are at this point. And so many of them are, as they usually do, they're moving quite aggressively on their own, at risk. Biotech companies and large and small pharmaceutical companies are trying to respond to the current outbreak. They're trying to move the candidates forward as quickly as they can as far as they can with the limited resources that they have. In many cases, they've set aside the resources from other large, very profitable programs for vaccines or drugs so they can turn their attention to try to work on the current outbreak. In these instances, they rely on the US government to be their partner and to share the risk and bring to the table our knowledge in reducing the risk and increasing the chances of success.



BARDA has used the approach in collaborating with industry a number of times and partnering with industry to accelerate the development of vaccines. Right now, BARDA has had the funds to support a collaboration with Emergent BioSolutions, and that is part of our infrastructure that we have in place for rapid response.

We're in negotiations with several other companies right now for the Zika vaccine candidates. Because of the limited funds that we have available, it's very difficult for us to build a strong portfolio of candidates with industry to take those through a clinical stage development and move those through the pipeline. We are fortunate for the reprogram funds, as has already been mentioned, for Ebola, for example, to be able to put some of those vaccine candidates in play. And hopefully, we'll have contracts in place over the next month. Unfortunately, without additional funds, those candidates won't be able to go very far and we won't be able to bring additional candidates into the pipeline.

So in those cases, many of those industry partners may decide without the government partnership to help them reduce the risk and accelerate those development pipelines to shift back to their other priorities. They may decide that they can't afford to do it on their own and have to go back to other priorities, as well.

So we're at risk at this point because we've made it such a high priority and we've engaged aggressively with industry. By not being able to partner with them effectively and quickly enough, we're at risk of losing some of those potential industry partners that have a lot of experience in developing vaccines for Dengue and Yellow Fever and other candidates, and reducing our chances of making a successful Zika vaccine in a short timeline.

MARILYN SERAFINI: Okay, great. So this'll be our last question. And while we are taking our last question, I'd like to remind you, you have a blue evaluation form in your packets. If you would kindly take a minute to fill that out before you leave today. So onto our last question.

JOYCE FRIEDEN: Hi. Joyce Frieden from *MedPage Today*. I just wanted to ask Dr. Hasbrouck to clarify when he said this is a health emergency and not a healthcare crisis, how you differentiate those two.

LAMAR HASBROUCK: Sure. So the distinction is of health, of the umbrella of health, there is healthcare and then there is public health. And so my distinction is that this is a public health emergency that is a population level, community level focus versus an individual one client, one patient at a time focus. And that it only becomes clinical when someone's infected and pregnant. Before that, all the upstream stuff has to happen in terms of the vigilance around communication engaging and the community in terms of mosquito control and surveillance and monitoring and identifying mosquitoes and personal responsibility in terms of wearing DEET and things.

So those are all the things upstream. So we want to prevent it from, you know, crossing that threshold to where it becomes clinical and now we've got to get physicians involved and we've got to get the, you know, therapeutics, hopefully, when they come down the line and some of the other stuff. Thank you.

MARILYN SERAFINI: Okay, great. Well, we've come to the end of our time. I would like to thank all of our speakers – Dr. Fauci, Kelly Murphy, LaMar Hasbrouck, and Rick Bright for being with us today to talk about this very important and pressing topic, the Zika virus. And once again, a big thank you to

the Jayne Koskinas and Ted Giovanis Foundation and to Health Affairs for their partnership on this series of briefings for reporters and we hope you'll join us next time. Thank you.