INTERVIEW WITH

Dr. BRUCE GELLIN

H1N1 ORAL HISTORY PROJECT

Interviewed By Sheena Morrison

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Interview with Dr. Bruce Gellin
Interviewed at Dr. Gellin's Office,
Washington D.C., U.S.A.
Interviewed on January 5th, 2009
H1N1 Oral History Project
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Dr. Bruce Gellin: BG
Sheena Morrison: SM

SM: The following interview was conducted with Dr. Bruce Gellin, Director of the National Vaccine Program within the Department of Health and Human Services on behalf of the National Library of Medicine for the Making History: H1N1 Oral History Project. It took place on January 5th, 2010, at Dr. Gellin's office in Washington, DC, and the interviewer is Sheena Morrison.

So, during our last interview you spoke about the U.S. commitment to donate vaccine to global communities in need, and one of the topics you wanted to get back to was the whole issue of vaccine and vaccine safety in general around international donation.

BG: Now those are separate. So, the safety and international donation are separate categories.

SM: Oh, I see. Okay.

BG: But I just wanted to mark off safety as a separate entity 'cause it deserves a whole, it deserves a lot of in-depth look, and perspectives from a lot of different people.

SM: Okay. Alright.

BG: But before...So, I don't know how you want to go with this, but on this international one, let's just pick up, because there's a lot of stuff that's evolving. And you know, from the perspective of whoever gets this five years from now, I think it'll be important to know how much things change in a relatively short period of time. So, we'll review just some of this. But this is a discussion that went on for a long period of time over the summer of 2009. Once it was clear that we're making vaccine, and it became increasingly clear that there was limited global capacity for a global pandemic of unclear dimensions, then there was a request by all camps about what was going to be availability of vaccine. We talked about that.

SM: Right.

BG: That led to this process where you had, at the level of the White House, the domestic view versus the international view, where there were clear differences of perspective. It went to the President to make a decision about how we're going to allocate our resources, recognizing that at the beginning of a pandemic, no country was gonna have enough for everybody the first day. And even in this one, before we knew how the vaccine would ultimately roll out, we knew that we would be giving vaccine away before every American had received their dose. And in part, that was part of the strategy, because part of the international perspective was that we're all in this together, and it shouldn't be just when we're done with it does it go to others. So that was all part of the decision-making process. That was mid-September. That was an opportunity...The timing of that was such that it was allowed to be discussed during the U.N. General Assembly. There were some other reasons for that. But going into it (and also, that was a point when no one in the world had been vaccinated), I think people were quite aware that the optics of all this would change once the countries with vaccine access began their vaccine programs, and those

without it would be clear that they were without. And people would be asking the question, well, what about them? So that proceeded over time. And we have been now working with the World Health Organization on the technical aspects. At the same time, really led by the State Department, working with a broad donor group that they have assembled as part of this - their effort in leadership - of, I forget, maybe 10, 11, 12 countries who've now pledged to be part of the donor pool. And we should fill in who those countries are cause they're not all who you would expect them to be.

SM: Okay.

BG: For example, Brazil has joined that. And there are probably other reasons why some of the other countries have wanted to be part of that picture as well.

But the point then is that as we've been working forward on this, there've been a lot of discussions about donating vaccine, and having WHO manage those donations so that they were not bilateral donations. I think people recognized that since there were many, many countries in need in a situation like this, donating to one or two or a few that

you were not donating to many, many more. I think that was part of the beauty of a multi-lateral WHO-led operation, which meant that many donors, both companies and countries (and I guess even philanthropies, but I'm not sure of the degree to which philanthropies could donate into that) would then be a general pool of goods: both the vaccines, finances to support vaccination, and things like needles and syringes would then be distributed by WHO on behalf of the donors to all - at least to a larger segment than any one country could do.

So that proceeded on, and now we've found ourselves frustrated, really, at how difficult it's been to do this. The carrying out, the logistics, of all the donations has really been quite substantial. There are a number of aspects to this from a technical standpoint: WHO has to be sure that the vaccines that are being donated are of reasonable quality. They don't want to just assume that, because that's not a good thing for recipient countries just to get some product because somebody else has donated it. And while we in the United States and other developed countries are quite confident of our regulatory authorities, and these are the same vaccines that we use, WHO has to treat all donors similarly. And there may be

other countries that don't have the same kind of regulatory structures, but may want to be part of a donor pool, so WHO needs to be clear that what is gonna be donated is of the quality that it should be.

SM: So how is this being done?

BG: Well, so, WHO has got a process for this. On the vaccine part, there is a process called pre-qualification, which they do for many products. 'Cause they want to make sure that recipient country x that may not have an FDA, when they're given something by WHO, they have some confidence that's it's been looked at and scrutinized with the same kind of inspections - both physical and, not only physical inspections, but, sort of, the whole process of understanding what the product is - that somebody who's got some significant experience has looked at that, and then deemed that this is appropriate quality to be used somewhere. 'Cause not all countries have such regulatory authorities, and not all manufacturers do the best job of keeping up with standards that would be applicable to different countries.

So, WHO has put in this process called pre-qualification, and frankly, this is one of the things that's been quite frustrating on how products...Now, here is an example: the vaccine from Sanofi Pasteur that we are pledging to donate - and we've had this really lined up to give to WHO for several weeks. So, here it's ready to go, and we've been working with the transportation, and USAID has been helping with the logistics of that. We're working with the company, working with the regulators, and having...This is the first of our donations, it's still not ready to go. It has yet to be prequalified by WHO. God knows why that is.

There has been a long...there is a document that WHO has about prequalification, but it's just hard to think what could take this so long. This is a product that's been licensed in the United States for four [forty?] years, and we've used hundreds and hundreds of millions of doses over time. It's the H1N1 vaccine; it's the same process that's been used. There's a document on the website that says that a product like this that has not previously been prequalified by WHO should take 10 days. Somebody has to, they have to review the production; they review all aspects of it. But it hasn't happened. And we were told weeks ago that it'd be prequalified, and it still hasn't been. I

talked to Sanofi this morning and they're still waiting to hear back from WHO. They've answered all the questions. So, in the large scheme of things, it's not a big deal. But you think if you have a global emergency and this is something that people have been thinking about for many years, have been thinking about pledging vaccines for many months, and here we are now in 2010 with one of the largest, maybe the largest influenza vaccine manufacturer in the world, is still waiting for somebody to do something with some paperwork.

Now that's...maybe I don't have all the facts, but this is one of these frustrations. And you realize how many of these little things need to happen, and need to happen in the right sequence for things to happen. So, the whole international donation has really been quite slow and slow for many reasons. This is one aspect of it which I think is relatively fixable, and I think these vaccines will go through the prequalification review in the coming weeks, or maybe a little bit longer, and it's not the worst thing that's taken so long. That's just one aspect of it.

The backend of it - and I think this is where the people looking at this thing years from now will need to have an

understanding of how much things shifted – now, here it is in January, it's seeming that in many countries in the Northern Hemisphere where there is data, it seems that the H1N1 peak is now behind us.

There is still disease out there. My wife's a school nurse in Washington, she told me that yesterday she went back to school and there was a kid with H1N1 who was sent home. And she too thought, well, its all over. It's just strange we're still seeing it. That's just the same thing on a larger scale. Many people think we've now passed this; the worst is over. Yet, we still have a lot of vaccine. And while we have our issues domestically as far as trying to continue to promote vaccination to people who are susceptible 'cause we don't know what's gonna happen in the spring (we don't know what's gonna happen beyond that), but we do know this virus is still around, and that there are still many people who remain susceptible because they haven't been sick, or they haven't been vaccinated.

This is a global situation as well. There's a piece that I saw today. It's been brewing in some European papers for a while, about many European countries now trying to get out of their commitments with some of the manufacturers. We

have similar things here. We have built into our contracts as far as what we reserve capacity for, and what we'd ultimately buy. But when you see how this plays out on the global scheme, it doesn't look quite...and I think that it has an interesting set of optics to it.

Particularly the French (and we should get you the articles so you can sort of read this into this), they ordered 94 million doses of vaccine assuming that people would need 2 doses per person. Now, they're only using one dose per person, and they're basically returning, or not continuing, the orders on 50 million of those doses of vaccine. They have relatively few people vaccinated. I don't have those figures in front of me, but now they're selling some of the vaccine that they're not gonna then receive from the company; they are selling it off to other countries. So, while that's a reasonable thing to do, it's sort of the optics of where we are now.

Where just months ago, as recently as early November, there was a cry for more vaccine: why can't we get more? Why are we using this old technology? It needs to come faster! And now, just six weeks after that, with seemingly, this recent peak behind us, little interest in vaccination. We seem to

just think that that is now a historical episode, and now we have vaccine for no reason; there's no reason to continue to use it. I mean we have in front of us, now that the new year is here and people are returning to schools, I mean, there's always the opportunity for people when they're re-clustered together for these diseases to transmit.

Next week, we are organizing what's called National Influenza Vaccination Week, which is something we've done for several years in the United States. Traditionally, it's been after Thanksgiving because in seasonal flu most of the push for vaccination is early fall, and after Thanksgiving, there seems to be little interest. People are doing other things: they're going on their different routines, they're getting ready for the holidays, they're going on vacation, and going and getting a flu shot has not been the most important thing to them. So, for several years we've had something called National Influenza Vaccination week, which is intended to send the message of: since flu isn't here yet (and seasonal flu), it's still a good time to get vaccinated, because the importance is, you get vaccinated before disease comes to town. We're in a different situation now, because we're not sure what the future is of

this virus. We don't know what's going to happen with the flu season going forward, but we do have seemingly less and less demand as the vaccine orders are coming in. And so, that's a domestic issue, but it's also a global issue as well.

SM: Wow. Well I read in the paper a couple of days ago an article where the government was given a grade on how it was handled. Did you read that article?

BG: Yeah, I did see that.

SM: And would you agree with it that - I mean, as someone who's watched it over time, I could see how, in sum, yes - a B+ could be doled out. But I think, overall, it was very simplified.

BG: (Laugh). Well, I think that that, it's true, it's simplified. I think that the problem of giving a grade is, I guess it's like a grade point average or a transcript. It may give you an overall picture of somebody's performance, but in the middle of that are some A pluses, maybe some incompletes, maybe some P.E. classes, and some other things all lumped together. So, I think it's hard to have an

overall grade for something that's this complicated, although people want to, wanna have a sense of, well, how did it go? But it really is quite complicated; I mean the vaccine's got several things within it. That's one piece.

The whole management of the public school closures is another aspect, how things are handled in travel, for instance. I think there's a number of different aspects. So I think it's hard to be perfect in everyone of them. And people will certainly have their own opinions on how things work.

But I do think that from the perspective of the project that you're looking at, it's probably worth (to the degree that you can) even looking further back and seeing where we were a year ago, two years ago, five years ago, to see what, how, given preparations at that point, of how much we think we would be able, how we'd rate with a performance of a similar pandemic then, versus how we did now with all the work that's gone into it. 'Cause I do think that it's hard for people to appreciate how far we've come in a relatively short period of time for something that's this complicated.

When we got into this (and I think in maybe our initial interview this got tasked), the reason I got into this in the first place was when I came here in 2002, the Department and the government didn't have a pandemic plan. And there had been, in the past, discussions about pandemic preparedness in the context of the National Vaccine Program Office, which was seen as a coordinating office for the Department. And since a pandemic would require a pandemic vaccine, and it would require all the components of HHS and others to be involved, it made sense for those conversations to happen in an office like the National Vaccine Program Office.

Flash forward, and clearly, vaccines is one of thousands of pieces of a larger picture, but I got into it early on, and therefore, while vaccine is in my title, I've done and been involved in a lot more. Because the more you drilled into it, the more complicated you saw it was, not just with vaccines and the antivirals, but the whole spectrum: from infection to control, international travel, international relations, and really everything in between, including some of the basic research science that feeds into some of the policies that we have now. So, I think that a grade is, you know, people will want to give it a grade. I think that

nobody will get an A+ for an event like this, and I think that people are glad that they didn't fail, because the failure would be much worse, not only in term of the grade you got, but what that meant for society.

I think the question outstanding though is: what does this mean for the future? I think we're gonna have to take a hard look at that. And there will be all kinds of people writing after-action reports about what happened. But I think that we need to recognize that what we've just been through isn't what we had prepared for. We have to then be realistic to try to think: if the thing that we are preparing for, an H5N1, or a very severe 1918-like pandemic, and if it came through, how would we do? What have we learned now that we would want to apply to that? So I think that we're gonna need to keep going on to make sure that we refine our plans, and exercise our plans, so we're prepared for the more serious one where the consequences for health and well being would be much more serious, because it could still happen.

And so I think we can't just say, "Well we got by that. It's now time to move on to other things." At the same time, people are tired of it, because they've been doing it

for a long time, and the big one didn't happen, and the little has been so overwhelming as what it was. But I think the lesson for all of us who are doing this all the time is that we're going to continue to have to do it all the time, and be prepared for the worst one, and be prepared for something that we don't really know how it will come through.

SM: This is just one point on the continuum.

BG: Yeah. And I think the other part of this where pandemic preparedness has been so different from some of the other 'disaster preparedness' is that (and I think this is one of the principles really from the beginning) a pandemic is not an incident. An incident is something bad that happened in some place over some fixed period of time, and then you're dealing with the consequences of what happened. This is the opposite of that. This is gonna start somewhere and grow and spread everywhere where everyone theoretically is gonna be involved, at least within the hemisphere at the same time, and so it's gonna require a lot more resiliency and resources in every sense of the word to try to manage that, because it's not gonna be easily centrally managed.

And I think that's where, in the setting of disaster preparedness, or broad emergency preparedness, a pandemic is different. And we've had the opportunity to now practice or prepare for a severe one, and I think we need to go back and look at those preparations, because this one was a lot milder than we what we had prepared for. But in so doing, it really, it threw us many curves that we just need to keep track of.

SM: So where are you right now? What issues are you dealing with right now?

BG: Well, right now, you know, one of the issues that we just talked about is this ongoing international issue that we're committed to. And part of this is the Administration's view on global health, and wanting to be sure that we were taking a leadership position in global health. So there's been some frustration on getting vaccine to the places that need it. Now, at the same time, I think we have to recognize that other places may see this similarly. They have a whole set of other health problems before a pandemic showed up, and is this something that they really want to do on top of that. And we need to - no

one wants to force a vaccine on anybody - we need to be realistic about any country's assessments of it's own needs. And it may be that there is, over time, less and less interest in this vaccine, which is fine. But I think to have some clarity on where we are with that so that we can get our targets clear, and what we and other donors are intending to do, executed as we planned. I mean there is a (phone rings)-

SM: Sorry.

BG: Okay.

SM: I'll just turn it off.

BG: So, I think that this system, this program that WHO is running is now just getting started. I don't believe as of today, January 5th, anybody's been vaccinated with vaccine that's been donated to WHO, but it's pretty close. And there are a few countries of the 95 countries that WHO has targeted as those without any access and the poorest countries, there's just a few countries now where vaccine is needed, but it hasn't been delivered yet. So, I think that we're all going to have to watch to see how that

experience goes and how disease trends are over the coming weeks and months, 'cause that may say a lot to what happens with ongoing donation. So that's a large part now.

I think another piece now is trying to make sure that we don't lose track of some of the things that were priorities, recent priorities, but aren't today's priorities. For example, the whole issue of how the science of the transmission of influenza virus is really not very well grounded. And we went through this last summer when there was...You'll need to get somebody to get into some more detail on this one about the science behind the use of masks and respirators. That's the theme. And behind that is the underpinning of how this virus is transmitted. And that would then give you some insights into whether or not you're protected best by a mask, or a respirator, which is a tighter fitting device, which is a lot more cumbersome, a lot more expensive.

The supplies are an issue as well. And there are different camps about this, where the science is not all that well grounded. There are believers in different camps that led to a institute of medicine trying to adjudicate this.

The bottom line though is that unless we have a better handle on how these viruses are actually transmitted, we're gonna be plagued by this. So, I think this is where when the science is good, the policies are pretty clear; when the science is murky, then the policy is driven by a whole other range of things. This one - decades after the influenza virus was identified in the thirties - we still don't have this one sorted out, how it's actually transmitted. And without some of that, we're gonna continue to be plagued by it. I say that because as we - if we are indeed winding down - we need to remember some of these things, because unless we continue to invest in the science, when it comes back, we'll be revisiting this all over again. And I should give you an article that I found from 1958. 1958 was in the middle of the pandemic then, and it sounds similar.

SM: Really?

BG: There are things in it that sound similar, where a guy named Richard Shope (who was one of the leading scientists then, and it was a lecture; I think he may have been at the Rockefeller University) was saying, "Do we have the science to make a difference, or are we just gonna do more

research?" So again, I think that this is a question that I think we still need to continue to ask ourselves, and to try to take advantage of what we've learned now, and ongoing, so that we can nail some of these down for the future.

SM: Okay. You mentioned a session that took place at NIH to focus on the influenza vaccine, research and development, and production capacity. And you drew a distinction between production technologies and new vaccine approaches, and mentioned that they're often confused. Can you elaborate on the distinction between the two?

SM: Yeah, it's a good point. (And that's another one where: how this gets preserved over time? There's a webcast of this thing, presumably, that gets locked in somehow, but it's probably just one that you should patch into your thing here.) But was a session, it was really designed to try to give education primarily to the science writers, so that they had a good understanding of what was going on. I think, in part, driven by the frustrations of the vaccine production and the idea that we're using these old eggs, and it's just taking us forever, and if we only use new

stuff instead of this old time stuff, we'd be much better off.

I think this is an opportunity to take a look at the whole range of these activities, from some of the basic science (just looking at some of the new technologies for new types of vaccines,) to, again, some of the production technologies. On the production technology, I think that we recognized that from the beginning, all of this (and we talk about this a lot) is about the eggs and the egg contract. I think we may have, if we didn't talk about that you need to get the-

SM: I did talk with-

BG: Did Robin Robinson talk about that?

SM: Jessie Goodman.

BG: Okay. Because that was when we got into this, in 2004. It became clear to us (and again, that means that somebody else has known it for a long time, but you need to look at it in a different context,) that fighting a pandemic with an egg based vaccine was gonna be a difficult thing. And

the first of the difficulties was gonna be that these eggs - which are live eggs, they're not grocery store eggs - these are fertilized eggs. They are 8 or 11 days old. And there are some type where they're all the right size. That's because they have to fit into the...they have grown together with the technology that uses them, so that they fit into the systems that the manufacturers use. They're eggs that are the most productive for growing viruses. All that said, that's the way the companies were making flu vaccines. They were done in a seasonal way that they would make vaccines essentially for the Northern Hemisphere between January and July or August, and then stop. That was the egg part. And then, they would have other parts to their production, but that's when they needed the eggs, because that's when they would inject the virus seeds into the eggs to grow up virus that would then be enactivated with the injectible vaccines to be turned into vaccines. So they would do that from that period of time.

The trivalent vaccine they would make one strain at a time based on what the selections were. And then by July they had each of the different viruses in vats, and they would blend them together to make the trivalent vaccine.

The point is that, after August, there really weren't eggs available, because it was all timed with the farmers (and again, this is thinking about Sanofi, which we would have been working with), with Amish farmers in Pennsylvania that were the source of the eggs. And they had contracts with these guys to make sure that eggs came in during the production time. So, essentially, between January and July, or August, they had hundreds of thousands of eggs each day that they would need, 'cause when you're not making vaccine you don't need all these eggs coming in. So it took a lot of planning, you know. I think it was about an eighteen month cycle of organizing the chickens to make sure that when the eggs came due they were coming in the right day, and everyday you had to have hundreds of thousands of eggs that were eight days old. So you can think through what that would take.

So, when we got into this, we actually learned a lot from Canada (who had been working with the manufacturer at the time in Canada on a similar program) that we needed to be sure that there was an egg supply that was available all the time. Because if you went to a manufacturer like Sanofi in October, at the beginning of the year, and said, "Hey, we have a pandemic on our hands, we need to make some

vaccine", they would say, "You know, we'd like to help but we don't have this kind of egg production coming in. We can go find some", but they would have nowhere near the number of eggs to meet their capacity. So, the first thing we did was to organize the egg supply so that there was a year-round supply of eggs that would be available to make influenza vaccines.

SM: Okay.

BG: Seems like rocket science, but that's what we had to do early on. And I think maybe the first pandemic funds were to work with Sanofi to organize the egg industry around that goal.

That said, the ability to make influenza vaccines from eggs is based on how productive the virus is growing inside the egg. And as we've learned again this year (and we learned every year with seasonal vaccine) is that this is all biology, and some viruses grow better in some formats than others. And the rate-limiting step was going to be the number of eggs and how well the viruses grew. And while the companies had their own ways that they can tweak this, they can change the temperature, they can do some things to try

to have the viruses grow better, that was gonna be your rate-limiting step.

And so, that's what led to the discussion early on, and the investments in cell culture technology where, basically, instead of growing viruses in living eggs, you're growing viruses in living cells, and then didn't have to rely on all the chickens, essentially, to supply all the eggs. And you could have cell cultures that were essentially waiting in the wings that you could then bring out as they would just be in vats essentially to then use. Therefore, the idea of a surge capacity - how much vaccine you could make in a given time - were going to be influenced either by the eggs, or by the number of cell cultures you had. And the latter you could actually make many of, and have on standby ready to go. You can't have the eggs on standby without a lot of waste. So that's where, again, those two huge differences in production technology. Essentially, it's the same thing: it's taking a virus and growing it in something living (which is what viruses do) to grow more viruses. Other technologies - I think that's where you probably want to talk to many others, and this is where - I don't know if you had a chance to talk to Dr. Fauci?

SM: Not yet.

BG: I would actually have him go through this with you ‘cause that was...Really, his lecture was a fundamental piece of that, of laying out the range of different technologies that were available for producing next generation flu vaccines - not a new way to produce the same type of flu vaccine, but next generation vaccines. And I think that some of the things you want to talk to him about: what are the attributes? Part of it would be speed: how quickly you could go from identifying a problem to then having a vaccine. We knew that with egg culture, egg technology, it was probably 20 or 24 months from the identification - if everything went well - from the identification of the virus to the creation of the first vaccine, and then time after that. Cell cultures may be a little bit faster, but not much, because you’re still growing virus; you have to isolate it and grow it.

There are a number of different molecular approaches now that can shorten that time significantly, and time makes a big difference. I think we’re all optimistic that all this experience (from even before this, I think from SARS to H5N1 and now) has highlighted the need for new

technologies. I sit as a member of the FDA's Vaccine Advisory Committee, and we had a sponsor, a protein scientist, come through this year with one of these new technologies. They're making their approach in a different cell called a baculovirus, which is a caterpillar cell. I think there's some limitations on the studies that they presented, and I think the committee therefore would want to see more about the follow-up, and about some of the studies than was willing to give this company a license for it right away. But I think what it signals is that there are a number of new technologies out there, so that in fifty years, we're going to be in a different place. How different, we don't know.

But I think as we've looked at this (and I think from the standpoint of how to advance the field), I think that we've looked at this in short, medium and long term. Part of the short term was to develop a stockpile, and we've done this with the H5N1. We didn't have the time with H1N1, because the vaccine needed to be used as soon as it was available. The stockpile, at least, it may not be the right thing, because if you put vaccine in a stockpile, by the time the virus causes a problem, it's different enough from the vaccine, what you've stocked may not be useful at all. But

it might be, which is why I've gone into it. So stockpile is, I think, a near term where you could have something ready to go, potentially, and hit the ground running. Now we have this other technology, which will take a long time. I think we now have at least in place, a new capacity for cell based technology, which will give us some surge capacity.

So what's next, really, is a couple of different things: one is shortening the time, and I think that's where some of these molecular approaches will make a huge difference. So that it's not 20 or 25 weeks, but maybe half that amount of time from when you identify a problem to when you have vaccine coming available.

And then, beyond that is a vaccine that's more broadly protective, so you don't have to create a new vaccine for each evolved new virus. And that's really the holy grail of influenza, is what's referred to as a universal vaccine that will protect against all of them. And if we get there, then all this stuff is now moot, because you'll then have a vaccine that's ready to go, that's protective against something that hasn't come yet.

So with that (and I think that will bridge into this,) is the safety aspects. 'Cause, while I think there's a lot of promise in the new technology, there's also a lot of leeriness about vaccines, even of old technology. So when you think about vaccines, of newer technology, then I think that raises concerns even more. We had a huge issue in the United States. I know that this...I think the piece you're referring to in *The New York Times* talked about the conservative approach that we took by using the same kind of vaccine we used for seasonal vaccine, and not using adjuvants.

Adjuvants are things that other countries have been using (and many other countries have used) for H1N1 that are added to a vaccine that can improve the immune response, that allow you to have a lower dose. You put those together, it means that you can have potentially more vaccine in a shorter period of time, and may then mitigate against some of the supply issues. In the United States, we looked at this, and we actually have a lot of adjuvant that we purchased for the stockpile with H5N1 in mind, anticipating that we would need it for H5N1. We won't get into that now, but it's clear that the way we made the H5N1 vaccine is gonna require an adjuvant to get any kind of

immune response, and to allow sufficient numbers of people to be vaccinated since, otherwise, it took a very high dose to get an immune response. With this, when we looked at the situation, we saw how the vaccine that we made with the seasonal approach was working, and felt that that was sufficient. And we at least had the science to go by, because we all have recognized that while there was already a lot of wariness about the vaccine, it seemed that the country is split down the middle between those who thought we'd gone too fast with this untested vaccine, and people who thought we hadn't gone fast enough, because we had huge lines of people and a pandemic on our...that we're facing.

We felt that there was significant leeriness about vaccines to begin with, and we've seen this with the other vaccination programs where people are concerned that vaccines are causing more trouble than they're preventing. And I think that part of the problem in the non-flu world, in the childhood vaccination particularly, is that the vaccines, which there are more and more, vaccinate against diseases that people are no longer familiar with. So what they see is a bunch of vaccines for diseases that they've never heard of, (a), or have never experienced. And they can't put it all together, and they hear all this chatter

about vaccines causing ill effects. And we know that no product is perfectly safe. And while any vaccine used in millions of people we're gonna expect to see some adverse event that may occur to somebody, there are a lot of other things that have been alleged to be caused by vaccines that then gets into the public's mind. And I think that then part of our concern on this was, if you had this opportunity for people to be vaccinated, you didn't want to have them decline a vaccine because they were afraid of it.

So we did everything we could to stick by a vaccine from which we had huge familiarity. Again, the seasonal vaccine's been made in the same way since the '40's, almost. I mean there's been some changes over time, but it's the same general approach of growing up a virus, purifying it, and that becomes the basic antigen of the vaccine. And we had a huge track record about that. So, we felt very confident about the safety profile of this vaccine, in contrast, because it was seen as an extension of our seasonal vaccine program.

Had we had the vaccine of some of these new technologies, in the same kind of a pandemic, I worry that there'd be more people who'd be refusing vaccine than would be opting

for it. That would change, I think, in a severe pandemic. As I mentioned with H5N1, we're fully prepared to use an adjuvant, because we know we can't get an immune response without it. And I think that should an H5N1 epidemic occur - and when I say that, it's recognizing that the case fatality rate for H5N1 (there've been relatively few cases), but the case fatality rate has been about 60 or 70%, depending on where in the world it occurs, but that's a pretty significant disease. And I think that when people are then faced with that question of making their balance against benefits and risks, and they see what the risks of the disease are, then they have a different understanding of what the risks of the vaccine are.

And I think that's where we need to do much more work in understanding people's perceptions of vaccines. And as we think about some of these new technologies, particularly for emergency purposes, how receptive people are gonna be to having a vaccine made by 'the Government', particularly one that doesn't have decades of history behind it? So we're encouraged by all the new vaccines. I think that the best thing that could happen is that these new technologies become used as seasonal vaccines, and as there's more experience with it, then people (like other new

technologies) would have a different comfort level with them, and also give us a chance to evaluate them in larger numbers over time.

But on the safety front (and I have to go in a minute now,) we've recognized that this was gonna be one of our larger challenges, in large part because of the experience of 1976, where (and we've all read the lessons of 1976,) the biggest lesson was the continuation from developing a vaccine to having an immunization program without a blink in-between. And I think that we were always very cautious about that. Early on, we talked about developing a vaccine, and separated that quite distinctly from having an immunization program, because you couldn't have an immunization program without a vaccine. But just because you had a vaccine didn't mean you had to have an immunization program. So, it was pretty clear as the epidemic progressed over the summer that a vaccine was warranted. We then made that transition from a vaccine development to an immunization program. And that was probably the clearest lesson from 1976.

But in 1976, there was this experience of Guillain-Barré, which is a severe neurological disorder. And people who

don't know anything about flu, or anything about 1976, have heard of Guillain-Barré. And it seems to be one of these things that now passes over time, in the same way that people have heard about Tuskegee and some of these other experience of the past that are now part of the urban street discussion. And so we needed to do everything we could to look for something like that, and to take a hard look and to see if it was occurring, and to communicate whatever we could about what we were seeing. And so with that, we put a number of different systems in place on top of the vaccine safety surveillance systems that we already have so that we could get as clear a snapshot as possible on what was happening. So, I can talk some more about that next time.

And that's why, when you want to, talk to Dan Salmon in some detail about what we've put in place, because I think this is something that is a great opportunity to see how, in this one case, something we put in place for this program now can evaluate how much of what we put in place for this program should now become part of our routine vaccine safety system. I think some of it will stay, some of it we'll know that we can turn on again if we need to, but I think that's where you want to get more details about

this. And there's a document that we have, it's called the Federal H1N1 Vaccine Monitoring System. But I think the idea is that there are many components to this system, and we've built up every aspect of it that we could, so we could take a hard look at it.

At the same time, we know that there is a lot of problems with trusting Government. And again, some of it relates to 1976; some of it relates to Tuskegee; some it of it relates to all kinds of other reasons why people may not trust Government. So we put in place at the recommendation of one of our advisory, our National Vaccine Advisory Committee, an independent review. So, not only would the Feds do what they always do, of looking at the data that came in, we have now an external group that reports to the National Vaccine Advisory Committee that looks at all the data that the FDA and the CDC and DOD and everybody is looking at, so they could have a separate assessment, so that the public could say these outside people outside of government looked at all the same information, and here is the conclusion that they drew. So, it's an ongoing thing. They meet every two weeks, and once a month they have to present to the full parent committee. That makes it a public presentation as part of the Federal Advisory Committee rules. So, at

least, we've gone to try to have independence and transparency to be built into the system so that people could see, people who might be skeptical could see, that we're asking others to take a look at the same information and tell us what they think. And so, that's ongoing.

And we'll continue to look at those assessments of what adverse events are reported on vaccines. There are a number of different systems that you'll learn more about, but that's all the data that we're...there's a lot of data there, but those are the things that we're looking at, to take a hard look at what's happening with these vaccines.

When you look at the literature around the world - I just saw something yesterday from Taiwan, where you can see how disruptive some of these allegations can be in a program. There were a couple of cases where it wasn't clear that what happened to people was related to the vaccine. It worked its way up to a pretty high level, and I think that there was some, you know, some fear by the public that there were things that weren't being told to them by the government. And so they had to bring in others to do, to take another look at the information. It's not clear that there's anything there, but I think that it just shows how

disruptive a vaccine safety signal can be in the middle of a program like this. That's clear that that happened in 1976. And one of our lessons going into this was to have the systems in place so that we could detect something that shouldn't go on, but at the same time, to be able to then report to people what we're seeing as we're seeing it so they would have confidence. People who took the wait and see attitude would know what they were waiting for.

SM: Well how does this trickle down to the average person in the street, if it's coming from the towers, so to speak?

BG: The average person in the street. That's a hard one. I mean we work with...Separately, we work with a lot of different places to try to get the word out. There are groups that follow this quite closely, and we make sure that they're aware of it as well. The media has reported on it. I think that it was interesting for this group; I mean, we've had cameras come to the premises of a working group meeting that we're...There's so much interest in vaccine safety (this is in early October) that the press wanted to report on it, because they thought it was so fascinating the government was going to this extent. So, the average person on the street. You know, who knows how they get any

of these things? But we've had a lot of...we discuss this with the media a lot. There are reports that are posted, maybe, sort of, in a typical government thing, but we do make this information as available as possible to everyone, so that in case people did want to know, they could find it.

So, the average person on the street. Who knows how they get their rumors sorted out? But I think that's a big part of the problem. Maybe, one of the things that's adjunct to this is to talk to Stephanie Marshall about communication challenges, and maybe, how we need to be thinking about social networking approaches to communication, and not just the usual traditional media approaches. Because, to me, I think the real question is: where does somebody get information? What information do they want to get from who that's gonna help them make a decision? 'Cause clearly, a lot of people don't want information from the Government, or can't fully trust what they get from the Government. So then, the question is: for any individual, where do they get information that's gonna be helpful to them? And that's a whole other field that a lot of people spend of a lot of time about. I think that from the Government, and public health perspective, we have to understand that. Because we

need to help those who don't wanna listen to us, but need to get this information from somebody, so they can then do what they think they need to do.

SM: Alright. Thank you.

Broad Themes

- Domestic versus international reviews
- International donations
    - Multilateral versus bilateral donations
    - Logistics
    - Regulatory disparities
    - Prequalification process
- Northern Hemisphere H1N1 peak before January
- Continued disease
- Global excess vaccine supply
- National Influenza Vaccination Week
- Government grade on response
- Pandemic preparedness plan and the National Vaccine program office
- Lessons learned
- Pandemic versus Incident
- Global health - U.S. leadership

- Countries without access and ongoing donations
- Priorities
    - The science of influenza transmission
        - Masks versus respirators
        - Supplies
- NIH session on production technologies
- NIH session on influenza vaccine development for science writers
- Production technologies
    - Egg based vaccine
    - Egg supply
- Rate limiting step – egg production
- Range of technologies for producing next generation flu vaccines
    - Molecular approaches
    - Baculovirus – caterpillar cells
- Stockpile
- Broad spectrum vaccine
- Safety concerns of new technology
    - Adjuvants – H5N1
    - 1976 lessons
    - Guillain-Barré
- Independent review of adverse events

- Literature around the world re: adverse events
    - Taiwan - adverse reactions to vaccine
- Communication
    - Social networking approach versus traditional media

Follow Up

Names:

1. 10-12 countries in donor pool.
2. Unnamed expert on the science of the use of masks and respirators.
3. Richard Shope – 1958 article on the science of transmission.
4. Dan Salmon
5. Stephanie Marshall

Documents:

1. Article in European papers about countries opting out of vaccine contracts with manufacturers.
2. Article from 1958 by Richard Shope