Universal Flu Vaccine — a discussion at the Milken Institute, featuring Anthony Fauci, broadcast on C-Span on Oct. 29, 2019. Link to video and official transcript with speaker identities.

Michael Specter -- Why are we even here? I will give one example. In 2009, there was a pandemic flu, h1n1. Some people called it the swine flu. I don't know why it should have been but that's beside the point. That outbreak infected more than two billion people. As far as I can tell, and I've done a lot of reporting on this, the WHO acted incredibly admirably and rapidly in getting vaccines out and the only reason that it wasn't one of the most devastating epidemics in the history of humanity is because that particular flu decided not to be virulent. We don't get a vote. But the Gates Foundation has mathematical modelers who are pretty good, and they have estimated that had it been anything like the 1918 flue, 33, 37 million people would have died, and then we wouldn't be having this conversation, or at least some of us wouldn't because we'd be dead. And what happens when these sort of things occur is if they don't kill a lot of people, we just move on, especially when it comes to influenza, which people seem to think is just a word that means, I don't feel well. It doesn't.

And I think for the first question, I'd like to ask, Tony, maybe you can explain a little bit about why would we want a universal vaccine, how does this work, how is a pandemic different than what we get every year, and where are we?

Fauci -- Okay, thanks, Michael. Just very briefly, because I know we certainly have a lot to talk about, but the situation with influenza, I think as many people in the audience know, is that unlike a virus like measles, which if you have a measles virus and you get vaccinated against measles or you get infected with

measles, that you are protected essentially for life for the simple reason that measles doesn't change from year to year or from decade to decade, whereas influenza is very unique in that it is a virus, a group of viruses. There are different kinds of influenza A, and let's just focus on influenza A, that tend to, we use the terminology drift from season to season in that there are mutations that change it enough so that you really need to get vaccinated each year, and you try to anticipate the right match between a vaccine and the virus that will be circulating.

And then every once in a while, as Michael alluded to, you have a very dramatic change, either by mutations or by evolutions, from animal influenzas that jump species, recombine or what have you, and you have something that's called a shift or a real big change. That's really unique. I mean, the viral infections that we deal with, polio, smallpox, measles, etc. don't do that, so we're dealing with a continual moving target from season to season and the threat of a pandemic.

So the title of this session is the quest for a universal flu vaccine. So when we talk about a universal flu vaccine, it really right now is an aspirational goal in that the quest being to make a vaccine that induces a response in the body to that part of the influenza that doesn't change from season to season, from decade to decade, or even that much when you get a pandemic. And scientists now throughout the country and the world have been able to identify components of the influenza that really do not change much at all and the critical issue is getting a vaccine to induce a response against that part.

Now a universal flu vaccine is not going to be today, we don't have it and then we flip a switch and then next year, we have it. It's going to be an iterative process because if you look at the display of influenza A's, they're in two major groups and there are 18

different H's, so there's a lot of wiggle room in there that you're gonna have to cover. So the quest or the road to a universal flu vaccine will be to for example take one of the group one of the influenzas in group one -- let's take H1 -- and we know that it changes a bit from season to season, to make a vaccine that would cover all of the iterations of H1. And then the next step would be maybe all of the iterations of whatever is in group one. And then there's group two that has H3 in it, and then the next goal would be to make a vaccine that covers all of the iterations of H3 and on and on.

So it's going to be a stepwise process with the ultimate aspirational goal of having a vaccine that you could give relatively infrequently compared to now, which you need it every year, that could be every five years, every ten years or what have you, that covers the broad array of the influenzas that we would be experiencing. So that's it in a nutshell.

Michael Specter -- Thank you. One of the things I've done as a journalist is constantly write stories telling people to get flu vaccines. But they really kind of suck and people always say to me, why should I get a flu vaccine, and I always say 23% is better than 0%, and as far as my mouth goes, that is true. But I'm wondering, like when I wrote something for a report that many of you have access to, the Sabin Salk vaccine report on influenza we put out last year, and I talked to literally dozens of people in this field, and not one person -- I asked them all at least one question: Is this as good as we can do? Not one person said yes. Not one person said we were close to doing it as well as we can do and I'm just sort of curious, why are we so bad at protecting ourselves from what many people consider the sort of most likely virus to cause the most damage to humanity? And I'm going to let anyone of you who wants to answer this do so.

Rick Bright -- Thanks, Michael, and I wish the

narrative would have come up on the video coming through because what's called out in that narrative is a sense of urgency to address this problem. I mean, there are still six hundred and fifty thousand people around the world dying every single year from seasonal influenza. And if we take that scenario that Bill Gates and the Gates Foundation funded from the Institute for Disease modeling that says if we had another outbreak like a pandemic virus today like what we saw in 1918, in that six-month time period, we would have 33 million people dead. And not only that, that virus would have been seeded all around the globe and two months after that, our best technologies to make vaccines would start releasing vaccines. And so we're still behind the gun on the tools we use to make the vaccines.

We have some reasonable vaccine foundations and we can make them better by adding adjuvants, high-dose vaccines that are not fully utilized, and a lot of parts around the world don't have access to the vaccines at all. And so I think that the sense of urgency needs to be there, Michael, but also the fact that we need to leverage the tools we have and at the same time envision what that universal flu vaccine is in a very rapid, urgent pace to get there.

Michael Specter -- So as part of my life, I teach at Stanford and people use this word in Silicon Valley which I mostly hate but I'm gonna use it now: disruption. Why don't we blow the system up? I mean, obviously, we can't just turn off the spigot on the system we have and then say hey, everyone in the world should get this new vaccine we've not given to anyone yet, but there must be some way that -- we grow vaccines mostly in eggs the way we did in 1947. I mean, we live in a world where I can download whatever song I want on to my phone at command and we grow vaccines the way we did 70 years ago. What is going on with that, Peggy?

Margaret Hamburg -- I think I can talk on my own.

Michael Specter -- I never knew that about you.

Margaret Hamburg -- Well, I think it certainly is the case that we are behind where we have to be in terms of the urgency of this threat and how we're harnessing advances in science and technology and how we're mobilizing as a society to also recognize the magnitude and scale of the problem before us. Clearly, disruption comes with uncertainty and it comes with uncertainty on many levels, uncertainty within the scientific community and how we do science, regulatory uncertainty, which I know something about, and also uncertainty about adoption and access and all of that. I think one of he things is and I think hopefully one of the messages coming out of this panel is that it's time to stop talking, it's time to act. And we've talked about these issues for a very long time and and that has taken the place of action sometimes, I think. But in terms of the why we're still growing it mainly in eggs, I think, you know, a part of it is that it's just the way we've always done it, it's the way we know we'll get some kind of vaccine out into the marketplace, and there's always been the hope that in the meantime, other work will be going on and we'll have the breakthrough and the aha moment when we have a universal vaccine. Clearly, that is not going to happen. I think it's also that we haven't had this sense of urgency.

Michael Specter -- Do we need to have lots of people die for that sense of urgency to occur?

Margaret Hamburg -- Well, the incredible thing is that lots of people do die every year and yet we aren't mobilizing, you know. I would have to say to be more positive since I can't really answer the question of why is it taking us so long because I think it shouldn't have and, you know, there really is not a good excuse. The science has had to move forward.

Gaps in the science still persist, including our understandings about, you know, immune protection in addition to understanding the nature of this particular virus, which has its complexities. Certainly part of the problem has been that it's much safer for a company to just keep doing what it's doing than to try to do something new but it's also I think we haven't funded all the the work that needs to be done.

On an optimistic note, there's a lot going on now and and Tony is leading efforts and there are other efforts, Gates Foundation, the European Union research, Horizon 2020, many other activities as well, but we're also not very good at collaboration and I think that needs to be addressed. We need to start sharing knowledge. We need a roadmap for research that really we follow. We identify what do we know, where the gaps are, how can we fill those gaps? We need to identify what are the ruts that we're stuck in that we have to get out of and how are we gonna use all the capabilities in science and technology today and the energy of our society and the scientific community to get the job done?

MS -- This collaboration issue seems particularly interesting and urgent to me because there's this vast amount of data out there and what happens is a lot of it just falls by the wayside. If you do a study and it isn't published, then it goes away and yet there may be good data. I think Casey has something to say about that, about openness and collaboration. Could we be doing --

Casey Wright -- Good day. It's my pleasure to be here. I think isolation is our enemy and there are opportunities to expand transparency and expand a culture of transparency and open data sharing that I think could unlock breakthroughs and create new insights to accelerate our progress. You know, we're the sole philanthropy on the group and we really build into our DNA a bravery about asking really hard

questions. For example, we've been asking, what is the role that publication bias may play in limiting our progress going forward? What are what are the opportunities for funders in this space to really meaningfully collaborate to build co-funding opportunities and build strategies together? What are the ways by which grantees can behave as cohorts in a collaborative fashion and less as individual contributors?

And one of the programs I think Michael is alluding to is that we just established a new collaboration with the Center for Open Science and the Public Library of Science to really create new incentives for researchers to publish null and negative findings. I think publication bias really does limit our options and if we can shed more light on data that's not published, can we create new incentives to bring that -- bring those analyses to the front and shed more light on them? I think it would be really wonderful. This new program that we've started, we're literally asking researchers to open their file drawers, pull out the floppy disks, whatever they have, and we'll pay them to reduce that opportunity cost and to draft those manuscripts and work and help them get those published because we think there are a number of opportunities ahead of us if we shed more light on that information.

MS -- I'm curious to what degree any of you think this and maybe, Bruce, you can address this, is a is a PR issue in some ways because people talk about the flu. I had the flu, I feel fluish. And about 80 percent of the time -- I'm making that number up but it's a lot of the time -- they don't really have the flu. Like last night, I had a bug. I do what I do for a living so I won't call it the stomach flu because I'm quite sure it isn't, but most people would call it that. Is that part of the problem, that we don't have appropriate nomenclature?

Bruce Gellin -- I think that there's there's

complacency I think on that side as well. Peggy also mentioned the institutional architecture that keeps innovation from happening. I think those two things are connected, that the people say well, the disease isn't so bad, I had the flu, I got over it. The vaccine isn't so great, good enough, I'll take it. I think there's that piece of it as well.

But I wanted to go back to the Sabin Aspen Report so the Sabin vaccine Institute is here in Washington. Knowledge and innovation is one of our pillars, and we teamed up with Aspen last year to pull together a group, and the idea was a diverse group of big thinkers, people from science, people from philanthropy, from industry, from journalism to take on issues in vaccine and vaccination. And not surprisingly, given that was the hundredth anniversary of the 1918 pandemic, that was the issue and that's where the urgent -- that's where that speechless video came from.

M**S** -- Silent movie.

Bruce Gellin -- But that's where the urgency came from and the recognition is, we need to do some things differently. I think there was a discussion there about the sort of cascade from communication to coordination to collaboration to convergence, and we need to sort of work our way down that pipeline to make sure hat we're actually getting all the way to the end to try to bring in as much as possible to take on this problem.

Margaret Hamburg -- You know, the complacency really is real. Reflecting back on when I was in government, not in the last administration but a few administrations back and I was starting to develop some public health preparedness programs. And I went to FEMA to talk to them about doing a tabletop exercise with us around preparedness for a biological threat and we were gonna do a flu-pandemic-like scenario. And they said, you

know, we don't do infectious disease. We do hurricanes, we do floods, you know, earthquakes, all kinds of disasters but, you know, disease outbreaks?

And I persuaded them to participate and it was a remarkable thing to watch them as events unfolded, realizing just how much this kind of an outbreak would undermine all of the sort of essentials of civic life, how it would undermine their own ability to mobilize and respond to needs, and also the recognition of the economic costs and productivity costs, in addition to the medical concerns, and ultimately the loss of faith of people in government and leadership because of the failure to be able to provide a vaccine in a timely way and other things. So, you know, people just still don't think enough about what this really means in our daily lives and what the impacts are even though every year, we're suffering a lot of preventable death, illness, and disability.

MS -- Well, that's why I asked the dark and unpleasant question, does something really bad have to happen? And it seems to me one of the curses of the public health world is if you guys do your job well, everyone goes along and is healthy.

Margaret Hamburg -- And they cut your funding.

MS -- But if you don't or if you do your job well and people get sick anyway, then somehow you just failed, and I'm not sure how you get around that. I'd like to take a half step back though and maybe Tony is the person to address this or Rick. Where are we? I mean, can you give us a better sense of how far we've come on our approach to a universal vaccine in the last, I don't know, decade?

Fauci -- Yeah.

MS -- Because it used to be not just that --

Fauci -- Well, we didn't we really didn't -- Michel, we didn't have the a real confidence in the scientific basis that we could actually induce a response or even what components of the virus, if you did have an immune response against, would actually be able to broadly cover. When we had the evolution of structure-based vaccine design, when we use cryo-EM's to look at for example the molecular configuration of the stem -- I mean, one of the big targets of a universal flu vaccine, certainly not the only target but one of the targets if you look at the hemagglutinin molecule, which if you kind of metaphorically constructed it, it's kind of like a head which is a mushroom cap with a stalk or a broccoli cap with a stalk, is that the part that the body makes an immune response against is the head. It's what we call immunodominant. When the body sees influenza, it much, much prefers to make a response against the head. When that gets it right, that's good news because you're gonna get protected. The sobering news is that that's the part that does the mutations that I mentioned a little bit ago.

The part that's the stalk or the stem doesn't really change much at all. That's potentially good news. The challenging news is that the body doesn't readily make an immune response against that because it's not immunodominant and it really hasn't been studied very well. Now that we know that if in fact you make a response against the part of the virus that doesn't change, that when you look at the response the body makes and test it against an array of viruses, you get a much, much broader coverage than against just the particular head of the hemagglutinin, which likes to change from season to season, whereas the stem sort of stays the same relatively speaking. That's not something we knew 40 years ago.

That's something that just now it's beginning to appreciate so what investigators are doing -- again, it's not the only target -- is to take that stem and get rid of the distracting head and stabilize that stem

and put it in a way -- not growing it in eggs, getting back to what you were saying, not growing the virus at all but just getting the sequences, getting the appropriate protein and sticking it on a self-assembling nanoparticle that is much, much more immunogenic, not only is it much more immunogenic but you don't have to grow it. You can make a lot of it and if you do it right and partner with industry, that's the kind of thing that doesn't have the vicisitudes of growing in eggs.
This is the thing that is 10 years in the making not the 40, 50, 60 years that you said we were doing the same thing. The critical challenge, and it relates to its and one of the things that that Peggy said, is that in order to make the transition from getting out of the tried and true egg growing, which we know gives us results that can be, you know, beneficial -- I mean we've done well with that -- to something that has to be much better, you have to prove that this works and then you've got to go through all of the clinical trials, phase 1, phase 2, phase 3, and then show that this particular product is going to be good over a period of years. That alone, if it works perfectly, is going to take a decade.

MS -- Well, I'm not a representative of industry but I'll pretend I'm one. I make a flu vaccine every year and it sells and it protects people to the degree that we can expect.

Fauci -- See, you have no incentive.

MS -- Why the hell would I go spend 400 million dollars to do this thing, which may be great and if it's really great, you give it once or twice or five times.

Fauci -- And that's where the federal government comes in. No, seriously, what happens is -- in fact, you bring up an excellent point. Our responsibility to the public health and not the profit line has to be able to push the process to the point where industry will find

it to their benefit to do that. I think if you're gonna sit back and wait for a company that's been growing virus and eggs for the last 30 years to spontaneously change without any incentive, without any de-risking, it's just not going to happen

Rick Bright -- Can I add to the story a little bit as well?

MS -- Please.

Rick Bright -- I think my mic is working out there. I mean, it's not that the field is not active. I mean as Dr. Fauci said, for 40 years or more there had been concepts and approaches and it's ebbed and flowed, the amount of energy from biotech and from academics and from large pharma. You know, for a while back in the 80s and 90s, the m2 target was too sexy target and a lot of energy focused around there and then, you know, big funding came available from government in 2005-2006 with that the threat of avian influenza h5n1 spreading. So a lot of new ideas cropped up but they were still focused on the framework that the government put out saying it should be an HA-based, antibody-driven vaccine. At the same time, we're learning so much about HIV vaccines and other vaccines through the field and we've been focusing on almost a dogmatic approach that an antibody only is what's going to save the day for influenza, and now there's so much science from investigators in NIH-led studies showing the how the breadth of an immune response is critical for so many of these lifelong or long, durable vaccine or immune responses. The energy now trying to pull that into an influenza vaccine approach is out there.

But what I think Peggy said is we're seeing a lot of these silent approaches where there might be at anytime forty different companies on the landscape right now in the pipeline attempting a broadly reactive, universal, or cross-reactive -- there's various different labels we're putting on it right now for funding primarily

reasons, but they're kind of siloed. You really don't see them leveraging the full scope of knowledge that we've learned about the breadth of the immune response and how it can play a critical role.

And we're still measuring the impact of our influenza vaccines through surrogate markers that were established years ago from egg-based vaccines, the HAI titer must be good enough. We're not conducting really large efficacy trials understanding the details of the immune response. We're not comparing the new technologies that we're getting licensed today for influenza vaccine against each other in the seasonal influenza world every single year around the world. Where we distribute a hundred and fifty million doses of a seasonal vaccine in our country every year, we don't even know how many people are getting vaccinated, how many of those doses are delivered to people, which doses they got and what the real outcome is so we can learn from that knowledge base on how to optimize or improve our vaccine.

So there are opportunities we have today with a wealth of knowledge and data that's been created for a number of years that has still been ignored because it's not pulled up into some larger brain trust for those forty different companies to leverage and make the best vaccine approach, or even for us to determine which vaccines we have today are working or are not. I think if we uncloaked the poorest performing vaccines on the marketplace today, it might be very revealing to tell us which of the technologies we have and allow us to go deeper into those technologies to determine why they're more effective. There are vaccines licensed today that are more effective. I think we're just afraid to admit the truth because we don't have the capacity to spread those vaccines widely once the truth comes out. But we need to identify those markers, those changes as differentiators. We need to build that brain trust, we need to move as quickly as possible and urgently as possible to get these technologies that address speed

and the effectiveness of the vaccine.

The Council of Economic Advisers from the White House just put out a report in line with an executive order from the White House saying that we need to prioritize development of vaccines for influenza that are fast. And so right now they're, as you said, mediocre and slow. A mediocre and fast vaccine is even better than a mediocre and slow vaccine, honestly, but we can make better vaccines and make them faster, but 361 billion dollars every year is our economic cost for seasonal influenza. In a pandemic, that goes into the trillions of dollars. We have to take that sense of urgency, that economic cost, that societal cost and the lives lost into perspective to think how do we gather this information and share it in a very targeted way to accelerate development of one of these better, faster vaccines.

MS -- So I'll ask Bruce this. One of the principal conclusions this group we had last year came to was we need a new entity. We need something special to do this because I won't say we're spinning our wheels, we're not, but we're definitely not accomplishing what we could accomplish and there are many people who think we're not going to do that unless we do something very fundamentally different I'm assuming you're on board with that, Bruce.

Bruce Gellin -- Well, that was -- I mean, that was the ultimate conclusion of that cascade of all the c's, from communication to convergence, and bring all those things together in a coordinated way. In addition to the to the research that Dr. Fauci's group supports, in addition to work that Bart is doing, there's a lot of private industry as well that has pieces of this puzzle. I think they've made a compelling argument that there are -- there's clearly more to learn from what we have now. But in addition, given the urgency, and I think that was the overarching theme of the report, given the urgency, we need to do things in

addition to what's already happening. What else can we do, how can we bring in new ideas to this to this space?

I think we need a Barry Marshall moment. When I was in medical school, ulcers were in a territory of surgeons. And then came the observation that no, there's a bacteria there and now with antibiotics and pepto-bismol, ulcers have gone away, gastric cancer is down, and the surgeons are doing something else. So we need to bring that as well. As I've been here -- I'm sure I've got this wrong for the people of Milken but I've been looking at this logo and it seems to me that that actually tells us part of this. We need to bring in strands from different places to try to think of how we're going to solve this solve this together on top of the work that is already going on.

MS -- I'm not exactly sure how we do that. And I have one other question that's been bugging me, and maybe I'm wrong about this. So it seems -- I know there's a lot of people doing great flu work but young, smart PhD students and post-docs go where there is funding and the funding exists but the there's greater funding in other areas. I don't run into an endless number of people at Stanford Medical School who are doing flu research. They're doing gene editing stuff, they're doing neurology, you know, there's a lot of things they're doing. This doesn't seem like it's principally one of the important issues on students or brilliant young researchers' minds. How do we change that or am I wrong?

Bruce Gellin -- I mean, I think you're right but one example is a year ago, the Gates Foundation with Flu Lab teamed up to put out a grand challenge for this and acknowledged all this stuff's going on, we've seen the NIH roadmap, the importance of some of the basic research. But on top of that, are there other people who we don't know from other fields who might have a solution this problem that don't know that they might

have a solution? That's I think a step forward. There's a lot of interest there with that. They're trying to forge better interdisciplinary collaboration. I think that's the kind of thing that, in parallel with what we've heard about from Rick and Tony is the kind of thing we need to layer on top of this.

Rick Bright -- I think also, it's just not sexy anymore. I mean, it probably hasn't been for quite some time. I mean, when I was in grad school, everyone was working on HIV vaccines. I was in the laboratory Harriet Robinson and working on DNA vaccines for HIV and I came to the lab and everyone's working the HIV says you can do what everyone else is doing or I've got a little bit of leftover flu money on a flu grant over there and no one's interested in influenza, so I took on that challenge. But to make it sexy I think we have to -- I like the concept of disrupting this field. If we are just continuing thinking we're going to work on a another iteration or -- no offense. I mean, I think we need to continue what we're doing but another iteration or another assay or another step, I don't know if that's enough to excite those really creative thinkers. So in addition to doing what we're doing we're so good at, I think in parallel there might be a need or even an urgent call for an entity of excitement out there that's completely disruptive, that's not beholden to bureaucratic strings and processes.

Fauci -- Well, the HIV field was galvanized when we put a lot of money into it so let's talk about reality. And and I think that the easiest way to get a grad student really excited about something that isn't sexy is to, you know, put a gown on it by having a lot of money. And as you well know, I mean, there has been movements among certain members of Congress, and Markey put a bill in for increasing the influenza for universal flu vaccine by a billion dollars over five years, which is 200 million dollars over each

year for five years. When you put in that kind of investment, you will get people excited not to do the same thing they're only doing, you'll get new people to come in with new ideas that are disruptive and looking at it from different angles. So when you have an infusion of resources, that's how the field changes because that's exactly what happened with HIV.

Margaret Hamburg -- And also when people care. I mean, Tony and I were talking yesterday about the early days of HIV/AIDS and how the activists actually helped to move the research agenda in powerful ways. But people also I think that go into science want to make a difference and if they feel -- if we really put this in the context of the burden of disease and what it means. You talked about PR before. We haven't done a good job of that and I think that will help both generate the resources and will also, you know, I think draw on the best instincts of people going into science who want to make a difference in this country and around the world.

Casey Wright -- I think we're being terrible PR people because we're flu ambassadors and we're saying flu is not sexy. It's very sexy. At Flu Lab, our ambition is to defeat influenza. 650,000 people died last year and they will die this year and they will die next year. And we seek a transformative product. I think that we can absolutely, in parallel with the pursuit of an iterative process -- I think in parallel, we can we can yes/and this we need to set an ambition for the ultimate vaccine. This is broadly protective it is once a year -- once in a lifetime. It is durable, it is for everyone on this planet, and it eliminates this annual scourge and it eliminates the pandemic threat, and I think it's -- we've all been talking about the need for urgency.

We see -- we're talking about a lot of increased passion in our field and I think that's very important.

But, you know, we've really been asking ourselves and our community sort of the really hard questions. Are we organized in the right way to harness the new scientific insights and this passion? Are we are we organized in the right way to make permanent progress and meet this goal and, you know, that's one of the reasons why we asked the Sabin Vaccine Institute and the Aspen Institute to really interrogate these issues, and their results are really quite clear. There's no clear global owner of the problem and there's no clear global owner of the solution. It's hard to imagine how we'll permanent progress if that, from a worldwide perspective, doesn't have some kind of ownership. I think this fragmentation is our foe and this problem, the scale of it requires unprecedented collaboration. It requires a new model for global collaboration and dedicated leadership and an ecosystem that's willing to engage and support it.

MS -- I agree with all that and you guys are -- Flu Lab is an exception but it seems to me and when I sort of furrow around in this field that philanthropers, they want to make a splash and they don't want to make a splash on something that everyone thinks is boring or that there's a vaccine -- don't tell me it isn't boring, don't you dare.

Margaret -- We gotta get you trained first. There's a communications issue.

MS -- You don't have to train me. I'm just telling you the people that I talk to who have a lot of money, their eyes kind of glaze over when you say this stuff. You are an exception to this and it seems to me what we're talking about, what we've all been talking about is a kind of two-track system where we do what we've been doing because we have no choice. We're not going to ditch that system right now but we develop something more powerful and permanent and that requires a different kind of entity. And I'm wondering who is gonna run that entity because I don't

really think the government is probably the answer.

Rick Bright -- And I'll speak as a government representative. I think you're right on that. I think we are so distracted by so many other things. I have at least 25, 30 different threats in areas I'm focused on. I know NIH NYAD has so many areas as well, and you know where you saw a lot of mobilization even in HIV world when a separate entity set up to focus on HIV vaccines. You know, there is no single focused entity on influenza and I think if there was a single focused entity on influenza, then that target and that time line would be accelerated to bring the best science, bring together those interdisciplinary thoughts.

I mean, we're in this room, we're probably vaccinologists, we're probably immunologists, we're probably working on some vaccine or made some vaccine at some point in our life, but we're not the chemical engineers or the other engineers or the anthropologists or others, who bring critical insight on how you disrupt and deconstruct an age-old problem. We've had these vaccine for 70 years so this is an age-old construct that requires those creative chefs that come out of the kitchen deconstruct the carrot cake and make it look like something different but the best carrot cake you've ever eaten your entire life. We need that for an influenza vaccine and we also need to not forget that for influenza, vaccines aren't the only part of the solution. I mean, it's so easy to get caught up -- if you want to get sexy with influenza, you do stay in the vaccine space. But if you go into the diagnostic space or the therapeutic space or non-pharmaceutical intervention, those are the early steps that will make a huge impact on bending that epidemic curve for seasonal and pandemic outbreak. And so we have to have that single focus entity and focus on stopping influenza, not only on making a vaccine.

Fauci -- Yeah. It is -- I mean, in case we haven't figured this out already, this is really very complicated not only from a scientific and public health standpoint but from a perception standpoint.

So, Casey, taking your point, certainly it's not boring when you delve down and see what the ultimate impact is, both cumulatively each year as well as the intermittent time that we get a pandemic. But let me tell you how things really fall into a different category. It's the diversity of what influenza means to the community. For some people, they get the flu, the real flu, not like I have a stomach flu but the real flu. They get better so there's sort of this perception if it's so serious, how come people get flu each year and it isn't a catastrophe?

When you're dealing with a disease like HIV, if you get HIV, it's serious whether you're young, whether you're middle-aged, whether you're old. If you get cancer, that's bad whether you're young, whether it's intermediate, whereas with influenza, for some people, they go throughout life and it doesn't impact them at all. There isn't anybody that's afraid of influenza. If you go in a focus group, when you say, are you afraid of getting HIV if you're at risk, oh, absolutely. Are you afraid of getting cancer? Absolutely. Are you afraid of the flu? Don't bother me. I mean, that's the reality of how people perceive flu.

As Rick said, we're responsible for a variety of diseases, making countermeasures, malaria, tuberculosis, zika, ebola. We're in the middle of ebola right now so you go to the DRC, where I went to a week and a half ago to visit our sites, and you ask somebody, are you worried about influenza, they'll laugh at you. What are you talking about, influenza? They don't vaccinate their people for influenza because they have enough problems with malaria and tuberculosis and now Ebola. So it is a perception,

which is a misperception, that it is not a serious disease but as Casey said, hundreds of thousands of people die of it each year and when you get a pandemic, millions and millions of people. So we really do have a problem of how the world perceives influenza and it's going to be very difficult to change that unless you do it from within and say, I don't care what your perception is, we're going to address the problem in a disruptive way and in an iterative way because you do need both.

MS -- In the long run, over time, amortised, if the 2009 pandemic had been much more deadly, would that have ended up being a better thing for humanity?

Fauci -- Would it have been -- no, no, because I mean, we had -- not as certainly as serious as the 1918 but we had a pretty bad pandemic in 1957 in 1968. That didn't change didn't change much.

MS -- But wasn't that before -- I mean, don't we have some bio-technological tools, you know, at our disposal that we didn't then?

Fauci -- Absolutely, absolutely.

Margaret -- The sad truth is that when there's a major crisis, it focuses attention and usually resources, and some significant mobilization falls. It doesn't necessarily mean that we are using resources in the best way possible, though, because it's done in the moment of crisis and there's, you know, throwing money at things that sound good without them being thought through. And then there's what we used to call the u-shaped curve of concern, where there's the initial increase in interest and resources and then when the problem fades and other problems emerge instead, then everything drops off. And, you know, I think we've been in that with many different outbreaks of disease and flu to some degree as well. I think part of what, you know, Casey was pointing out and others on this

panel were pointing out is that we need, number one, this time to be different and we also need to really organize ourselves in a way where there will be accountability for sustained action and not just response.

MS -- So let's talk about the science a little bit more. Craig Venter, who is a controversial person but interesting to me, has written that he thinks we ought to have a vaccine such that if you take off in a plane from Hong Kong and are infected, by the time your plane lands in New York, there ought to be a vaccine assembled and deliverable to you. How crazy is that, how far are we from that? Are we ever going to get there?

Rick Bright -- I'm not gonna say how far away but I don't think that's too crazy. I think that if we move towards the era of synthetic-based vaccines, I think we remove the tendencies of thinking the vaccine has to be something that we have grown into something else, in an egg cell or insect cell, any type of dependency and growth. If we can move into more synthetic, the nucleic, acid-based, messenger RNA-based, those sequences can be rapidly shared around the world. Enzymes that can synthesize the small fragments of the messenger RNA necessary to go into a vaccine can be made in a shoebox-sized system right now, which is translatable into a 3d printer-like or inkjet printer-like thing.

Now putting those in a system to print those on a patch that a self-administered vaccine could happen, the technologies are out there. We haven't demonstrated their true effectiveness and the ability for a vaccine but it is not too crazy to think that an outbreak of a novel avian virus could occur in China somewhere. We could get the RNA sequence from that, beam it to a number of regional centers, if not local, if not even in your home at some point, and print those vaccines on a patch and self-administer. We're

a ways out but the technology is there to be adapted, assembled, to put a futuristic view of a rapid response to an emerging novel threat.

MS -- How much more do we need to know about immunology to get this right?

Fauci -- Well, I mean, not immunology in general but the immunology associated with protection against flu. We didn't mention it but I'll just briefly mention it now because it is important is that one of the other complicating issues with flu is that as the human species evolved, you developed an adaptive immune system, which means that if you get exposed to something and then later on, you get exposed to the same or similar thing, your body will remember it and make a good immune response. That really helps you, it saves civilization, it's very good in the immune system.

The trouble with influenza is that since it changes a little bit, your body for the first influenza you get exposed to, every time you get exposed to subsequent things that are a little bit different -- because if I get exposed to measles and get measles and then a year or two or three or four from now, I get exposed to measles again, I'm protected because my body sees that measles and is gonna make a good response against the virus.

With influenza, there's a thing called imprinting. People refer to it somewhat inappropriately as original anagenic sin. And if you get exposed to an h1n1 when you're an infant, every time you see any influenza, be it h3n2 or h2n2, your body is gonna make a response against that but it's going to be very distracted and it's going to back and make h1n1. I was born in an h1n1 year and when I get exposed to h3n2, my body will want to make a response to h1n1 as well as
h3n2, so it gets distracted.

So getting back to what you ultimately want to do, and I think Casey mentioned it. When you do get a universal flu vaccine, you're going to want to give it to six-month-old kids because the universal flu vaccine even for me at my age is not going to be universal. It's going to call up other things that I've been exposed to. So to answer your question, Michael, we know a lot about the immune system but influenza, by the way it induces a response, really complicates the immunological response to it.

Rick Bright -- One of the interesting things about that, too, of where technology is going -- when you're thinking about synthetic- based vaccines, we're also driving in synthetic-base monoclonal antibody production in vivo. So at the same time, you could or someone could put that vaccine dose messenger RNA into a patch or a way to administer it to your body. They can also deliver this same messenger RNA sequence for a monoclonal antibody. So you could actually help the immune system while it's making that immune response to the vaccine by delivering an encoded monoclonal antibody. So you can have an antibody response come up within a period of hours that would bridge your body while you're making the immune response, even if it's maybe a partial immune response, to the vaccine strain. So -- I must be speaking too much. The combination of helping the vaccine response by coupling it with synthetic delivery, rapid delivery of a monoclonal antibody or other sort of passive immunity might be an approach to give us that rapid protective immune response.

MS -- I don't want to beat up on industry too much. Well, I don’t mind beating up on the industry but how eager are they -- presumably, there would be a profit incentive even for a universal vaccine. There's a lot of people who would need it. How eager our industry players in your experience -- maybe Peggy would be the first to answer this -- to embrace something new like

that?

Margaret -- You know, I think that there are certainly companies big and small that absolutely would. I think, you know, we've seen -- Tony was mentioning the Ebola outbreak. You know, we've seen several major companies and some smaller ones step up to the plate in ways that aren't really benefitting their bottom line but are important in terms of public health. But I think we do have to try to create a context for them to do this in which they will get rewarded. Some of it is appreciation, some of it is, you know, the sense of contributing and, you know, really harnessing science for the benefit of humanity. Andsome of it is helping to decrease some of the barriers and the uncertainty in the process, and I think that goes back to the collaboration. I think what we really have to think about is how to align the different capabilities, the different funding streams, the different incentives towards a common goal. And for the industry, I think it is really, really important for them to not feel that they're just going to sort of walk off a cliff with a completely new approach without any idea whether it will be successful.

So I think, you know, what we've seen in various areas and certainly something -- a lesson I learned when I was Commissioner of the Food and Drug Administration is that the sooner everybody can sit at the table, government, industry, academic researchers, and in many cases, the people who are actually going to have to either consume or deliver the product as well, and really get together map out a plan and sort of identify what are the critical questions to ask an answer? What are the unknowns scientifically, what are the unknowns in terms of the regulatory process and and what's the level of risk that people are willing to accept and how can we reduce some of that, either through financial incentives or guaranteed purchase or, you know, really clarifying and making more predictable the regulatory questions as well.

Casey -- I think to add to that, Peggy, sort of part of it getting everybody around the table sort of it acknowledging of what everyone's strengths are at that table, and then what's really hard for those individual organizations to do and take on. I think that's that's that -- there's a potential role for philanthropy to play there, too, and have a role at the table.

Margaret -- Absolutely.

Casey -- I think we are in a position to take on a little bit more risk to, you know, open to a little bit more experimentation with methods and how we do things. That's what I think is unique about Flu Lab and it's unique about other philanthropies, and I think playing -- they could play a really important role there and fund a set of sort of bolder, maybe earlier promising concepts but also take on smaller creative initiatives that might have an outsized impact.

Bruce -- So what Peggy and Casey just described is the rationale behind that call for an entity. It wasn't necessarily a building with a logo but it was just putting it all together. And I think it's important that when the group looks at this, they recognize that calling for some of this wasn't easy. Do we need another global this or that? But the recognition of, given the urgency and given the importance of this and given we heard about the risk, it really was worth pursuing that to try to figure out how best to align all those different things that Peggy laid out to make sure everybody's around the table, and it would advance things rather than keeping things in their own lands.

MS -- So that report has been out for a little while now. Are you finding that it's catching on?

Bruce -- What does catching on mean? It was released in July. We've talked about it a lot. It's gotten a lot of attention. I think the group was wise in prioritizing what they called for. They called for this entity, which again is this collaboration we talked about. They've called for the need to to infuse innovation, to find some of these people who we don't know might be part of the problem to come into this, and to try to think about how we talk about this differently so that your stomach flu doesn't keep us from making progress.

MS -- We only have a couple of minutes. I was wondering what people think is the single biggest obstacle. Is it money? If we just had a ton of money focused on this problem, would that make it go away?

Fauci -- It wouldn't make it go away but I think an infusion of more resources would bring people into the field that would not normally be into the field because scientists do that. They do things that are interesting to them but they also follow the money. And I think an infusion won't make it go away but an infusion of resources I think are gonna bring some people who are interested in other fields to add a fresh new look, so I think it would make a difference.

MS -- And does that have to be something that comes from philanthropy, does it have to be something that comes from the United States Congress, a little of both? I mean, where do we get the financial firepower to do something that hasn't been done?

Fauci -- I think both. I think it's -- it's not just unidimensional. I mean, clearly, there's movement and discussion at least in the Congress. I mean, we have fiscal constraints now but, I mean, people like Ed Markey and Rosa DeLauro have been talking about the need to make a substantial infusion of resources into the entire field, not only the field of science to get

new discovery and innovation but also in the field of developing better processes to make the vaccines. And that president's executive order actually specifically talks about the kinds of things that need to be done. It doesn't mention resources in it but it clearly delineates the kinds of things that we're talking about.

MS -- Do orders like that spur resources to get allocated?

Fauci -- Anything that calls attention to the kinds of things that are going on into the problem would either directly or indirectly at least bring attention to the need for resources.

Margaret -- And I think we just we really do need to have some accountability. We can't just keep talking. We have to really demonstrate progress towards goals and I think that, you know, that's part of what -- again, what the Aspen Sabin group tried to do, was to sort of define some things that need to get done and create a system of accountability.

Rick -- Mike, I think -- I know we're out of time.

MS -- Keep talking.
Rick -- I do think we need this moment of energy, this burst that complements everything that we've been doing for these years and collecting lots of information. This advocacy group that is single focus, that goes to Congress, goes around the world. People are dying. The urgency -- the time is now and this group is focused on it. It is the advocacy group, it is the lobby group, it is whatever the group does. But it's got to get money from philanthropy, it's got to get money from government. It's got to not be distracted by these cycles and bureaucracy to get the job done.

MS -- We're out of time. Things are flashing at me.

So I would just like to thank the panel very much for a provocative conversation and their time.