[Crosstalk]

Thank you, David. That was quite an introduction, I must say. Maybe you were doing it just because I followed you but thank you very much and I'm glad to be here and David has been one of my close colleagues and I've learned an enormous amount from him over the years about the inter-section of the life science and health and security issues and we've been trying to get together to do an event like this for a long time so I'm glad it finally worked out. So where to begin? I will say, I asked David if we could not do it in a format of a speech because after six years as FDA Commissioner, I'm just sick of giving formal speeches, so we decided we'd do it as a conversation. It'd probably be more interesting, we can probably cover more ground and hopefully we can engage all of you as well in those discussions.

Well, maybe stepping back just underscoring what David said about how unique and essential the FDA is to the health and safety of every American, but also more broadly. I feel I have to underscore this. At this moment in time, when some are questioning the role of government, questioning the role of regulation and I think, also, this renewed focus that's more nationalistic, much of what I learned at the FDA really tells me that we need to proceed with caution along those avenues of thinking because, in fact, to me, FDA represents what government can uniquely contribute to society, to health and well being and it also is a time in which we have to really think very differently about science and about the global nature of the world we live in so that it is a much more collaborative and integrated approach. As David said, FDA is responsible for regulating somewhere between 20 and 25 cents of every dollar that consumers spend on products ranging from overseeing the safety and efficacy of medical products, biologics and vaccines, the safety of the blood supply, medical devices, the safety of things that emit radiation, safety of cosmetics and dietary supplements, food safety and the food supply, 80 percent, it's a shared responsibility with agriculture.

We used to joke that FDA oversees 80 percent of the food supply and gets 20 percent of the money and just the reversed for agriculture that does meat, poultry and eggs. And during my tenure, we also got oversight of tobacco products, which was a hugely important step because tobacco and its use remains the leading cause of preventable death in this country and around the world. So a huge set of responsibilities and at a very challenging time, when science and technology is advancing rapidly and as was mentioned, the world is becoming increasingly global. So when I arrived at the FDA, I have to say I was sort of shocked. I had no idea what I had gotten myself into and was uncertain where to really begin but I would say that some of the critical aspects of my tenure were really positioning the FDA squarely for the 21st century and its challenges and one aspect of that was the area that very much relates to the intersection of health and security that David mentioned, which is the globalization of both food supplies and medical product supplies. It was a shock to me, maybe you all are more sophisticated, but to learn that on the food side, 50 percent of fresh fruit, 20 percent of vegetables, over 85 percent of seafood were all coming from places outside of our borders.

These are the products that Americans were consuming and those products, you might also note, are among the most vulnerable in terms of potentials for contamination. On the medical product side, the numbers, I think, are equally startling. Forty percent of the finished drugs that Americans take are actually manufactured elsewhere. Eighty percent of the active

pharmaceutical ingredients in the drugs we use are coming from overseas, mainly from China but not exclusively. About 35 percent, probably more, of the medical devices used here are coming from other countries. So there really was a requirements, that even though the mission of FDA is to promote and protect the health of Americans, there was a requirement that we step outside our borders and think in new ways and the original vision was that there have always been some imports but the FDA inspector at the port or even at the airport could decide what to inspect and decide, okay, that tub of molasses is safe, let the ship in. But the volume now is just so huge and growing and the number of facilities around the world, the number of countries around the world that products are coming in whole or in part from so enormous that we really had to rethink our models for how to respond, not just how to better protect the borders as sites of entry, even though there's several hundred airports and trains and trucks that are coming in every day carrying products.

We did need to have a strategy to address that and actually using the tools of computational science, we created a computer-based system called Predict that used information about the nature of the product, the history of the manufacturer, the region in which the product was coming from to help prioritize and red flag the things that truly needed to be inspected and green light the things that could just sort of move through. But we also began to think about how do we work around the world setting up regional offices for interacting with counterpart regulatory authorities and companies but also, really trying to create a new strategy for global governance because the only way that I, as FDA Commissioner, even as the head of the most well-financed and most sophisticated, I'd have to say, regulatory authority in the world, we couldn't possibly do our job alone. So setting up systems where we would share information, share work load, trying to harmonize standards for inspections and regulatory review and really trying to create a new global governance approach, which I found was much easier in theory than it was in practice. But all of that was fascinating.

All of that, I think, really, also, very much, is at the intersection of critical public safety and security issues that the public doesn't recognize but that every single day, when you go to the supermarket, potentially, you're at risk without the good work of the FDA and responsible oversight by companies and other regulatory authorities around the world. It used to be, at least when I was little and we'd go down to Mexico for a vacation or whatever, I was instructed, 'don't eat anything that you can't peel or boil.' Now you go to the Safeway and you buy it. So that was one important arena. The other incredible challenge was keeping up with evolving science and technology and the truth is that FDA is an agency with enormous history. We're now over 110 years old, having been founded in 1906 by President Teddy Roosevelt in response to a lot of serious problems that were occurring in both the food industry and with the sale of medicinal that were unsafe and unproven and the publication of Upton Sinclair's 'The Jungle,' I think, was the final bit of -- I don't know if that was an early form of social media that influence policy making. But anyway, much of the legal regulatory framework of FDA came in response to serious problems that needed to be remedied but was really and still is, mired in a different era of science and technology which has exploded in recent years.

So to try to not be a barrier to innovation as many think of the FDA as being, but to help foster innovation that's meaning for patients and consumers because it actually benefits them because it's demonstrated that the benefits outweigh the risks. If FDA is gonna keep up with evolving

science and technology, it really requires a very different approach and a breaking down of what was the model that really, I found, when I got at the FDA of the FDA as a unique entity as a regulator that needs to sit in its own domain and interact with stakeholders at appropriate times under appropriate circumstances and you wait for the package for a drug approval, for example, to cross your threshold and then you look at it. Really, it became clear that the only way for FDA to work effectively and meaningfully in the modern era was to break down that black box approach and really engage with partners, with stakeholders to actually bring what FDA could offer to bear on the R&D process in many instances so that the right studies would be done so that the research agenda would be elaborated in a way to make sure that the critical questions were asked and answered rather than after the fact saying, 'why did you do that study and not that study?' But also, FDA can't possibly have all of the expertise within its walls that it needs to be assessing emerging technologies and new areas of science and the complexities that they raise for the regulatory process.

So to also engage FDA scientists more broadly with the scientific community and of course, in the modern era as you all appreciate, science is a globalized enterprise as well. So those international activities become even more important, too. The other thing I'll mention, I said I wasn't gonna give a speech and here I am, giving a speech but I didn't appreciate until I was in the midst of it, what a critical role FDA, in fact, plays in responding to emergencies and of course, it had been an interest of mine, going back to my days as Health Commissioner of New York City, when the World Trade Center was bombed the first time. We sometimes forget but for those of us in responsible positions in New York City, that was a seminal event when we all started to think about the threat of domestic terrorism differently and I, as Health Commissioner, began to think of the range of vulnerabilities that I would be directly responsible and that's when I discovered the threat of bio-weapons and bioterrorism, probably when I first began to intersect with work you were doing as well.

And I also had the good fortune to have grown up with a family friend, Josh Letterburg, here on the Stanford campus who was then at Rockefeller and he really took me under his wing to educate me about the world of biological threats and I've worked on those issues thereafter from various points of reference and leadership. But when I was at FDA, that was not an issue I thought that I was gonna be spending much time but in fact, FDA is right at the center of advancing the development of new medical counter measures for deliberately caused biological threats and also, naturally occurring serious biological threats, diagnostics, drugs, vaccines, critically important and also overseeing other important medical devices like masks and respirators and even rubber gloves but it was the role in developing medical counter measures that was fascinating to me in terms of the importance of the FDA role and the forward leaning nature of the agency because it's very hard to actually develop and assess a product to be used for a disease that isn't naturally occurring for a disease where you don't have human populations to study it on to be able to think about ways to get products as ready as they possibly can be when you don't know what the threat will be.

So the idea of developing platforms for vaccines that could be pre-approved in terms of the basic concept but then adapted in a specific setting, etcetera and then how do you think about how to structure some of the important research that needs to be done when the crisis actually occurs to move it as quickly as possible. So we've been deeply involved in many aspects of medical

counter measure development including developing an approach to the pre-approval of drugs that is unique in the regulatory world which was the animal rule, which enabled approval based on two animal models that could be demonstrated to have relevance, although not perfect alignment with human disease. When Ebola occurred, Ebola, as you may remember, was not a new disease when we had the outbreak in West Africa but the impact of Ebola was very different because it occurred in three countries that were still struggling to get on their feet after years of conflict amongst the poorest countries in the world and countries with very minimal health infrastructure and other social and public infrastructure to support response and also conditions of considerable urban concentration, a lot of movement amongst regions, though, and across the borders of the three countries involved and also, a set of traditional practices for dealing with dead and dying that actually increased risk in terms of exposure 'cause it involved washing and being in direct contact with bodily fluids in ways that enhanced Ebola transmission. So it was a perfect storm to really accelerate this Ebola outbreak in ways that ultimately garnered global attention and concern and response but it created an environment where there was a rush to do whatever could be done and huge pressures on agencies like the FDA in terms of there were some products in the pipeline that were actually a result of programs that the U.S. government had created after 9/11 and the Anthrax letters when there was a recognition that we needed to better define potential threats and start to develop products to address them and Ebola was seen, at that time, more as a concern in the possibility of it being weaponized to cause deliberate harm rather than the kinds of outbreaks that were occurring in remote villages in Africa.

So there were some preliminary Ebola vaccines that were a fact in development, which we won't be so lucky in all instances. Some therapies that were less evolved but potentially useful and the diagnostic domain was rapidly ramped up. But how, in the midst of this terrible crisis that was increasingly politicized as well, I might add. President Obama said it was actually one of the most challenging episodes of his eight year tenure as president. How to try to make, potentially, useful products available to people as rapidly as possible but not to potentially expose an already vulnerable set of people and communities to something that was untested and might actually cause more harm than good and it raised a lot of issues about not just one of the ethics of all of this but also, how do you help to build capacity to actually do studies, how do you educate the public and policy makers to understand what the options are and how do you make sure that when a crisis occurs, you can collect critical information but also, I think, now, what we're grappling with is how can we be better prepared for the future so that we don't go through some of the unfortunate lessons learned in Ebola again and again and again.

Yeah. Well, I guess, first and foremost, I would say to a new FDA Commissioner and I have said it to the nominee to be FDA Commissioner, that it's crucially important that you hold onto the sense of mission about what the FDA is and what it does. It is a public health agency that makes science-based regulatory decisions to promote and protect the health of the public and it sounds a little bit trite, but that is the core and that has to be the guide post. It is an agency that is constantly being buffeted by competing priorities, different stakeholder groups with strongly held views, by politics and ideology by huge financial interests and the most poignant of all pressures, which is the individual or families of patients that are seeking something to help treat or cure a devastating illness. So it is really hard not to get off course and I think keeping science as your guide and recognizing the unique and essential role that the agency plays as a public health agency, is crucial and should never be forgotten 'cause once you start to go off course, you

can wildly off course. I think, also, even though it may be unattractive in this environment, I think that you have to be prepared to defend the role of regulation and it's easy to say that regulation is a barrier to innovation, that regulation is job-killing, that regulation is holding back all kinds of wonderful treatments and cures for a range of serious disease but if you really step back and look at the role of regulation, I think that history and experience tells a very different story, that regulation can actually help to improve the quality of products, can really help to define the risks and benefits and the best, most appropriate uses.

Regulation that is smart and science-driven and done in an open and transparent way, actually, I think, strengthens industry both because it can enhance the value of the products and the quality of the products but it also improves consumer trust and confidence in those products which really matters in the marketplace and it also creates a level playing field for companies because the worst thing and we certainly saw this in the history of the FDA is when there are literal snake oil salesman out there and you're trying to create a quality product. Well, the pressure if that snake oil salesman is out there with a good marketing strategy to actually reduce the quality of what you're making to compete is very tempting but at the end of the day, we have certainly seen, over and over again, at the FDA, when there's a problem, it's devastating. It's not just devastating to the one company that has a recall, whether it's a food recall or a drug recall, but it's devastating to the whole class of products, it's devastating to the whole industry. So I think that while industry isn't always out there with their placards advocating for the FDA, industry will tell you that they benefit from a strong and well-supported FDA, an FDA that is well-supported in dollars and in people because the quality of the people who work there really matters and that's the other thing that the FDA Commissioner needs to be prepared to advocate for is that FDA needs the resources that it can do, that it needs to do the job.

FDA funding, it's the best bargain around. If you look at what every citizen of the United States spends to support the FDA, it's about eight dollars a year and probably in the course of one day, most Americans consume more than eight dollars worth of FDA regulated goods. So right now, I'm happy that during my tenure, every year we got a bump up in the budget, which was a new trend. It wasn't anywhere near what I had hoped for and anywhere near what the agency needed. This is obviously a moment in time when it's likely that resources will constrict and that would be devastating and I would say don't succumb to the pressures to turn inward because, more than anything, because of what I was talking about before, we need global engagement and a global perspective and I think in this environment, also, sadly, the commissioner of the FDA is gonna have to fight to remind policy makers and the public that expertise matters and that actually, FDA brings enormous experience and strong science to the table for the benefit of the public.

Well, it's a strange time in Washington. I was actually enjoying several thousand miles between me and Washington out here. It's hard to know how this new administration is really gonna settle out but right now, it certainly isn't looking all that promising for science or for regulatory agencies. I think that for lots of reasons, including the fact that whether you like government in regulation and concept, at the end of the day, most members of Congress and members of any administration actually do want safe food on the table and drugs that work. So I don't think that FDA is as vulnerable as agencies like the EPA but I think it is a worrisome time, the fact that there has been no clear effort to put in place a science advisor, no clarity about whether the White House Office of Science and Technology Policy is going to be maintained or not. Many of

the appointments to critical leadership roles in parts of the government are people that actually actively have disavowed certain important aspects of science, climate science being one good example. All of those things are worrisome. I would say there's one little glimmer of hope, but I don't know if it's really gonna pan out but with respect to some of the global health security issues that we began talking about a bit, there does seem to be an effort underway to actually build a focus on global health within the White House from the get go, which sadly has not been true of past administrations.

The Clinton Administration, partway through, for the first time, put someone with a health background on the National Security Council as a health advisor, Ken Bernard who's sitting over there. We thought that was the breakthrough and that would become practice thereafter and I can tell you, he made himself invaluable but when the next administration started, the Bush Administration, they made a conscious decision, Stanford's own Condoleezza Rice and others that health was really not a security issue and they would abandon that approach. There were several important studies done before the Obama Administration came on board, one from the institute of Medicine that I participated in, all making the recommendation that global health focus be part of the National Security Council and there be an organizational and operational focus within the White House for this important set of issues and they, too, decided not to put it in place but both the Bush Administration and the Obama Administration put it in place partway through in response to a crisis. So I think maybe now, we actually are seeing what may be a focus in the White House. So it's still all in evolution, but that would be good, that would be a positive step forward and time will tell. But I think the trends, anti-government are worrisome. The devaluation of expertise and science more broadly is very worrisome. The sense of nationalism, I think, is coming at just the wrong moment when we really need more global strategies and solutions to problems and I think the desire to cut certain critical areas of government to protect or expand other areas is also potentially devastating, whether it's cuts to foreign aid or cuts to research at NIH, cuts to an agency like the FDA. All of those things are going to combine in ways where I think the negative impacts are gonna actually be more profound and worse than any of those cuts in isolation.

Well, really an important question and one that I spent a lot of time thinking about and working on because again, even if you look through all of FDA in the most selfish way of trying to protect American citizens, the best way to get there is to actually help to build regulatory capacity in other countries and especially when you're looking at products and supply chains that are coming from many, many countries that are developing economies without a lot of resources, with very immature regulatory systems at best with companies that are also very underdeveloped and under resourced in many instances and often, unstable governments and institutions. We spend a lot of time, as we thought about our globalization strategy working on that issue and in fact, I used to get teased by some of my colleagues in the FDA, reminding me that FDA wasn't a development agency 'cause it was very easy for me to offer the services of FDA to help Bangladesh or Myanmar or Uganda develop their regulatory capacity but for the FDA, it's actually a near-impossibility to spend much time at it because they're already stretched so thin and doing any overseas inspections is a much greater demand in terms of time and resources. So the additional training was hard but we actually developed some great partnerships and programs and I think it's an area where there is some momentum, I hope, with philanthropy now getting interested with the Bill and Melinda Gates Foundation. I actually seconded someone from

the FDA to work with them. He now works full-time for them and they have a whole program in regulatory capacity building and have done really good work with East Africa, there's a regional regulatory harmonization activity there, some work in Southeast Asia and a fair bit a work in China, which is more than a developing economy, of course, but they have huge challenges in terms of regulatory capacity and for better or for worse, they've also been a major source of adulterated and contaminated goods, both on the food supply and on the medical product supply, in terms of risks to this country. India's another example and it was shocking to me when I learned about the heavy metal contaminants in spices and I have a husband who's a bit of a hypochondriac.

He'd cut out certain things all together when I'd come home and tell him stories but there's enormous amount of work to be done and really, it is a situation where the only way we're ultimately gonna achieve it is to get other countries to care. I used to argue with my colleagues at USAID and we actually did some good work with the World Bank and they're spearheading some activities, but it is really a good return on investment in terms of development because in addition to the benefit here at home, you're helping improve health and quality of life in countries that are potentially unstable. You're helping to build industry that can strengthen the economies of those countries and again, the stability of those countries and you are building trust and confidence and bridges between different countries in new ways that have much broader value when you think about national and international security. So it really is a great return on investment but unfortunately, regulatory issues are not the most compelling when you just hear about them superficially and in some instances, it's a turn off.

In fact, that was Bill Gates' reaction, basically, keep regulatory agencies as far away from us as possible but then, he realized that in terms of both return on investment, in terms of the moneys that they were putting in to developing new products for use again important public health problems around the world, getting that regulatory perspective in helped because it made it more likely that their scientific investments would pay off but also, recognizing that it, as a development activity, had these huge payoffs and ultimately, the desire to be able to produce products in the countries or regions where they're gonna be used has great appeal, as well. So we're making progress and I think it's a really important approach but it's a bit atypical in the development world but becoming more important. The other aspect of it that you probably are aware and sorry to give such a long answer but it's a really important question, if you worked in Southeast Asia, I'm sure you appreciate the problem of counterfeit and substandard drugs. Part of the problem is that we don't know the nature and scope of the problem 'cause nobody tracks and actually, while I was at FDA, we started funding WHO to start to do surveillance and again, the Gates Foundation actually stepped in to take it up but until then, nobody was really looking or monitoring and still, the systems are very poor. But as much as 30 to 50 percent of drugs in Southeast Asia may be substandard and not only does that mean that healthcare systems are wasting their money on ineffective drugs, patients aren't getting treatments that work and in many instances, Malaria being classic, you're actually breeding drug resistance as well, that has huge public health implications for all. So if you're providing drugs as part of various programs around the world, if you're a government providing drugs, if you're a healthcare system, you have a huge interest in knowing the quality of your products but if you live and work or your programs are operating in an area with an immature regulatory system, there isn't a screen and you usually learn about the problems when it's too late.

Well, let me clarify because I don't believe that FDA and its regulatory apparatus is emasculated, I actually believe it is stronger and more effective than people realize. I think it's at risk and the demand's way outstrip the resources but I think that almost anyone in any country would rather have an FDA-regulated product than not and in fact, an interesting thing that's been going on in recent years is many countries have adopted legislation to enable them to use an FDA approval for their own approval, which has been great for those countries. Mexico used to make me very envious when their commissioner would cite the statistics of how much money they were saving by letting FDA do the approval for them and they were putting it into expanding access to care, which is certainly something that I valued. But if FDA's gonna become the world's regulator, then I hope we'll get some more money. But I think what I really wanted to convey was let's not fix the wrong problem and I think that's part of what's going on now, is that there is a perception that regulation is bad and the answer is to get rid of it. But in fact, the answer is to help support meaningful and smart regulation which adds all kinds of benefits.

Yeah, well, I don't think I can give you that message, either, and I think that this a challenging, vulnerable time and I think that the great danger is that rhetoric will get in the way of reality, in fact, and rather than look at the facts, in terms of what works and what doesn't, there will be a sense of blow it up. One of the things that's very interesting, for example, is that if you really wanna reduce the time for research and development and regulatory review, the best thing that you can do is better resource FDA so that they have more scientists with the right expertise and exposure as well, so that there can be early and continuing engagement by the FDA team with the researchers, so that the right R&D strategy is in place from the get go so that the FDA can help inform the decision making so companies or researchers don't go down dead ends, so that there can be real feedback, instead of waiting until it's too late. But the response by many right now is FDA is slowing R&D, so let's cut them back because they're just a problem and it's the exact wrong solution.

Yeah, but what can you do to help? Well, I think, I wish I really knew how to influence policy making and political ideology at this moment in time but I think a voice in support of the important work done by FDA really does matter. One of those things that was very frustrating to me was that there were various advocacy groups that meant well in Washington and national groups that were informally supportive of the FDA but whenever they did anything, like the organization, Research America, you may have heard of, they've been very valuable in enhancing budgets for NIH but I was constantly on the phone saying, 'well, what about FDA?' If you don't also enhance the budget of FDA, then it's not going to efficiently serve to deliver on the promise of all that scientific investment at NIH and in fact, I think regulatory science, which is a term going back to regulation not being the sexiest thing. When I first started talking about regulatory science, everybody said to me, 'just stop it,' because people's eyes glaze over or they have an automatic aversive reaction and anything you say, they won't listen to. But there really is an area of science that's very important to the overall scientific enterprise that's being underappreciated and under invested in for a long time. There really is that last bridge. I mean, translational science gets you into studies and humans but if you really want to efficiently translate opportunities in science into real world products, developing new tools for predictive toxicology, so you're not doing a bunch of animal studies that usually don't have that much value but do take time and money and get PETA at your doorstep, thinking about innovative clinical trial designs that are adaptive and bring in Bayesian statistics and utilize different kinds of so-

called real-world data that may exist, using big data to help look at the real world experience in terms of use of drugs and emerging safety issues or indications for use or as we know more about genetic markers, being able to look at data from studies or groups of studies that might have looked like a product didn't work or had unacceptably high side effects. But as you know more, you can begin to subdivide the groups and look at subpopulations of responders or subpopulations that have unacceptable toxic side effects and continue to evolve your understanding about drugs and their use. So really, being an advocate for FDA as a science-based agency and the science needs of FDA is very important, too.

Yeah, well, I think AAAS can and should play a really powerful role at this moment in time, in terms of engaging the public about the importance of science. I'm not quite sure how to do it but I think that there does seem to be an attack on science on many fronts and of course, AAAS is much broader than just life sciences, which is the area that I know best but really, a questioning in Washington of science as a public good and when you have the director of OMB actually saying that he doesn't think government should fund science, it's a worrisome trend. So I think AAAS has a very fundamental role about engaging the public and in turn, policy makers about the important of science and why science matters to people and restoring people's belief in science because I think there's the political environment but I think there's also been a parallel trend that's probably related but it is a little bit distinct, where people just don't have as much confidence in science as they used to. It's partly concerns about data reproducibility and one week you read something in the paper that says, 'eat this,' and the next week, you read something that says, 'don't eat that, but eat this.' People are sort of wondering and then it does get tied in with ideology and other things. So I think this is really an important time and it's hard to know. I would welcome other perspectives on how AAAS can usefully assume this role but I think we have to learn and it's a broader issue about how you reach people that aren't part of your already converted but actually reach people that are skeptics and science denialism takes on many different forms in many different contacts and requires different partners but that's one thing that I think AAAS really needs to work on and I think AAAS has always been very, very important as being a source of credible information on important science topics and also, a source of credible information about what's going on in terms of the world of science policy, how science is being funded and what are the implications. So I think that should continue. This weekend is gonna be a very interesting weekend I think. Probably, all of you know there is gonna be a big science march in Washington and satellite marches in other places and in other countries. And within AAAS and I think within the science community more broadly, there was a lot of debate about is this a good idea or not? Do we want to politicize science in this way? Do we want to become the opposition in terms of the way the Trump White House thinks and will it ultimately serve science or will it actually be detrimental? Of course, it remains to be seen. The decision for the AAAS was to participate but to not participate would be a very strong statement and that there were things that were happening in the world of science and policies in response to scientific issues that were simply too egregious to step away from the discussion but how to make it into a positive pro-active 'Why Science Matters' kind of a focus and not Trump-bashing. So we'll see, but that's another area that AAAS has been focused on, of late.

The world has changed. I don't know when you were in the White House. Many people think that FDA is an independent regulatory agency and actually, I was on a conference call earlier today with six other former FDA commissioners on a project that we're doing about why FDA should

be an independent regulatory agency but it's not. In fact, the authorities of the FDA Commissioner, actually, by law, are given to the Secretary of Health and Human Services and then those are then, in most instances, formally and sometimes informally, given to the FDA Commissioner, but some of you may have actually witnessed, in real time, that playing out when the FDA recommended that a certain product called Plan B, a morning after contraceptive, be approved for over-the-counter use for women of reproductive age and the Secretary of Health and Human Services overruled that decision and she was well within her legal rights although she was supposed to use the same criteria that the FDA uses for regulatory decision-making which is a science-based criteria which was not used and ultimately, the courts supported the FDA. But that was an example where it was not FDA, as an independent agency. I don't know when you were in the White House and I hate to pushback, but _____ didn't exist then, which is the Office in OMB that has to sign off on every regulation that goes forward and for the FDA that does a lot of regulations and they also extended their mandate to guidance so that many important activities that the FDA are delayed for months, years, as they are reviewed within the White House and decisions are made that go beyond, necessarily, the framework that FDA was using. You can argue that that has benefits in many instances and it does also demand a look at the economic implications of regulations as well as the public health regulations. It also provides a nice opportunity for other forces to come to play but the influence of the White House on the FDA is intense.

Yeah, I mean and that's why I think FDA has never been hit as hard as EPA, for example.

You know, everybody complains and points fingers at the FDA. I learned early on -- I mean, I appreciate everybody thanking me for my service 'cause believe me, there weren't that many that thanked me on a daily basis when I was in the job and I tried to follow advice that I got when I started the job which is, when bitten by sharks, don't bleed. But it's sometimes hard. I think that pretty much Congress is never happy and the White House is never happy with the FDA because there's -- FDA, every day, is making a lot of really important decisions and someone is unhappy and they convey it to their member of Congress or the White House, whatever, but at the end of the day, you don't do these jobs to be well-liked and that brings me back to the point I made about recommendations to the next Commissioner, that if you let your criteria for decision making get influenced by all of the many factors that swirl around you, you get into trouble and you need to be able to come back and wrap yourself in the mantle of science and public and say, 'this is what we do and you don't have to like it,' but nobody loves the FDA.

Those are the two options.

Yeah, I mean, I have to say that one of the things that was really an eye opener for me when I got to FDA was the quality of the staff. Corruption or incompetence were not words that immediately came to mind.

The questions about industry capture and concerns of undue influence, either political or industry are real but in my experience, exaggerated a bit or considerably. I don't think that's true in every regulatory agency around the world and I think the problems of both corruption and I won't say incompetence but inadequate experience and training are huge and add to the problems in terms of poor quality of food and substandard manufacturing and other things. But within the FDA,

there used to be very high standards about conflict of interest and disclosure and divestment and I certainly never had anything paid for by an industry executive and that was true for others within the FDA. I would say that, in all honesty, the pressures from industry were more shared desire to see things get through the system. People think that FDA is always more cautious and actually, it's easier not to approve than to approve and make a mistake but generally, you want to see. I can only imagine when the recent Alzheimer's study failed that people within FDA were devastated 'cause everybody wants to see a treatment for Alzheimer's. So there is that alignment but it's not a corruption. I would say, what worries me a lot, at the moment, is social media and pressures that come from that domain as well because that has really intensified in recent years and the campaigns from patient groups and people with kids suffering from a disease and the organized campaigns that bring in political pressure as well, that's very powerful too. That's what makes the FDA a really hard place to work because you're always grappling with complex scientific decisions. You do have to put the science in the broader context of social values as well and weighing risks and benefits and then there are these intense pressures that people are training to resist and there are systems of oversight and transparency to reinforce that but it's not easy.

Two separate but very linked issues, one is the global supply chain, which are enormously complicated. So much more complicated than I had ever imagined, in terms of the many different countries and places that a product will go before it ends up here. The number of different handlers from the producer to the distributer to the packager to the re-packager and the exporter, the importer, I mean, those supply chains are hard to track and that's one of the reasons why the only way to get a better handle on it is through collaboration with other regulatory authorities and a closer collaboration with industry as well and common standards and approaches. So progress is being made but it's still very, very spotty and the opportunities for problems to occur, either unintentional contamination or damage from improper storage or repackaging or deliberate adulteration for economic purposes or potentially as a form of terror. All of that is enormously possible with the kind of open and complex supply chains that we have today. Even within the U.S., though, the supply chains haven't been adequate and to be honest, there were many things at the FDA that really surprised me, where I did not understand why anyone would question the value of a certain approach and yet, I found myself in a maelstrom of disagreement and opposition. One was trying to actually track medical devices. It turned out that medical devices didn't have serial numbers and tracking systems in the way that your toaster does. So once a device was implanted, if it hadn't been written down in the record, you didn't even know what type of a device, necessarily -- if you had a transplant, an artificial hip, you wouldn't necessarily have a way of knowing what it was. So legislation was passed while I was at the FDA that was very controversial but we pushed hard for it, to get a unique device identifier system implemented and industry pushed back incredibly hard. Eventually, it went through and it is now being implemented but to me, it seemed like a no brainer because you'd even want it just for inventory, I would think. So I can't explain it but we're better than we were but on the drug side, the system within the U.S. is better defined but it still does create challenges.

Well, both important questions. On the first, I was trying to find something to be positive about and I do think that the notion that a couple of good people I know are under consideration to work in the White House on global health issues, so that's a good. When that's paired with drastically cutting back foreign aid at state, cutting back on things like the Fogarty Center and its important health programs and ideology of American first, that fails to recognize that in fact,

America's health, whether it's in the FDA realm or in so many other realms actually depends on acknowledging and building on our interconnectedness. Those are all worrisome signs and any one of them but certainly, all of them together will make it not matter how smart someone is that might be sitting at a desk in the White House. So I think we all need to keep our eye on that and push hard but provide positive reinforcement if something good happens. _____ the education, it's a huge issue and it probably goes back to the early question about what can AAAS do? We have to make progress in terms of science literacy and understanding about science-based issues and technology because it underpins almost everything these days and it is --

Yes but it still is very challenging and certainly, we see issues, vaccine safety is one, GMO is another where sections of the public and members of Congress are very locked into certain positions and it's hard to change them.

Well, I share your view and in fact, the FDA, when I got there, was only inspecting, I think, one percent of products coming in. So it was clearly inadequate at best. We tried very much to adopt a much more globalized approach, including trying to create this new global governance mechanism to really share information and workload. But every country has its own sovereign laws around how products are regulated and you will always have to deal with that if you're running a regulatory agency. One can begin to harmonize approaches and then there's the issue that not every country is equal, in terms of capacity. So it gets back to the question of, how do you also bring up the ones that are weaker and I think that is a huge challenge for us, as we sit here today.

Well, progress has been made there. There was just a mutual recognition agreement with the EU. We do share inspectional data with other countries now. You have to prove yourself before you're allowed into this group that does inspections and actually, they put us, even though there is no question that we are the gold standard, FDA, when it comes to regulatory inspection, they put us through a lot of hoops to prove that we could meet their standards. So there's more and more of that. What worries me a bit is that the trend is against it but it is the only way we can possibly. I mean, FDA regulates products that come from at least 150 different countries responsible, by law, for doing inspections in several 100,000 different facilities. I mean, no generic drug can be approved for use in the U.S. without an FDA inspector having been in the facility that's making it. Whether it's in Milwaukee or in Mumbai. So it's a huge challenge and then the notion of being able to inspect everything that comes in is, of course, absurd. But that doesn't mean you stop inspecting things, but you have to have a better strategy.

Thwarted might not be something that I can speak to, although there have been, certainly, various episodes or potentials that have been addressed, David probably knows more about some of the intelligence.

Yeah, right but we weren't talking so much about bio-weapons and bioterrorism at this session 'cause it was more FDA but certainly, within the realm of FDA, there have been many problems with deliberately adulterated drugs and food products.

Well, both, but one of the big challenges is what is government enabled or not? One of the most shocking involved Heparin, a blood thinning drug and this is an interesting story. I said I was

gonna try to be short but Heparin comes mainly with important ingredients from China that come from pig intestine. There happened to be an outbreak of something called Blue Ear Disease in swine. So the pigs were dying out and the cost of pig intestine was going up. So some clever person figured out that there was a certain substance that could be substituted that on chromatography for screening of quality would look, it would have blips in the right places and look like it was real quality Heparin but it wasn't and then it turned out that that substance that was added actually created allergic reactions and it's hard to know exactly how many people died or got sickened as a result of it because most people that are getting Heparin in the hospital are already pretty sick but it clearly caused death and worsened disease in this country and in others. It was never known whether that was a government sponsored entity and this was before we actually had FDA employees working in an office in China. By the time FDA inspectors got Visas to go into China, the facility where this product was made no longer existed. So there's one Congressional staffer who's still intent on solving this mystery but what FDA did was put in place measures to try to prevent it from happening in the future. Melamine in dairy products was another example and it was the same kind of thing. It was a very shrewd economic adulteration where a substance was replaced for an actual dairy protein, Melamine, which could pass certain screening tests but actually, proved poisonous and many dogs were killed by it because it was in dog food. Sadly, I think more than 100 infants in China actually were killed by its presence in infant formula and it was only because of an outdated FDA regulation that that didn't happen in this country because there's an old regulation on the books that nobody has bothered to take off but it'd be one of the ones that, in the Trump era, you'd look to and say, 'this is silly,' that prevents infant formula from being imported into the U.S. It's one of the few food products that can't be imported and it did show up in other dairy products in this country and caused damage. So this isn't a fantasy and then, in the FDA world, intentionally counterfeited products is very commonplace and it's actually -- I mean, the mob is an active player in that and some of the penalties around counterfeiting drugs have been increased in recent years but sadly, it used to be that the penalties were worse if you counterfeited a Gucci bag than if you counterfeited a medically important drug.

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