Speaker 1: Welcome to Conversations on Healthcare. This week we welcome FDA Commissioner Dr. Robert Califf on challenges to drugs long approved for medication, abortion, upcoming tobacco regulations, and FDA's quest to combat misinformation. Now here are your host, Mark Masselli and Margaret Flinter.

Mark Masselli: Abortion rights have eroded in America since the Supreme Court overturned Roe v. Wade. And right now we're seeing some of the starkest examples of this reality. Our guest is one [00:00:30] of the persons trying to navigate a rapidly changing legal situation while keeping patients safety front and center.

Margaret Flinte...: Dr. Robert Califf is an accomplished cardiologist and scientist. In his second stent as the FDA Commissioner, he previously served as the FDA Commissioner under President Barack Obama.

Mark Masselli: Oh, well, commissioner Caleb, welcome to Conversations on Healthcare.

Dr. Robert Cali...: Good to be here.

Mark Masselli: Yeah. We'll start with the breaking news about the bans on abortion medication, which is the [00:01:00] choice of approximately half of all terminations in the country. 22 years ago, as you know, the FDA approved a medical abortion regimen for up to 10 weeks into pregnancy. Now Wyoming has become the first state to explicitly ban their use in the mail order option may be at risk in Wyoming. I'm wondering what the Biden administration or what your thoughts are in terms of communicating on this.

Dr. Robert Cali...: Mark, unfortunately, [00:01:30] in a case of pending litigation as it relates to FDA, I'm not really able to say much about it. I'll just comment the FDA did its review over 20 years ago. The science is unchanged, our decisions are unchanged at this point. But because there is pending litigation, we'll have to wait and see what the courts have to say.

Mark Masselli: Commissioner, as I think about that, there was a number of years that went into that decision [00:02:00] 22 years ago. Maybe talk a little bit about the rigor that went into that decision back 22 years ago.

Dr. Robert Cali...: Well, all of our decisions are based on the best available science. The data come in, they're evaluated by civil servants who have no vested interest in any, they're not political appointees. I'm a political appointee. I'm the commissioner. So those decisions are made by career civil [00:02:30] servants who are assessing the science. So science and medicine is what we go by and that's where we were 20 years ago and where we still are today.

Margaret Flinte...: Well, commissioner, if I could just pick up on that for a moment. FDA approved really means something to all of us. I want you to know out in the world of practicing healthcare, whether it's primary care where we are or cardiology where I know the focus of your clinical career has been. [00:03:00] But I think

people often are confused about where the sort of boundaries end with some of these things.

My understanding is once the FDA has weighed in on safety and effectiveness, right? The two big issues, that it's not something that could be overturned externally. And I guess, the question is do you have the regulatory discretion to avoid enforcing a ruling that goes against what the FDA has included? Just educate [00:03:30] our listeners about that.

Dr. Robert Cali...: I'm afraid I can't really get into the details here because they're separate branches of government. The judiciary is different than the executive branch and there could be a variety of different circumstances. But so that's really all I can say about it while the litigation is pending.

Mark Masselli: And we appreciate that and we have a lot of topics to talk about. But [00:04:00] I do think it was sort of an unprecedented act where Walgreens indicated that they were not going to make the drug available in 31 states. I'm wondering your own thoughts about pharmaceutical companies or the large manufacturers deciding which states they can sell FDA approved, forgetting this particular drug, but just as a precedent I guess. [00:04:30] Has that happened in any other case and...

Dr. Robert Cali...: Well, I do appreciate your interest and I do have personal opinions, but in my role I can't really comment on these things at this point. I'm sorry. I look forward to talking about it later.

Margaret Flinte...: Well, we look forward to future conversations and obviously we're following it closely, but you do have a enormous span of issues that you're responsible for. And one of them that I'm not sure the public has always understood is that you have oversight of [00:05:00] infant formula manufacturers and certainly very much in the news this year was that the plants have been plagued by bacterial outbreaks. I think that's led to some shortages in some areas. You've proposed changes to the agency's human foods program to address the problem. Tell us what you're doing. And does more need to be done even than the next steps?

Dr. Robert Cali...: Well, glad to talk about this. Infant formula course is a very precious [00:05:30] component of a very large food system that we have. The food ecosystem that we regulate has over 600,000 entities. I was just on a call this morning about imported seafood safety, for example, where over somewhere between 70 and 95 percent of our seafood that we eat in the US comes from overseas. So it's a vast set of responsibilities that we have. But of course, infant formula is special because infants can be totally [00:06:00] dependent on formula.

And as we ran into the problems that we had with contamination of a plant with bacteria of one manufacturer, that was the dominant manufacturer in infant formula, we had to stop production in that plant and entered into a consent decree with Abbott to oversee the restart, which took several months. That led

to a shortage. And it also [00:06:30] surfaced a lot of issues within our human foods program. I have to say, upon being nominated, as you know, this is my second time around at FDA. The first time was relatively.

Mark Masselli: Congratulations.

Dr. Robert Cali...: Brief before the election, I got a lot of calls from inside and outside the agency that the foods program needed more attention and support. So I was ready for it. But it turned out that recall at Abbott was on the day I was confirmed.

Margaret Flinte...: Wow.

Dr. Robert Cali...: So I was presented with this right from the beginning. [00:07:00] What we're doing is restructuring the whole program to upfit it for the future. But one really important point to make, which we didn't talk about much, right about the time I was confirmed because you were in the middle of a crisis with infant formula that we needed to handle first.

The Economist did an assessment of all the countries in the world and we came in third, right neck and neck with Canada and Finland for the [00:07:30] safest and highest quality food in the world. Unfortunately, availability, we didn't come in so high as a country.

And as you know, there are many factors beyond the assessment of quality and safety, which is our mandate that come into play there. We have many inequities in this country that we need to deal with. And so we're really putting a lot more effort and energy into the program. We're elevating nutrition. We're losing millions of Americans to chronic diseases that [00:08:00] have a nutritional basis, as you well know.

Margaret Flinte...: Yeah.

Dr. Robert Cali...: And we're also getting support from Congress to beef up our infant formula program. We don't make infant formula, we can't tell companies to make it, but we have a marketplace right now which is heavily concentrated and not diverse enough, and in which we had very little ability to get insight into the production that was going on. All the companies are now collaborating and our in stock [00:08:30] rates are back up to where they were before the recall, but there's a lot more to be done.

Mark Masselli: Commissioner, the diabetes drug Wegovy is FDA approved for treating obesity and there's concern about the side effects even with the FDA approval and acknowledged obesity issues in the country. Are the side effects worth it in your mind to prescribe it as a physician? What would you be prescribing?

Dr. Robert Cali...: [00:09:00] You keep drawing me into this tricky position of I'm FDA commissioner, so I have to be careful about being too opinionated right now.

Mark Masselli: Yeah.

Dr. Robert Cali...: Relative to the role of the FDA. But I have a few things to say about this. You know that we in more than almost any other country, are suffering from this enormous amount of obesity, type two diabetes, hundreds of thousands of teenagers now with type two diabetes. [00:09:30] And the biology of the weight gain that we've experienced as a country has been poorly understood.

And I think as much as anything else, these new classes of drugs are giving us insight into something that a few scientists knew about, but most of us were oblivious to, which is that the connection between the gut and the brain that affects our appetite is a complex neuro hormonal connection. And so these drugs intervene [00:10:00] in those pathways.

And what I would say is that obviously the FDA has found one of the drugs to be safe and effective, not only for diabetes, but also obesity. And there's another one, which the data will come in soon from a large trials that'll give us the insight that we need to have. I feel like this is going to be the beginning of a revolution in the way that we control weight, not just with the pills, but because we'll [00:10:30] understand the biological mechanisms better.

There'll probably be multiple therapeutic is including better use of the integration of digital technologies and medicines. So would I prescribe it now safe and effective for the intended population? I think the biggest issue in front of us is going to come from very large trials that are underway about people that have obesity [00:11:00] but don't have diabetes.

And in that population, the results of those trials will tell us what we need to do. If you have a reduction in death, a reduction in disability due to orthopedic conditions or cardiovascular events, then by all means on average, the benefits will outweigh the risk. But all drugs, all interventions, there are side effects and toxicities.

We have to be aware of those as clinicians and we need to inform patients. [00:11:30] The good thing about these drugs, like many others, is that most of the side effects are symptomatic. And so if someone's having symptoms of side effects, you can stop the treatment. That's kind of a nice quality of this kind of intervention.

Margaret Flinte...: Well, we look forward to results of that further research. And as with the National [inaudible 00:11:53] project, we certainly hope that it embraces people of all backgrounds, ethnicities, races, when that research is done so [00:12:00] we have a good understanding. But I have to say it's March and I don't think I'll ever experience March again without thinking of it as the month that the COVID Pandemic started.

Three years ago now. A little more at least in our rear view mirror. But you've been proactive, I think, about how important it is that people get the COVID vaccine, that they're safe, the treatments are effective. And I read that you actually [00:12:30] reached out and sent an official letter to the Florida Surgeon General about his views being very public that the COVID vaccines could be quote "Harmful." Have you heard from him? Did you get a response? Do you think that there'll be a change of position on that?

Dr. Robert Cali...: I wouldn't expect a change in position. Dr. Ladapo sent us a letter, so we were just responding to his letter. And his letter indicated [00:13:00] that maybe we weren't paying enough attention to the side effects which are recorded in the Vaccine Adverse Events reporting system and other places. We just responded saying we are paying attention.

All effective interventions have side effects and toxicities, and we need to care for people that are unfortunate enough to have those and try to understand them better. But in the case of vaccination for COVID, the vaccines have an overwhelmingly beneficial effect on reduction in death [00:13:30] and hospitalization and a modest effect on transmission now.

And initially, as you may remember, when the vaccines were first developed, they had a huge effect on transmission. But as the variants have come along, that effect is smaller and wanes over time. But the effect on being dead, I'm a cardiologist, I'm used to dealing with life and death, almost everyone would rather be alive than dead. And you have a free simple intervention.

And we made the point that while we should be aware and pay [00:14:00] attention to side effects and toxicities, if we do that and don't talk about the benefits at the same time, we could be misleading people into avoiding getting vaccinated, which would be avoiding a life saving intervention.

I used to spend a lot of time convincing docs to give, to open the artery of people with heart attacks and feeling that if you had someone with a blatant heart attack and you didn't open the artery, [00:14:30] you were subjecting them to the risk of dying unnecessarily. And I think the same as here. So I don't expect Dr. Ladapo to change his view, but we felt it was important to respond to the letter that he sent us.

Mark Masselli: I want to stay on that theme of misinformation in COVID because you've been very clear that almost no one in the United States should be dying from COVID, but misinformation really is impacting the death toll and the FDA is more aggressively trying to stop [00:15:00] misreporting incorrect social media. I know this is very important to you, but is a more proactive approach needed? And do we need to go after the social media algorithms that spread this information? Because as you noted, it's a matter of life and death.

Dr. Robert Cali...: I think this is one of the most important problems we faced. I've publicly said, I think misinformation is actually the leading cause of death in America now because [00:15:30] so many people who die could have done things to change it had they gotten better information in a way which motivated them to act in very simple things like taking proven medications to prevent cardiac events, for example.

And certainly vaccination is another example of the same thing. But this is a very complex and difficult issue. We're in such a different environment now [00:16:00] with the advent of the internet and the use of algorithms in social media. It's just an article last week that really got my attention that demonstrated a social science article that if the headline of an article has a negative word in it, it gets more clicks than exactly the same headline without a negative word.

And so there's also an article that shows that physicians are just as affected in their recommendations by [00:16:30] which news outlets say watch as laypeople are. So these things are telling us that if we believe that a federal agency like FDA can just make a determination and put out one statement and things will happen, that's a very naive perspective.

On the other hand, we highly value the first amendment and the right to free speech. So finding where that appropriate middle ground is [00:17:00] really difficult. And I'm not arguing that we know that right now, but we've got to be constantly working on trying to get accurate, reliable information to people.

And here I'm glad we're on, whether it's physicians, nurses, nurse practitioners, physicians assistants, pharmacists, we really need everyone to pick up their activity on this and make it part of every day. [00:17:30] Because in the same way I described it for federal agencies in, I worked at Alphabet between my two FDA stents, and it's really obvious that if you think that people are coming in just to listen to you for 15 minutes and then to go out and do what you say with no other influence, you're out of your mind. The minute they're out that door, they're Googling and looking at...

Mark Masselli: Yeah.

Dr. Robert Cali...: Other information and hearing from relatives. And if you don't ask them [00:18:00] what they're thinking and what their information sources are, you may never know that they didn't do what you advise them to do or what you thought they had agreed to do because they were influenced by some influencer that you'd never heard of.

Margaret Flinte...: Well, commissioner, maybe that ties a little bit to this next question that I wanted to ask you, but I've been reading some and really appreciating the health equity lens that the FDA seems to be taking towards tobacco [00:18:30] regulation and prevention efforts and that recognition of just another huge

disparity between who is starting to smoke these products at what ages and what communities they come from. Maybe you could share with us a little bit about what we might expect to be hearing more about or seeing over the coming months in terms of labeling and messaging from the FDA about tobacco.

Dr. Robert Cali...: Here, this is really a tough [00:19:00] one. And I grew up in South Carolina, in North Carolina. I've was a cardiologist at one of the busiest hospitals in the Southeast and saw many people die or have lifelong disability from tobacco. We're going to lose almost 500,000 Americans this year from tobacco related illness. When I came to FDA in 2015, I sort of felt like we understood this problem and we had it under control. It is getting better.

[00:19:30] We have about half the rate of use of combustible tobacco that we had when the Center for Tobacco products was started at the FDA 13 years ago. But we got a long way to go. One of the most important areas is menthol in tobacco. And we have a rule which is been out in draft form. We've got all the comments and we hope to finalize that this year that will make it illegal.

And there's a very important [00:20:00] equity sort of double twist to this that we have to all pay attention to. Menthol has been marketed specifically to African American people preferentially leading to higher rates of use and higher rates of death and disability. But when we make it illegal, there's a risk that if we don't handle this appropriately, it can bring law enforcement inappropriately to the individual user and not to the manufacturer.

So we're [00:20:30] working hard anticipating this will be finalized to make sure that the enforcement is against the manufacturer, not individuals in the community. We're also dealing with flavors in cigars. Our youth are starting with cigars almost as commonly as with combustible to regular cigarettes these days or even more so.

And we have on the agenda the hope that we'll [00:21:00] be able to write a proposed rule that will bring the level of nicotine and tobacco products below the addiction level. So it's an interesting question, how many people would use tobacco products if they weren't addicted to nicotine? Then I think we may be able to take care of that. So there's a lot coming. It's complicated and every step is a battle with a bunch of really smart lawyers on the other side.

Mark Masselli: Commissioner, let me get in one last question. The president [00:21:30] is, and I know something, it's important to you as well. The president at Stanford University's under fire for allegedly falsifying research data. And drug makers, Amgen and Bayer have looked at this issue and they are finding it show as much as 50% of all medical research cannot be reproduced due to flaws in research quality. Is it that truly a broken system?

Dr. Robert Cali...: My answer to the last part of what you said [00:22:00] is no, I don't think it's a broken system. But reproducing science has multiple dimensions to it. But if you

ask me, is there room for a considerable improvement in the integrity of the scientific enterprise for the reproduction of research before it's published to make sure it can be reproduced?

Because some cases just slightly change the conditions under which the experiment is done and you get a different answer. In other cases, [00:22:30] there are temptations to take shortcuts and skip things or copy things over, which are really bad. So yeah, I spent a good part of my academic life actually working on these systems, mostly in clinical trials where blinding and the use of double data entry and...

Mark Masselli: Right.

Dr. Robert Cali...: Audits and keeping track of where the data came from electronically is a really important part of it. And I think these methods, which are very common [00:23:00] in industry regulated applications to FDA, in other words, the industry has much more rigorous standards in that regard.

The academia's been a little more free flowing, which is understandable in a way because when it's discovery research, it's sort of self-correcting. But we can do a lot better in terms of producing reproducible research. I've written a good bit about this and would welcome people to look back at the things [00:23:30] that I think about it. It's an important problem we should all pay attention to.

Margaret Flinte...: Commissioner Califf, we thank you for your service to our country. We hope that you'll join us again in the future. And thanks to our audience for joining us. There's more online about conversations on healthcare, including a way to sign up for updates. The address is CHCradio.com. Commissioner, thank you so much for taking the time to join us today.

Dr. Robert Cali...: Thank you. And I'm glad we could talk. Take care.

Mark Masselli: All right.

Margaret Flinte...: Thank you.

Mark Masselli: Thank you so much.