SCIENCE BOARD TO THE

FOOD AND DRUG ADMINISTRATION

9:00 a.m.

Monday, April 23, 2018

FDA White Oak Campus

Building 31, The Great Room

10903 New Hampshire Avenue

Silver Spring, Maryland

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P R O C E E D I N G S

[9:00 a.m.]

DR. MCLELLAN: Okay. Good morning everyone. Welcome. Let me just start with a couple of general comments and of course start with the proverbial please mute your devices, so we can have an enjoyable meeting. I'd like to remind you that our meetings are webcast and live, so we hope you will stay engaged and of course speaking clearly and slowly.

I'd like to welcome you all. I'm going to start by doing some quick introductions around the table and then we'll move onto our formal meeting. So my name is Mark McLellan, I am the Vice President of Research at Utah State University and Chair of the Science Board here. And maybe if we'd just start here and work our way around.

DR. WILSON: Carolyn Wilson, Associate Director for Research Center for Biologics Evaluation Research.

DR. MARKS: Peter Marks, Senate Director, Senate for Biologics Evaluation Research.

DR. REISS: Hi, I'm Ted Reiss, Head of Clinical Research and Development at Celgene Inflammation and

Immunology.

DR. BALDI: I'm Rhondee Baldi an Interest and a Medical Director at Inovalon.

DR. TOSI: I'm Laura Tosi, I am Director of the Bone Health Program at Children's National here in DC. I guess we're not quite in DC, but next-door in DC.

DR. BAHINSKI: Hi, Anthony Bahinski, Global Head of State Department Ecology at Glaxo Smith Klein.

RADM HINTON: Good morning. Denise Hinton, Acting Chief Scientist.

MR. RAGHUWANSHI: Hi, Rakesh Raghuwanshi, Designated Federal Officer for the Science Board.

DR. STEELE: Scott Steele, Associate Professor, Public Health Sciences and Director of the Regulatory Science Programs at University of Rochester.

DR. KOWALKCYK: Barbara Kowalkcyk, Assistant Professor in the Food Science Department at the Ohio State University.

DR. SARWAL: Minnie Sarwal, Professor of Surgery Medicine and Pediatrics at the University of California San Francisco, and Director of the Precision Transplant Medicine Program at University of California.

DR. AFSHARI: Cindy Afshari with Amgen Incorporated. I lead the comparative biology and safety sciences group.

DR. YASZEMSKI: Mike Yaszemski, Mayo Clinic. I'm an orthopedist and a chemical engineer. I do spine surgery and musculoskeletal oncology and I direct our GMP facility at Mayo for biomaterials.

DR. XIE: Xiang Xie. I'm a Professor Pharmaceutical Science at School of Pharmacy University of Pittsburgh. And also I'm [inaudible] Research of School Pharmacy and a Director of [inaudible] Center of Excellence for Computational Drug Abuse Research.

DR. BYRNE: Hi, I'm Barry Byrne from the University of Florida. I'm a Professor of Pediatrics and Director of the Paleogene Therapy Center there.

DR. MCLELLAN: Very good. Now we'll listen to a statement on conflict of interest. Rakesh.

CONFLICT OF INTEREST

MR. RAGHUWANSHI: Sure, sure. So good morning everyone and welcome to FDA. I'd like to thank the members of the Science Board for traveling from coast to coast to be here. And those of you whose flights

were cancelled and had to drive thank you to you too as well. And sorry that you had to do that. Welcome to the public and to the FDA staff.

Today the Science Board will hear from the CBER Research Program Review Subcommittee Chair. The Board will also hear about FDA's patient affairs initiative and will engage in a high level discussion on various topics as outlined in the agenda. All members of this Advisory Committee are special government employees and are subject to federal conflict of interest laws and regulations.

The follow information on the status of this Committee's compliance with federal ethics and conflicts of interest laws covered by, but not limited to those found at 18 USC 208 is being provided to participants in today's meeting and to the public. FDA has determined that members of this Committee are in compliance with federal ethics and conflict of interest laws. Based on the agenda for today's meeting no conflict of interest waivers have been issued.

We have one open public comment period scheduled for 3:30. There have not been any requests to speak

thus far, but if any member of the public wishes to comment during this period please announce yourself at that time and we will accommodate you within the period allotted.

To those of you on the phone, please remember to unmute when speaking and go back on mute when you're not speaking to help minimize any feedback and so that the transcriber can easily hear those in the room and you guys on the phone. I will note about these microphones at the table. I've been told that if more than two or three are on at the same time the volume drastically drops. So once you're done speaking just hi the red button and make sure your red light turns off.

I just wanted to add one more thing about conflict of interest. As all of the Science Board members are aware in the past we have delved pretty deep into specific drugs or a class of products. And we have done extensive screening for those meetings. You all recall the opioids meeting of March 2016 and the sheer volume of paperwork you had to fill out.

Today's meeting the idea is not to have a

discussion around specific drugs or a specific class of products. Rather the intent is to have a high level discussion on FDA's processes, its approach, its tools and its authorities and to discuss ways the Agency can better utilize those and better engage with relevant stakeholders to maximize its positive impact on public health. So I just wanted to note that for the record. Thank you.

DR. MCLELLAN: Okay. Ladies and gentlemen we do -- I can call the meeting to order. We do have an agenda in front of us. We'll be discussing the CBER Research Program review. We've got statements from Rear Admiral Hinton, as well as our Commissioner. And then our afternoon will be jumping into a fairly extensive discussion covering electronic health records, drug repurposing. If we can get further along we'll get into FDA's secure computing environment issues and the use of real world data in terms of augmenting clinical results.

For the Committee Members if there's anything else to add to the agenda this would be the time to speak up.

[No response.]

Hearing none we'll set the agenda as is. Our minutes are transcribed through webcast so they are verbatim. No approval of minutes is needed therefore.

So our discussion today is sort of at a 30,000-foot level as we get into that. And as Rakesh reminded us, we want to stay absolutely clear of specifics in terms of specific products so we are absolutely safe in terms of our conflict of interest.

I would remind you that we are in the spirit of the Federal Advisory Committee Act and the government in the Sunshine Act. And we ask that all members here take care that they're conversations about the topics at hand take place in the open forum of this meeting.

So with that I think what we'd like to do is invite Rear Admiral Hinton to address us as our new Acting, it's not even new, you've been around now for a while, as our Acting Chief Scientist. Thank you, Denise, for being here.

CHIEF SCIENTIST'S UPDATE

RADM HINTON: Thank you. Good morning. And thank you to our Science Board Members for traveling to be

here today. And thank you to those on the phone. I appreciate your time and commitment as well.

I know you have been in great hands with my Chief of Staff, Rakesh Raghuwanshi. And we look forward to working with and getting to know all of you over the years to come.

Since this is the first time we are meeting in person I'll share a little bit about myself. I started my career as a nurse officer in the United States Air Force where I served for eight and a half years before transferring to the United States Public Health Service Commission Corp. I've been here at the Agency for about 16 years. I started in Cedar at the Division of Cardiovascular and Renal Products and followed by working in the Division of Training Development. And then later for eight years in the Office of Medical Policy in various positions as Deputy and Acting Director where we focused on development coordination and implantation of medical policy programs and strategic initiatives in collaboration with other Cedar program areas, FDA product centers and a broad variety of stakeholders.

Last summer, of course, I began my position as Acting Chief Scientist. In working at the staff senior management level and now executive leadership I have become quite familiar with how things work around here and know how the importance of effective communication, collaboration and putting process in place to be able to facilitate and implement our decisions in order to succeed. I also know have valuable advice and recommendations can be from external resources such as this Board. I also understand FDA is a science based agency. We succeed when we make decisions based on sound science and data. Part of my role and responsibility is ensuring that our scientists have the tools they need to stay at the forefront of emerging science and help FDA maintain its reputation as a world class regulatory agency.

As you can tell by today's agenda we hope to utilize your collective expertise to get some insights into what works, what doesn't and your experiences dealing with issues in the academic and private sectors. You are all leaders in your fields and I know this is a very strong group that has been both

complimentary and critical of the Agency at times. But as always we provide honest advice and recommendations to further the Agency's mission. And thank you. As public servants that's what we do, we do our best and stay open-minded so that we can support to continue to protect, promote and advance the health and safety of our nation.

Switching gears a bit let me briefly talk about what has been going on in the Office of Chief Scientist. OCS at its core is here to support in the advancement of science at the Agency, especially within our centers. We are working with leaders, management and staff across the office and centers to enhance our processes and procedures to ensure we provide the best service possible. We do this by providing resources, including subject matter experts for scientific projects and infrastructure so that our scientists can make the best regulatory decisions.

We also lead numerous crosscutting efforts in areas including, but not limited to, health informatics, women's health, minority health, scientific integrity and counterterrorism and emerging

threats. Here are some recent highlights. We executed a memorandum of understanding between FDA and the Reagan Udall Foundation for the development of a Reagan Udall Foundation fellowship at FDA. And my understanding that a subcommittee of this Board studied this issue and provided recommendations of this very matter. So thank you for that. As you can see your suggestions are very useful and are often put into practice.

We also launched a committee for the advancement of clinical and scientific education to address priority topics as opioids and adulteration to offer continuing education for physicians, nurses and pharmacists.

We participated in the Science and Engineering Festival in Washington, DC. And I bring this up because we're always looking to recruit the next generation of regulatory scientist and reviewers who are interest in public service and public health. So if you know anyone please let them know that the FDA is a great place to work and we can make a positive impact on public health.

Our Office of Regulatory Science and Innovation is working to leverage centers of excellence that we have established to address recent agency priorities, such as compounding, patient reported outcomes and real world evidence. In collaboration with FDA centers, NIH and the Office of Information Management and Technology our Office of Health Informatics, which manages and curates the substance data used in regulatory product, is working with the Netherlands to help implement the global substance registrar system in Europe. This system is a highly curated database of substantives that are used in regulated products. And this implementation in Europe will assist FDA in better collaborating with our international partners to ensure global product safety.

The Office of Minority Health established a Memorandum of Understanding with Yale University to form the basis for development of scientific collaborations, outreach and education extrication activities and initiatives and intellectual processes and partnerships. The types of initiatives expected to develop from this MOU include, but are not limited to,

collaboration to cultivate and advance the Yale cultural and master's program and the engagement of community partners to increase participation of diverse and historically underrepresented or underserved populations in clinical research.

The Office of Women's Health is hosting a debate on May 16th as part of the National Women's Health League to help increase the number of women who participate in clinical trials. They've also developed a research impact and outcome framework which serves as a guide to qualitatively assessing the impact of the research that we fund. As I'm sure you'll all agree metrics are sometimes difficult. So we are constantly thinking of ways to better measure and capture the impact of our scientific research on public health.

Our Office of Counterterrorism and emerging threats in collaboration with the Wyss Institute of Harvard has developed the first model of gastrointestinal acute radiation syndrome in a human organ chip to support the identification and screening of medical countermeasures. This work was recently featured in *Nature Cell Death and Disease Journal*. And

last, but not least, the National Center for Toxicological Research's scientists were authors or co-authors of seven out of fourteen original research or mini research articles in *Experimental Biology and Medicine* journals, "Thematic Issue: Biomarkers and Their Impact on Precision Medicine."

So as you can tell we've been quite busy and the progress we have made is in part to address some of the recommendations of this Board made in its recent last major report *Mission Possible, How FDA Can Move at the Speed of Science.* I'll continue to keep this Board posted on our progress as we work to tackle the many public health challenges we face. I look forward to a productive discussion today and I appreciate you for letting me take a little time to provide this update. Thank you.

DR. MCLELLAN: Thank you, Denise. Any questions or comments from Board Members? I'm sure there will be others later as we get into our discussions.

RADM HINTON: Okay. Well, thank you.

DR. MCLELLAN: Thank you again. Let's see, we had another member of our committee join us. Lynn, would

you introduce yourself?

DR. GOLDMAN: Certainly. I'm Lynn Goldman, I am Dean of the Milken Institute School of Public Health at the George Washington University. And it's my pleasure to have served on this Board for a couple of years. Sorry for being late today.

DR. MCLELLAN: Glad to have you back. I believe we also have members on the telephone. And forgive me for not making room for them to be introduced. So at this time why don't we pause. We'd like to have those of you on the phone to introduce yourself, please. Do we have members on the phone?

MR. RAGHUWANSHI: Maybe not yet.

DR. MCLELLAN: Maybe not. Okay. All right. So some time ago we as a committee voted to establish a subcommittee to study CBER's research programs. And today we're going to be hearing from the Subcommittee Chair Dr. Barry Byrne. Welcome Dr. Byrne. Glad to have you with us and look forward to your presentation.

FINAL REPORT FROM THE CBER RESEARCH PROGRAM REVIEW SUBCOMMITTEE

DR. BYRNE: Thanks very much. I'll just stay

seated, if that's okay. And thank you all for inviting me to present before the Committee. It's really been a privilege to participate in this Subcommittee. I have to thank Dr. Marks and Dr. Wilson for their enormous effort in putting together all of the review materials, which really over the greater than a year ago from January of 2017 began this review process, culminating in a site visit last June.

Just a little bit of background. I am a member of the Cellular Tissue Gene Therapy Advisory Committee. I had the privilege to serve as the Interim Chair of an Advisory Board for the Consideration of Luxturna, which is now the first gene therapy to be an approved product. So it's been an interesting experience. Valuable to me as a medical professional involved in this space. So it has been great to see all the work that's being done in the Center. Feedback.

DR. MCLELLAN: If you're on the phone could you please mute your phone.

DR. WEAVER: Mark, this is Connie Weaver. Apparently you couldn't hear me when I tried to introduce myself. But I'll get off the phone and I can

hear you fine.

DR. MCLELLAN: Connie, thank you for joining us.

DR. BYRNE: Okay. So just to dive into the discussion that we had over this past year and the review of the scientific activities. I'll just say from my perspective as an outsider I think one of the fascinating things about CBER has been that the consideration of the Center goes from the individual subject who might be in a clinical study to the enormous issue of the public health concern. So you see this spectrum of consideration both scientifically and in their policy and review activities is enormous.

So and we had a thirteen-member review panel, five of whom are members of the Science Committee who are here today. So we'll feel free to call on them as well during this discussion.

So just by way of overview, the vision as stated here really the sound science and regulatory expertise too, as I mentioned, protect and improve public health and individual health in the US and apply their regulatory expertise to these main topics, particularly for developing, approving and excessing safe and

effective products and new technologies. And that's one, I think, of the things that the scientific activities within CBER truly embrace because there are many emerging technologies that they -- is part of their oversight.

And then really how could the Center be strengthened and what are the opportunities for growth. So if you can go to the next slide. This just states the mission of CBER for those that are unfamiliar. Certainly the goal is to ensure that all the products they review are both safe, pure, have established potency and effectiveness of biologics. Which includes such a wide variety of activities, both vaccines, blood and blood products, cellular and tissue therapies, as well as the gene therapy that I mentioned as my own area of expertise. And then some of these will be to prevent diseases used for diagnostic purposes and specific treatments. Which we all know have -- I think it's been stated, even in Dr. Gottlieb's overview from a few months ago, a tremendous opportunity in the coming months and years to see a very highly specific transformative therapies, particularly in the rare

disease area.

And then these really, as particularly in the vaccine area and the Office of Vaccines Research and Review, the public health is the main concern against emerging infectious diseases and bioterrorism threats, as well as to develop, maintain and support this diverse workforce that they have within they agency and the model of the scientist reviewer. I think that's another key take home that the need to support that type of activity so that the scientist reviewer has -- remains on the cutting edge of their scientific interest. And then because of that they have to conduct cutting edge research that helps them make science based decisions in their review activities.

So if you go to the next slide this touches on what we reviewed. And this is the charge to the Science Board. So do the scientific endeavor, support the Center's regulatory mission. The Committee considered changes in its regulatory science research portfolio that would really help accomplish this regulatory and public health mission. And then whether there are any gaps in regulatory science capabilities

or expertise. And I think probably a lot of our discussion was really focused on these opportunities and crosscutting opportunities between the agencies, both in FDA and the NIH to leverage their regulator science programs.

So if you go to the next slide this is the composition of the thirteen-member committee. Dr. Arnold Monto, whose expertise is in vaccines, was the Subcommittee Co-Chair. And then the other members are listed here. As I said, five of whom also serve on this Committee.

So the next slide shows the valuation process. So we conducted -- received extensive background materials and then conducted six teleconferences with CBER leadership. This was very time efficient and well organized. And in addition we had specific presentations from research management and staff during those teleconferences to delve into the details of some of the key scientific programs. And then we conducted a one-day site visit, including presentations from the CBER leadership and key research staff. And then were able to collect responses to questions that we had in a

post-site visit series of additional teleconferences. So the next slide covers the major findings in the six areas with their recommendations. So if you can go ahead one. Yep.

So the research priorities. So this is often challenging to fit the interests of the investigators with what's emerging in the field. And the recommendation of the Committee was to develop a center wide horizon scanning process, which would allow them to identify new key topic areas for which future investment was warranted. And I think they're particularly well suited to not only build from within, but recruit others to this campus to conduct their basic research.

And then, you know, at a time when this began obviously there were many considerations about resources available to the Center. And it meant that they had to be adaptive and have contingency plans to shift resources and projects. Because at any time a large review activity might come forward or there might be budgetary changes that would affect the overall mission of the Center.

And then a focus on research collaborations because this is really a way, I think, to build a broad base both within the Center and colleagues across the offices in the Center. And so there was a focus on having also these, as well as external collaborations to allow for personnel exchanges with other agencies, particularly here in the Bethesda/DC area with colleagues at the NIH, or even the possibility of having mini sabbaticals done with outside laboratories.

So if you can go to the next slide. This is actually an important part of the backbone of the scientific program is the reviewer scientist or researcher model. And given the review burden that exists for every intermural scientist it was important, felt important by the Committee to have a protected time for their research activities because certainly the commitment to comprehensive review and under the federal statutes for a timely return of those reviews is challenging when you have an ongoing active research program. So having sufficient depth within the Center to allow those responsibilities to be shared evenly among all of the research reviewers was considered

important. This would be particularly relevant to having sufficient budgeting, budget leeway to maintain a sufficient number of research reviewers to shoulder that burden.

And then as I mentioned, this sabbatical program would allow shared time with academic labs and to either develop a new technique or to collaborate on publications on specific topics. And I think this is particularly important in the cellular tissue and gene therapy activities of the Center where there's really a very rapid pace of discovery and clinical research ongoing right now.

And then to maintain people's level of currency and visibility within the field it's important, felt important that the scientists have the ability to attend national meetings. This seems to be challenging sometimes to manage that budgetarily, but we thought this was really a key part of both recruiting new junior scientists to the laboratories, as well as maintaining the visibility of the staff that are there.

So the next slide, so this relates to expanding mentorship, professional development. National

meetings was part of that. Obviously there are also internal resources that could be used to continue to grow and maintain the competency of the workforce.

And lastly there was a strong recommendation to maintain and/or expand the core facilities, particularly as they related to the Office of Biostatistics in Epidemiology. That will probably be touched on I guess later in your meeting regarding electronic health records, safety reports and the work of that office. So as well in the genomics area, the core facilities contribute to the scientific undertaking of all of the groups here.

So that really were our key recommendations. So I can go to the last few slides for conclusions and then have any discussion or further questions. So our view was that CBER really had developed a very robust research program. And the research reviewer model I think is, at least in my own personal experience, is a in submission of INDs from our institution we see a level of expertise and that is really important to understand the core science in order to adequately review such proposals. And so in that sense I think

been very successful. It's relevant to the overall mission and is advancing key questions for the Center and for the scientific field in general, which have national and international implications. Obviously many sponsors now seek to bring the studies that are done in the US to our EU counterparts, so and elsewhere in the world. So this is really an important time for that activity.

And the last slide really just says that the leadership has maintained really a great grip on the resources. Managed to maximize the productivity of what is really actually a very closely knit group. And then develop those programs with the limited resources they have and an outstanding research effort. And that that can be expanded without further taxing those resources by developing cross-FDA and external collaborations and continuing the horizon scanning process, which will continue to enhance their ability to impact health and their own research within the Center. So I can end there with questions.

DR. MCLELLAN: Thank you, Dr. Byrne. Appreciate, that's an excellent thorough report. And I'm sure

there will be some discussion questions. For those of you interested in questions please lift your flag if you would, your name tag and we'll call on you. And I'll open the floor at this point to comments or questions. Lynn.

DR. GOLDMAN: How did you know? I didn't even put my -- oh, I guess I had my thing turned on still from introducing myself. But I do have a comment.

DR. MCLELLAN: (Inaudible.)

DR. GOLDMAN: And that is, you know, in reading through the draft report I was very impressed with how thorough it was. And I think that, you know, we had a prior report about CBER. And it's very heartening, you know, to see that there's been a lot of progress. And at the same time to see that some, you know, some of the same issues exist in terms of the support of the researchers and support of the science. Which I think it's important for this group to continue to, if I may, you know, double down on. I think that the recommendations are completely reasonable and doable and I think that they're very well supported.

Again, you know, I've been impressed in reading it

with the quality of the science in CBER. And I think that, you know, your review bears that out and that's very heartening, you know, given the relatively austere environment frankly that the scientists exists within. And so I think that's also worth noting.

DR. MCLELLAN: Go ahead, Scott.

DR. GOTTLIEB: Just a quick comment. I also wanted to acknowledge the work of Mark and Carolyn with CBER supporting us throughout the process. It was really helpful through the entire review. And as was noted, some of our recommendations are certainly broader, things around the training and in workforce and scientific engagement. And as Denise mentioned, some efforts related to addressing that and maybe we can continue the discussion about that going forward, which impacts obviously CBER, but other centers and offices.

DR. MCLELLAN: Sean.

DR. XIE: It's very sorrow [sic] work and I like it a lot. So I have just curious. You mention about sabbatical. That means academic and coming to spend time at FDA, right. So related to this I follow Lynn's

-- if anything data outcome sharing, how you're managing the CBER academic come with its own IP. And then are you going to create a portal to allow all the data outcome sharing?

DR. BYRNE: Yeah, I think the consideration was whether intermural scientists could go to academic laboratories, particularly to learn new techniques or to just engage one-on-one with all levels of trainings from students through post-doctoral candidates. I don't know if Peter you want to expand on that notion.

DR. MARKS: I think we appreciate it. I think it's something we want to look into. There's the pathway towards the sabbatical program is one I think we have to kind of work through because there are some limitations on what can be done within the federal system. I think we've actually had people go for several weeks to learn a new technique and that's something we're doing currently. People will go for a month to -- in fact, we've fact, we've had people go to Europe for a month to learn technique in somebody else's lab. But for more academic style sabbaticals for going for six months or a year we have to see if we

can work that through. Because that becomes more of almost a secondment [ph?], as we'd call it. And that has -- there can be limitations on that. But I think it's a great suggestion to look into and we continue to investigate it.

DR. MCLELLAN: Great. Laura.

DR. TOSI: I don't think it was in your charge at all. But let me just ask you about something I find very troubling in my own profession. So I'm an orthopedic surgeon. And the biologics have become a financial whizzbang for a lot of people. There are allegedly 500 orthopedic stem cell centers in America, none of which by the way have orthopedic surgeons involved. But people have stolen our name, so we're very aggravated.

But the use of step cell therapies is taking off and is essentially non-evidence based. Do you see yourself coming down with helpful ways to regulate or to see CBER come up with better ways to regulate how the use of these materials is being done? People are paying cash here, there and everywhere, whether it's plasma rich -- what is -- P -- what is -- help me. P -

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DR. MCLELLAN: Platelet rich plasma.

DR. TOSI: Platelet rich plasma or stem cells, per se. How do we help protect the public?

DR. BYRNE: Yeah, that's a good question. As you said, that wasn't really part of our prevue as understand the science of the reviewer scientist. But maybe Dr. Marks can comment the regulatory efforts.

DR. MARKS: So the work that goes on in our laboratories has been trying to help define the scientific parameters, standards that might go behind manufacturing stem cell products. Our hope is by creating the right scientific parameters the right standards people will actually develop these products into real products. And your point is extremely well taken that right now there are a lot of what I would I dare say, I would call the pseudo products. They're things that are products but they don't have the supporting safety and efficacy data that would make them into a true product.

And we in November of this past year put out a regulatory framework for generative medicine products

where we're trying to help people understand how they can gather the correct data that they need to support these products in terms of clinical data, which would include safety and effectiveness data. But it is a very big challenge because people can manufacture these things pretty easily with things they can get their hands on.

We have put down a marker to say though that when people are making products that trigger our regulations for being biologic products that require a biologic license application they need to come in for investigational new drug applications. And we also made clear that over the next couple of years we'll be starting to increasingly enforce to get people to do so. So it's not an easy thing. And I do take the point very well that in certain areas it's proven very challenging because there are so many people out there. So hopefully with a combination of good regulatory science, applied scientific research will help people understand how they can make these products and then good regulatory policy will kind of reign in what's going on. Thanks.

DR. MCLELLAN: Barb. Go ahead.

DR. KOWAKCYK: Yeah, just a few comments. And it was a real pleasure to serve on this Subcommittee and to hear all the presentations that so much preparation went into and to participate in the site visits. You know, I was really impressed with the quality of the scientists, but also their passion and the quality of the laboratories as well.

You know, I think just a few things to add to the comments that came out. I mean clearly the reviewer regulator researcher model is a strength that's unique within CBER. And you can really feel that in terms of what CBER delivers. I wanted to call out that the future horizon scanning piece, married with the talent development piece I think is the sweet spot that comes forward in the recommendations. And clearly the treadmill's going faster with respect to scientific and technology evolution and the scope that CBER has to regulate.

And so I think, you know, the Committee, and Dr. Byrne reflected this, we tried to put forward recommendations and knowing, you know, there's flat

budgets or declining budgets, how do you best balance that with the focus on really the scientific manager leader and integrating kind of the new younger kind of next generation of scientists coming together?

And so I think one of the questions overall between the Committee and the next kind of the auctioning of this will be, you know, as you think about all the different options, how do you best balance those? Because without strong scientific leadership it's hard to develop the next generation talent who may be more transient, but obviously are your future leaders. And on top of this evolving landscape, as Dr. Tosi, you know, suggested in her field.

And so I think that that's one of the questions that the recommendations are there and we definitely were saying this is important for the strength of the future of CBER. But I guess the Devil's in the details. And I want to make sure that, you know, CBER has everything they need in terms of from us as a committee in terms of any recommendations that are in that intersection.

DR. MCLELLAN: Thank you. Barb.

DR. KOWAKCYK: Thank you. I really enjoyed the report as well. I had a couple of comments, one particularly around professional development and workforce development. One is I really like the recommendation to promote travel for scientists within the Agency to attend meetings and conferences. And that's something that his Board has recommended almost every year I think. And so I would hope that the Agency would take some steps to address that. I mean I've been on the Board now for three or four years and it seems like every report, every -- we've written letters, we've done different things. And so I'm glad to see that again, but I'm almost disappointed that it doesn't seem to be resolving itself. And I understand the current economic climate is contributing to that.

As an epidemiologist and biostatistician, you know, I'm very much in favor of development of pipeline of epidemiologist and biostatisticians. And that's something that we're going to talk about it later this afternoon as well. But I can tell you there is really not enough young people going into those fields. And

developing a strategy within the Agency is good. But I also think looking to your academic institutions as partners for developing students and the next generation that will have the skillsets that the Agency needs. And I think there's a lot of opportunity for a partnership there. And I didn't quite see that in the report and I didn't know if the Committee had talked about those things.

DR. BYRNE: Yeah, there hadn't been a formal plan about how to integrate. But I think your comments are well taken because the integration with the sources of training is going to be important to the future workforce. So there were some general comments about workforce development, but not the specifics as you bring up and the important topic areas for each office.

DR. KOWAKCYK: So I think at a minimum it would be good for the agencies, and I say agencies here because yours I don't think is the only agency dealing with this problem, is to identify some core competencies that you're looking for, that the agencies are looking for. A lot of academic institutions are developing data science programs and things like that, but that in

my mind is a bit different even than epidemiology and biostatistics. And so having at least outlined the needs that you have so that you can then partners with academic institutions to develop new professionals that can meet those needs I think would be a good idea.

DR. MCLELLAN: Mike, go ahead.

DR. YASZEMSKI: I'd like to follow up on Laura's comment as your other resident orthopedist. Bottom line upfront I'm going to ask our CBER colleagues to consider direct education to the public about these things. In that the folks who are doing this, as Laura said, they've taken our name. They call themselves -- I've seen one group call themselves regenerative orthopedic physicians. I don't think they're orthopedists. But what they've -- they're very shrewd. This one that I possess to look into this group in another venue, what they've done is they've found from CMS they've found CPT codes that all they need is patient consent to do and then they link those into a treatment. This particular one that I looked at was a treatment for knees. And I saw these fellows on TV. The two codes that they used were a bone marrow biopsy,

if they get patient consent they can do that, and a knee injection for knee arthritis. They linked those two, harvested bone marrow and in the same procedure took the needle down to the knee and injected it. And they said we get the magic stem cells from the bone marrow, we just put them where the problem is and they know what to do. Now, they're getting paid by CMS for these two codes. I don't think a bone marrow biopsy and a knee injection was ever envisioned to be done together. There's no science behind that.

So I don't think you folks are going to have trouble with the companies. The companies are going to behave well. You're going to interact with them. You're going to do good science and approve what is reasonable to approve. But if you could please educate the general public about these folks that are doing these things that have no science at all, and I don't think in total are doing any patient any good.

DR. BYRNE: I just want to thank you for that. That's a great observation. It's not just even educating the public, but something you bring up that I think we have to investigate is whether we can even

educate CMS about looking into those two codes coming up together. Because the two codes probably shouldn't be used together because they define what we would call a non-homologous use of bone marrow. Thanks.

DR. MCLELLAN: Ted.

DR. REISS: Thanks Mark. So my comments I think will echo some things that Cynthia was saying, actually most things that Cynthia was saying, but I think they're important to emphasize. I first want to thank my CBER colleagues who I thought they did an excellent job during this review process providing all the information sort of about exactly what they were doing and they were clear and transparent and extremely helpful. And I really appreciate all that work that they did.

The thing that I just want to emphasize is the future really. Now, they're doing an excellent job from a scientific point of view at this point. But the environmental scanning sort of is the issue I think that touched on a lot of us. So while we're doing this adequately today the world is moving incredibly fast in this arena, in this area. And so how, you know, how is

the organization going to keep up from a process point of view and an organizational point of view to meet those challenges? I think to emphasize that to come out of this report I think is absolutely critical and critical for the future.

UNIDENTIFIED SPEAKER: Dr. Byrne, I guess I have one follow up I'd like to do and that is your comment about core facilities and your review of core facilities there. And I'm curious if you could go maybe a little bit further and give us some pointers as to what you're observing and any particular soft spots that need direct attention.

DR. BYRNE: Yeah, well, we were able to visit the advanced computing core facility as one example and they have really strong infrastructure there and are developing new informatics technologies both for understanding safety reports, identifying trends that might influence other agencies, other offices within the center. So that was one example. Then there are much smaller entities throughout the scientific enterprise where, for example, cell phenotyping might be done or sequencing cores. So those are not as big

an effort, or at least from a funding perspective, but they're critically important to keeping the budget of an individual lab at a manageable realm because they're centrally supported. Do you have any other comments about the care other core activities?

DR. BYRNE: Well, maybe just to add what I think some of the comments we had were, that just the sustainability to ensure, you know, both technologically, but also to continue to attract and retain the personnel, the experts in that area.

UNIDENTIFIED SPEAKER: So, excuse me, so in addition to the core facilities that Dr. Byrne just mentioned we also have core facilities that supports a number of different biotechnology needs, in addition to high throughput sequencing traditional sequencing, as well as A logo peptides and so on. We also have flow cytometry, core, confocal core, TEM and micro array. And so for especially confocal and flow this year we actually did quite an intense review of what those facilities provide, how they're being used and how to provide a funding model that will make sure that these are sustainable resources and available to our center

scientists. And so we actually have come up starting in FY-19 with a combined model where at least half of it will be fund centrally so that there is this idea that the Center is providing these resources and making sure they're available. And the other half will be sort of charged on a prorated basis to the offices to their usage so that there's some accountability also on the part of the scientists and the offices in terms of their hopefully not abusing these resources by making them completely funded at the top. So we're hoping that that will be a nice mixed use model that will provide the sustainability and the accountability that we need to continue to provide these critical resources.

DR. MCLELLAN: Great. Sean.

DR. XIE: Just a quick question. I want to come back with Dr. Byrnes. You mentioned about several [inaudible] bioinformatics computing. Those are under FDA or FDA combined or regulated?

DR. BYRNE: Yes. Yeah, from my understanding.

DR. XIE: So something -- under -- it's under FDA 21, Chapter 11 they just combines on the software of

the computing facility security.

UNIDENTIFIED SPEAKER: So the resources that Dr. Byrne was mentioning is our high performance computing environment, which has authority to operate under the FDA. And so we are in compliance with all the security requirements, if that's what you're asking.

DR. XIE: Yeah.

UNIDENTIFIED SPEAKER: Yes.

DR. XIE: Okay. Thank you.

DR. BYRNE: Great. Are there other comments? Go ahead.

UNIDENTIFIED SPEAKER: So first of all, I just want to take a moment to really sincerely thank all the site visitors, Dr. Byrne and the entire site visit committee. Because I think really we -- they did an incredibly thorough job. We really, we went through the reports quite carefully. We really appreciate it. We've already taken steps to put some of the recommendations into place. For instance, we very much heard the need for horizon scanning. Which has been echoed by the fact that in the past two, three years

things have been coming at almost breakneck pace of having to deal with CRISPR/Cas9, really a surge towards continuous manufacturing and other manufacturing technologies, and having people and keeping up with that has been critical. So we are actually, as part of our strategic plan, will incorporate for each of our offices that are involved in research, a horizon scanning process that we will do on a regular basis so that we actually do make sure that areas that are emerging I can have resources devoted to them.

That dovetails very nicely with something we put into place a few years ago after a consulting engagement that we had, which includes kind of research prioritization process that we do internally which addresses our ability to be able to shift resources. So there are some areas which we have, although we continue to research in them, we kind of have lower priority and some which have higher priority. And what will happen as we see with this horizon scanning process, that there are new areas emerging. Again, things that have very low priority may sunset as we have limited resources and need to bring on people to

work on other areas which have higher priority.

Right now obviously higher priority in some of the areas of gene therapies we are in the process of looking to make sure we have plenty of strength in that area, as well as increasing our strength in this area of advanced manufacturing technologies. Because it's very clear that the field is headed there with continuous manufacturing of biologics, following on the continuous manufacturing of drugs.

So we really do hear your recommendations. We really appreciate them. I hear also the issue of travel. We are trying -- I think right now we are in a somewhat better place with travel. We are lucky that the funding situation is not quite as severe as we thought it would be, and I hope it stays that way. To my knowledge I don't think we've had to really decline people wanting to go to meetings. Sometimes we have limits on the number of people that can attend a meeting, but in terms of total number, but we try to make it possible for people to go as much as they can.

And finally I should acknowledge the work of Dr. Wilson and her staff who have done an incredible job

really making sure that our research and enterprise stays current and that the recommendations here have already been really put in large part into strategic plans or into place. So thank you.

DR. MCLELLAN: Sean, your flag's up. Barb.

DR. KOWAKCYK: Thanks. I was happy to hear that. I had a follow up question about your prioritization activities and how does the -- how do you go about doing that? I know prioritizing where you allocate resources is always a difficult task. So I was wondering, you know, what is your process?

DR. BYRNE: So it is as always it's a complicated way to have to do this, but I think for us the prioritization process goes through looking at the -- essentially looking at the research work on a variety of different aspects. How relevant it is for the regulatory work that we're doing at this time, how current the research is for vis a vis others in the field, and whether -- and finally probably a very important point that I don't want to miss is that how unique is the research compared to what's done externally. For instance, there are certain areas

where if we don't conduct that research nobody else is going to do it. And so it's this combination of regulatory relevance, quality of what we're doing and our ability to fill a unique need, public health need that might not be addressed by others that we work with.

And I'm sure I've forgotten something else that probably Carolyn can respond to. And it's not easy. But I think it is necessary. Because if we don't do that we will be in a position where when the next pandemic comes around, which will happen, we won't be able to rapidly shift resources in a way that we need to. I think we've done a reasonable job doing that in the past. And in the past at least before our most recent consulting engagement it was done on a more informal basis. Now I think we have a more formal process so that we can be a little bit, feel a little bit more confident that when we shift resources we're not shifting them from programs that are otherwise really important in some other ways. So obviously time will tell, but we appreciate the challenges here and we'll continue to try to do it better.

UNIDENTIFIED SPEAKER: That's very good to hear. It sounds like you're using some sort of decision analysis to set your priorities and that's really excellent.

UNIDENTIFIED SPEAKER: So I'll just mention Dr. Marks referred to some new processes and one of which is the Regulatory Science Council, which is composed of center and office leadership and they develop center wide goals, office goals and objectives. And then this past year we've had a series of discussions of Regulatory Science Council and we've developed an impact framework which is a whole series of metrics which we're applying this year for the first time going forward to look at the impact of the work as part of that annual evaluation process. So we continue to try refine our processes to get closer to that sweet spot.

DR. MCLELLAN: Go ahead Scott.

DR. STEELE: Dr. Marks, you mentioned the travel situation has improved, which is very good news. I was wondering about -- I know that at some point there was some challenges with the process or mechanism to bring in fellows. Is that something that's improved or is

that a work in progress?

DR. MARKS: It's still a work in progress. But I'm hoping that with an FDA fellowship, which should be in place in the not too distant future, that will help address some of the issues. I think that will -- that may make things better. Carolyn, do you want to add anything?

DR. STEELE: Is that a -- because that's an FDA wide issue, and is an FDA wide solution or --

DR. MARKS: Indeed this is an FDA wide solution to an issue that right now the challenges have been that the fellowship process involves contracting. And it's probably best not to have to treat our fellows as contractors and to be able to have them as -- have a fellowship program more like an NIH fellowship program.

DR. STEELE: Great. Thank you very much.

DR. MCLELLAN: Any other questions, comments? Dr. Marks and Dr. Wilson, thank you for your being responsive to the report. Barry, if I could I'd like to ask you as Chair to the Subcommittee to make a motion for us to accept the report of the Subcommittee along with its recommendations.

DR. BYRNE: So I so move.

DR. MCLELLAN: Is there a second on the Committee please? Thank you, Lynn. Those in favor please say aye.

(Multiple ayes.)

DR. MCLENNAN: Those against?

(No response.)

DR. MCLENNAN: They ayes have it unanimously. Thank you very much. Barry, it's a great report. Appreciate it. We're going to take just a five minute stretch here. We've got a little bit of time built into the agenda. So let's pause right here. Thank you.

[Recess in conference.]

[Conference resumed.]

DR. MCLELLAN: I think this was one Board meeting that I probably had more reading to do thanks to Rakesh here. He gave us lots and lots of background. My airplane ride was full. Okay. I think we have our quorum back and we're ready to proceed. So we'd now like to hear from the FDA's Patient Affairs Initiative. Joining us today is Samir Shaikh and Julie Andrea

Furia, if I got that right.

MS. FURIA-HELMS: Andrea Furia-Helms.

DR. MCLELLAN: Andrea Furia-Helms. Thank you very much. Welcome guys. Looking forward to hearing your report. The floor is yours.

PATIENT AFFAIRS INITIATIVE AT FDA

DR. FURIA-HELMS: Thank you so much. Good morning everyone. Thank you for the opportunity to be here today and to talk with you about our newly established patient affairs staff. Thank you, Rakesh, for inviting us and thank you, Dr. McLellan, for having us.

Just a little bit of background about myself. I started my first ten years in the federal government at the National Institutes of Health. And at that point I transitioned here to FDA. And it's been about over eleven years now. I was in the -- what used to be the Office of Special Health Issues and now is Office of Health and Constituent Affairs running the FDA patient representative program. And when Patient Affairs was established late last year I transitioned over there to Acting Director. And that's my current position.

So as I mentioned the Patient Affairs staff was

established late last year. And we're a small staff, it's just Samir and I. Hopefully to grow in the future. We report into the Principal Deputy Commissioner for Medical Products and Tobacco. And our aim is really to have a unified and to enhance a systematic patient engagement process across the medical product life cycle. And ultimately we are trying to meet the needs of patients as best as possible.

We work closely with the medical products centers and other offices in the Office of the Commissioner. And in collaboration, of course, with our patient community stakeholders. And we want to support and compliment the ongoing patient engagement efforts that are currently underway across the medical product centers and the Office of the Commissioner.

Our aim is to coordinate crosscutting activities and programs. And we're trying to leverage best practices and enhance the patient engagement process across the medical product centers. And this is really facilitated under the FDA's Safety and Innovation Act. And specifically under that there is a Section 1137 for

including patient perspectives in the medical practice discussions. And now with FDA Reauthorization Act and the 21st Century Cures Act there's a lot of legal basis for including patient perspectives.

And at this point I'd like to turn it over to Samir Shaikh and he will get into more of the details of what we've been working on and our objectives.

MR. SHAIKH: So good morning. My name is Samir Shaikh. I'm currently the Deputy Director for Patient Affairs, as Andrea mentioned. A little bit about myself, I've been fortunate to work in three different sectors of healthcare. I started off working in clinical research at University of Chicago. Then transitioned to pharma as a vaccine chemist and now on the regulatory side where I've been for the past five years.

I should probably make a disclaimer. We don't have a slide where we can quickly kind of skip through this part. But, you know, are comments are not reflective of the views and opinions of the FDA and our non-binding. With that said I want to pose a question. And that is how many people are familiar with any kind

of patient engagement activity at the FDA? Okay. So a couple. And how many people are familiar with the patient affairs initiative in any way? Okay, great.

And I think we should probably just clarify what we mean by patient engagement. And this is defined as draft terminology under the patient focus drug development initiative. And it's involving patient and patient stakeholders in sharing their experiences, their perspectives, their priorities, their needs to help inform FDA's public health mission. And so patient engagement has been happening across all the medical product centers. From patient focused drug development in CDER and CBER to the Patient Engagement Advisory Committee that was founded and in CDRH.

So our focus, as Andrea mentioned, being in the Office of the Commissioner, being situated there is to focus on cross-center initiatives, right. So not necessarily in any of the particular centers, but looking at it from a cross-center perspective. And having services that's specifically directed to patients, right, specifically for patients. And so in thinking about drafting our objectives we considered

different viewpoints. The first is public voice. We had a public docket established last year. And through that we received comments on what some of our considerations in creating a patient care staff. We also had a third party assessment that was done around patient engagement across the entire agency. And then the last component of some input that we're receiving for our objectives is through our internal colleagues, right, the folks that have been in this space for many, many years, working on patient engagement.

So what I'll do is I'll quickly walk through a couple of our proposed objectives and then we can ask some -- or respond to questions that you may have at the end. So the first of our proposed objectives is to create a central entry point, a front door of sorts for patient inquiry and patient requests. There are various entry points to the FDA that patient and patient advocates are using. The goal isn't to put locks on those entry points and to have them all then come through the front door, but rather for new patients, patients and advocates who are not familiar with the FDA, who don't have the existing

relationships, how do we give them an opportunity to engage? So that's really one of our proposed objectives.

The other is focusing on education and navigation. It's important that we are informing patients of how they can contribute to drug development. What are the different vehicles of engagement? Also, how can we help educate patients about some of those nuances of our regulatory process? So in this space specifically what exactly is patient experience data? What is a clinical end point? We would define these terms, but how do we convey say getting from patient experience data to a regulatory decision? I think as the science matures educating and being transparent about this process is going to be important as we engage with these constituents.

And then the last proposed objective I'll talk about is our public and private partnerships and expanding on them. And I'll turn it over to Andrea to talk about a couple of them.

MS. FURIA-HELMS: Thanks, Samir. So just to give you a little bit of insight as to a couple of

public/private partnerships we've been working, in December of last year is the one of the first initiatives of the Patient Affairs staff. We opened a docket to request nominations for a patient engagement collaborative. And this is going to be a forum to bring patient stakeholders together to interact with the regulatory staff here and to better understand their experiences and our experiences in engaging with patient communities. And from those experiences learning from each other and hopefully finding new ways to engage, better engage and maybe learn from each other, provide education and try to implement more systematic patient engagement across the FDA.

So we had the docket open through January 29th and we received 200 nominations, which was a pleasant surprise. We're currently going through those nominations to establish the 16-membership of that forum. We are working collaboratively with the Clinical Trials Transformation Initiative. And they also have some steering committee members that will be part of this collaborative as well who are patient advocates.

Just a little bit of background. What's the impetus for developing such a collaborative and have this forum? For one the laws. The laws are telling us in FDARA and 21st Century Cures we need to engage with patients and patient communities and caregivers more to better understand how we can meet their needs better. Understand their perspectives in terms of disease burden and treatment burden, quality of life issues and how symptoms impact their daily activities.

We listened. Under FDASIA 1137, as I mentioned earlier, there was a provision to understand how we can include patients and caregivers in the regulatory discussions. And we had a docket open at that time and one of the things that was recommended from our stakeholders was, you know, can we have -- can we be part of the process regularly? Not on a reactive way all the time as we have been doing sometimes in the past. But just regularly so that we can learn from each other and hear what's going on and be up to date and current with FDA. So we listened to those recommendations and here's the implementation for this patient engagement collaborative.

And thirdly we have a model. The European Medicines Agency has been doing this for about ten years. They have the Patient and Consumers Working Party. And they've been engaging with patient organization representatives in this kind of collaboration for this long and understanding how they can better engage and better include their perspectives in their regulatory process.

So just a little bit of information on the membership criteria for the patient engagement collaborative. We're looking for patients who have personal disease experience either directly or indirectly. Either they're living with a disease or survivors, primary caregivers of patients that cannot represent themselves, such as a parent of a child or someone who has Alzheimer's who has progressed to the point where they really can't participate in this type of activity. And also representatives from groups. So they are interacting with their communities from an organization perspective. They can represent their community's perspectives from an organizational standpoint.

So a couple of things that we are thinking about is we're hoping to have the first inaugural meeting in late summer, early fall. And some of the topics we have discussed that could come out of this is improving transparency. We heard from the community that they want to better understand the medical product, life cycle process and how to engage at certain touchpoints where they would be effective and efficient in helping us understand their needs. Other things are how to include more systematic patient engagement, as I mentioned, across the medical product centers. Strategies for engaging with patients and new models for collaborating with our stakeholders.

However, even though we have these topics that we have sort of addressed that could be possible, areas to focus on and to explore with the patient engagement collaborative, we really want this patient drive. There is going to be a chair and a co-chair. And the co-chair is going to be a patient advocate. And we want the advocate members and we want the co-chair to really drive the topics for this collaborative and really have ownership and feel like their voice is

being heard and that we are trying to implement some changes that would assist in engaging better with our patient community stakeholders.

So now I'm going to talk about another initiative that we're currently working on in our initial stages. To kick off rare disease week in February we launched an initiative to do listening sessions, rare disease listening sessions. It's going to be a pilot. We have a Memorandum of Understanding with the National Organization of Rare Disorders to help us collaborate on this effort. And the reason why we established this, especially in the rare disease area, in my work and experience in the Office of Health and Constituent Affairs I would get a request from medical officers to better understand certain rare diseases in their work. They would want to understand quality of life issues, disease burden, those types of things, so that it would help them understand what's important to patients. So we would help establish those typically phone calls where it's a conversation with patient communities in better understanding their needs and how their disease is impacting them on a daily basis.

So we're going to pilot this and we're going to select a therapeutic area. And hopefully once we do an assessment to understand is this valuable on both the review division and on the patient community stakeholder end, maybe expand to other therapeutic areas. And it's all an effort to really help enhance the work of the review division, better understand the patient community needs and for giving the patients a voice in the process.

And that's what we have for you today. We truly welcome your questions. We thank you for your attention and we're happy to address any recommendations you have.

DR. MCLELLAN: Thank you both. Great report. Comments and questions from the Committee? Yes.

UNIDENTIFIED SPEAKER: Thank you. I think this is extremely timely, really important. And I'm involved in a number of initiatives through the NIH right with regards to kidney and transplant precision medicine where the patient engagement piece is becoming more and more important. I'd just like to come back to the rare disease kind of network that you're working with. I

would like to congratulate you because that is so needed.

But just as a thought there I also work with a lot of rare disease networks. And I think one of the main kind of patient pain points, something that you may be wanting to focus on and be aware of is that a lot of these patients actually their participation in some of these clinical trials for getting drugs approvals for their rare diseases is integral. And they do it with a lot of enthusiasm because if they didn't participate they wouldn't be able to get those kind of approvals. Yet once those drugs are approved those drugs actually get priced at a very high price point because of the economic model of generating drugs for rare diseases, it's a small market so you hike up the cost and you have to pay for it.

So a lot of these patients are then coming back and suffering because they are then unable to afford the kind of cost of those drugs. And so we've been trying to work with a couple of organizations for these rare disease networks. In Europe where this has happened where I think some kind of, you know, some

kind of confirmation from these developing -- these pharma companies that are developing these drugs for rare diseases that those drugs will be made available back to the patients and the families who participated and how to work through that conundrum, I think really encouraging that patient voice to come back in in the earlier planning stages for some of those trials so that pharma can also hear it I think would be quite critical.

MS. FURIA-HELMS: Yes. I think that's very important to take into consideration. And I think that's part of the education piece. I think the patient community they're very excited, they want to participate in clinical trials. They want to see approved therapies, especially in the rare disease and ultra-rare disease area. But I think the education piece and understanding what happens after that and how it impacts them after the fact financially is something that definitely needs to be further distributed and understood.

DR. MCLELLAN: Sean.

DR. XIE: This is a very interesting program. I

Googled it and it seems I thought that we discussed this before in 2017. Yeah. FDA has a committee special for patient engagement. But my question is how do you -- you have a detailed plan already developed to access outcomes. Back to [inaudible] about what kind of diseases, common disease or rare disease and also if it's new to come out how do you educate a patient? And the key is this is a [inaudible]. Patient posts a question online and some expert has to answer the question. So assuming this is a big team supported, including MD or PharmD partner with you on this system to answer the question. Is that right?

MS. FURIA-HELMS: Yes, I think it is important to partner with those that can -- the experts that can address those specific questions. And that's something that we would also explore as well. As we are in the initial stages of development we truly appreciate that recommendation. It's something to explore for our future endeavors as we move forward in developing our programs and initiatives.

DR. XIE: Yeah. [inaudible] we have a school pharmacy, we have UPMC, we'd be happy to [inaudible]

with you.

DR. MCLELLAN: Barb.

DR. KOWAKCYK: So I had a quick question. And I wanted to know, I know you said several times this is about the centers involved in medical development. Do you plan to engage CFSAN at all in this initiative? Because, one, there is a significant public health burden due to food borne pathogens and those patient perspectives should be included. Not only that, many patients fall into the vulnerable populations which are more susceptible to food borne illness. And some of the outreach and education activities that CFSAN does could be informed by the patient perspectives of this Committee. And I was just wondering if you were planning on engaging CFSAN.

MS. FURIA-HELMS: I think that's an excellent point and I do think that's something that eventually we will be moving toward, especially in the area of medical foods as that further develops, and understanding the food borne illness. I think it is something that we certainly need to explore as we get further established. I do know that when I ran the

patient representatives program we did not have the capacity to include food borne illness issues in that. But it's something we certainly should include in this role now in patient affairs.

DR. KOWAKCYK: So I think I would strongly encourage you to do that, particularly with patients that have had hemolytic uremic syndrome, which is a significant food borne illness that does fall within the rare diseases. And I think that there is a need for outreach and engagement of these patient populations. A lot of them are at higher risk of serious consequences. And there are food restrictions that they have to follow. And CFSAN should be aware of what's happening. I mean there needs to be better coordination.

So for example, I recently heard of a co-op that was being developed, a pharm co-op for cancer patients so that they could access fresh produce that was located, would be located near a dairy farm. This proposes a very high risk. I mean cancer patients in general are often recommended that they don't consume fresh produce. For example, there's a big outbreak

right now from E.coli in romaine lettuce, okay. And so these patient perspectives I think CFSAN would benefit from hearing them. So I would encourage you to do that sooner rather than later. Thank you.

UNIDENTIFIED SPEAKER: Absolutely. Thank you. Can I -- I'm sorry, I didn't [inaudible].

DR. MCLELLAN: Would you like to -- go right ahead.

UNIDENTIFIED SPEAKER: Yeah, I was just going to say just something briefly. And I know in working with Andrea in the Office of Chief Scientists and of course our shared family in the Office of Medical Products and Tobacco, we'll be working together to kind of identify any gaps in engagement across the Agency. So of course we're working with Dr. Susan Mayne and then we also have Rear Admiral Andy [ph?] from Food Science and Med, along with Dr. Ostroff. So we'll be working with them to work up these issues. And of course we could tap into your expertise here on the Board. So thank you.

DR. MCLELLAN: Good. We're going to go with Laura, then Cynthia, then Lynn. Laura, go ahead.

DR. TOSI: This is very exciting. My own practice

focuses on kids with rare and ultra-rare orthopedic disorders. And the challenge has been helping the patients understand who they are. Because so many of these diseases are, even though they're rear, are incredibly heterogeneous. And will you be, and is it even your role, to help develop the tools that help stratify patients? Because what we're finding is, okay, you have osteogenesis imperfecto. Well, nobody knows what kind they have. And you won't know the improvement that they'll have from a therapy if they can't stratify themselves well.

And you might say, well, people will be in clinical trials. Yes. But that's short term. And then going forward often times patients are putting themselves forward to be part of this, that or whatever, not knowing what their patient -- what their type is or how they should be organized. Is it within the prevue of your office to starting thinking about how do we help patients think about who they are? So that when they answer quality of life instruments, or answer PRO instruments that you know who you're starting with, rather than trying to compare apples and

oranges.

MS. FURIA-HELMS: That's a very good point. And actually that does come out of the conversations we have with the review divisions when we're determining who we want to speak with in those listening sessions. With rare diseases, for example, a recent one, there were three subgroups within that particular rare disease community that the review division wanted to hear from. And they wanted to hear specific experiences related to those subgroups with their current experience with certain treatments that they're using to manage their symptoms and other related issues that are specific to those specific subgroups. Yeah, so I think that does naturally come out in certain areas. But then also in some listening sessions, and this is all contingent upon the need of the review division, it may be more general those questions. But I think that does come out naturally.

DR. TOSI: Just I think your focused on review and I'm focused a little bit more on communication and helping patients after work has been done or while work is being done to be understood. And if patients don't

understand who they are, and rare disease people are, you know, distributed worldwide, often not able to come into your meeting or to a clinical trial or anything else, is there any work on communication tools is really the bottom line here?

MS. FURIA-HELMS: Currently that is one of the things we plan on working on is communication and education and helping our communities better understand the different regulatory process and where they fit into that. We do plan on doing some education.

MR. SHAIKH: Yeah. And I think specifically on the methodology and tools that you're referring to, a lot of that's happening through the guidance work under the Patient Focused Drug Development Initiative. But as you mentioned, we need to couple that with communication. I think that's where our staff can work with the medical product centers to ensure that that's happening and that we're engaging with patients and their advocates.

DR. MCLELLAN: Cynthia.

DR. AFSHARI: Thank you for the presentation. It's exciting to hear about this. And I think as you

articulated there's these ongoing activities and now this is something new coming in. And I guess I have two comments/questions. The first one is you talked about the front door for maybe patients and groups that aren't already present or interacting somewhere in the Agency. And I'm just wondering as these other groups and initiatives have come up across the different FDA centers they probably all have their own look and feel to them. And so is part of the goal here of your office with the Commissioner to try to maybe introduce a similar framework across all of these so that you can determine best where the value is in the Agency? And again, if you have to rob Peter to pay Paul so to speak that you have kind of a systematic approach for doing that in terms of where the priorities are. Because I imagine there's a lot of tension in the wires there.

MR. SHAIKH: You know, certainly I think a standardized approach or framework across the Agency will be critical. I mean we're a little early in the process. And first trying to understanding who is engaging the FDA? What are some of the matters that we're engaging patients on? But ultimately, as you

mentioned, I think once we have the information and we know the sources of input, it's understanding how can we have a uniform kind of process for how we engage patients? But we also have to understand there are specific nuances to say a drug conversation, versus a device conversation, versus biologic conversation. But at some I think baseline there is kind of a unified framework that we can have and how we take in information and how we engage patients.

DR. AFSHARI: My second was you talked about cross collaboration, which I heard as being across the FDA agency. But as you think about patients and what their caregivers may need and think about access to healthcare and drugs, or whatever that is, it could quickly take you out to other agencies and other types of groups. So how will you engage there and what's the process?

MR. SHAIKH: Yeah. One of our goals in the early phase is to understand what's happening in say, for example, Health and Human Services. We've already reached out to AHRQ. And my colleague has actually had experience NIH. And so these are, you know,

conversations that we're just starting to facilitate now. And, you know, I completely agree that understanding what are the best practices? Because there is patient engagement happening outside of FDA and understanding what valuable, you know, pieces of those conversations we can also have. Thank you.

DR. MCLELLAN: Lynn.

DR. GOLDMAN: Yeah, I have a few comments. One thing that strikes me is that, I mean, we are the Science Board. And so I think that it behooves us to think a little bit about how science could inform what you're doing and in particular behavioral science, which there is such a thing. We don't have very much strength in that area on this Board. But when we're talking about engagement of patients and communication with patients there's a lot of rich, very rich science involved. And a lot of people who could bring expertise to you, perhaps even within the Agency. But I know certainly in academe.

And some of the things that I wanted to mention, I mean, one is just even, you know, how you wrap around your arms around who is a patient. And, you know, you

made a comment, you know, that people with Alzheimer's probably couldn't serve. But probably one in ten of us in this room have it. We don't know we have it. You don't know we have it. But, you know, so, you know, who is a patient I think is major issue.

The same with actually Barbara's issue, I mean all of us. I ordered a Cesar salad for lunch, so you know, I'm a romaine lettuce eater. And so I haven't had, you know, I can't get, you know, hemolytic uremic syndrome. But I think, you know, who is a patient I think is a major question. And then I think you're already getting them.

I really admire the efforts that you are making to widen your circle of connections and brining more people in. But you can apply science actually to understanding, you know, what are those social networks of patients that you can tap into. They're not necessarily members of organizations who read the Federal Register. So that's a problem when you reach out through the Federal Register I think you're very unlikely to reach a lot of normal patients or would be patients. But there are scientist who can help you

with that. And there's a lot. I'm not saying hire Cambridge Analytica or something like that. But I do think that there are ways, you know, to get into these networks.

And I mean the other thing is that I think that the behavioral science can help you around coming up with strategies to communicate. Because I also think that these -- I mean even the rare diseases, they're compl -- the communications issues, and I don't do this, Minnie does this, but I know they're completely different. If you're dealing with the communication is to parents of infants with a rare disease versus adults who have a rare disease and are trying to transition into independent life. And so, you know, and then, you know, we, you know, we're a multi-cultural society and it's complicated to communicate.

You know, a couple of things that I also wanted to mention. I mean one is certainly the reach out to other agencies is really great, I think ARC. I think also to think about CMS. I think a lot of the frustration for patients is that, you know, FDA reviews medications and devices and so forth and approves them,

but that doesn't mean that CMS is going to pay for it. You know, so the broken, in my view, connection between FDA and CMS it's really, really hard for the public to understand. And partly because it doesn't make any sense, you know. Because you have expert bodies that review things and then another agency in the same department gets another expert body to review things. And, you know, I think that we can listen to patients about that, but we could also think about, you know, trying to fix that disconnect and make it better for them.

PCORI is another agency to think about. They're doing a lot of research on patient oriented outcomes. And that patient centered approach that they're doing I think is eliminating a lot of issues that are really important to you. And there may even be opportunities, you know, to partner with them on some of this. So I just wanted to mention that as well.

The last point, [inaudible] PA we had issues about, you know, just communicating to the public about what was on product labels. And we actually were able to have very productive partnerships with the industry

around doing surveys, survey research to actually understand what words that we were using on labels meant to actual people. And it was really sad too because what my people thought was kind of a hierarchy of words that described risk. The public had it turned on the other side. So, you know, our experts, our regulatory scientists and stuff who come up with some of these words, don't think -- don't understand the words the same way the public understands words.

And the industry does have a lot of connection with these networks of patients. You know, they use them in some ways that's sometimes not the best I think. But I think if you can have an honest to God partnership arrangement where you're just aligning on things where you have things of interest, like understanding things about language that, you know, the industry and the FDA need to both understand that and could collaborate on that. We felt we were able to leverage a lot of resources around that where we didn't have funding to go out and do the science and we could get it done. So --

MS. FURIA-HELMS: Thank you for all those

comments. I think you bring up a number of good points. I think health literacy is a huge issue and I think that's something that we will be involved in and really exploring in terms of our efforts here at Patient Affairs. There is an HHS health literacy group that we are a part of and we will be exploring those types of things. I think the other point of view, you know, engaging with other federal agencies, as Samir has said, and really further engaging with other entities as well.

But CMS is also something that we should look into for the future. And I just think that the behavioral piece is so important, the around social science piece I think. In my experience with -- I used to run the Back the Sleep campaign at NIH and, you know, we had one brochure that said "Back to Sleep." And when you go out and talk to people they thought it was some kind of mattress ad, you know, so not around sudden infant death syndrome. So, you know, we really learn what people are interpreting when they're reading when you go out there and do that kind of focus group research. And I think that's important as well to include in our

work. Thank you.

DR. MCLELLAN: Other comments, questions? Go ahead.

UNIDENTIFIED SPEAKER: So thank you for that introduction to the work that you're doing. I think it's incredibly important and needs to go forward actually quite expeditiously. You know, the patient really is the focus of what we do and but yet sort of the voice of the patient really hasn't been heard in a lot of the things that we've been involved in. So obviously incredibly important, I think people have woken up to it.

But I have a strategic question for you guys. So you've gotten a lot of, you know, issues and feedback and thoughts and ideas. It sounds like what you're really trying to do is to just start to sort of understand or level set or get involved or get involvement in the Agency and then in the reviewing division. But I haven't heard yet from you guys about any specific goals that you might have, some specific goals where you guys are headed, what sort of the end game is. Because, you know, from what you're hearing

from people there's about an enumerable number of things that you could be doing. So the question is what do you -- what are your short term goals? And then what do you see for your long term goals and where might this initiative be headed, given the fact that the sky is almost the limit for anything that you can do, since the patient voice really hasn't been heard in the things that we've been involved in to date?

MR. SHAIKH: So that's a great question. We're actually working on that right now. As I mentioned in my initial remarks, we are getting feedback and input from various sources. And some of that is both internally and externally. And it's going to be important that we do create kind of strategic priorities that are tied to the Agency's overall public health mission. And so we're in conversations right now. I think it's too early to kind of establish them, but hopefully in the next I'd say month or two we should have those solidified and we can share those with public.

MS. FURIA-HELMS: I also think being the Science Board there's opportunity for us to engage in the

future as we have gone further along in developing our objectives and goals. And one of the things for the future is really how can we take that patient experience information and tie it to a regulatory decision? And so we would need your expertise in understanding and really finding a pathway to move forward in that direction.

UNIDENTIFIED SPEAKER: Just one quick follow up follow comment. And I thank you for that. We look forward to hearing from you guys also. Just one of the things, you know, that sort of come out in the conversation is sort of, you know, getting different types of groups sort of involved in the social science aspect of things. Because patient experiences can be enumerable basically based upon sort of the culture, background, ethnicity, these sorts of things. So that's something that has got to be baked into what your strategic planning is and how you address all of that.

MR. SHAIKH: Thank you. Rhondee.

DR. BALDI: Yes, thanks. My comment was about the strategic planning and whether you might consider how

that patient engagement work dovetails with medical adverse event reporting, being that front door for the broader public to report adverse events. It certainly sounds like the, you know, rare disease community is the first big group you're trying to engage. But thinking in the future about how the larger public can engage in that medical event reporting, adverse event reporting and make it easy for them in ways that the rest of the -- in ways that we engage with other institutions really easily. So thinking about that for the future as well.

MS. FURIA-HELMS: So one of the things that we did when I was in the Office of Health and Constituent Affairs, part of that office was focused on Med Watch and assisting with that process. And there was a lot of education in helping stakeholders understand and our patients and caregivers understand how to fill out a Med Watch form appropriately. There were some videos made and some webinars and things we did at that time. But I do think there is a lot more to do in that area. There are also groups of patients that we've interacted with that have been harmed by medical devices and want

to find ways to engage with us so that it doesn't happen with others and how we can improve in that process. And improve basically our products so that it's meeting their needs with as minimal risk as possible. So those are the types of things we also could continue to explore.

And I know that also in OHCA we had developed a consumer form. It was a little easier to work through than when a physician would submit or a researcher. So that was also developed at that time. I think there is still a lot more education that's needed to understand how much detail to provide in there. Because there are some components that get missed and then that information could not be utilized the way it should be in terms of adverse events and how that impacts in the surveillance area.

DR. MCLELLAN: Lynn, did you have -- okay. Any other questions? Let me just end with a commentary. You know, I appreciate the focus that you've been and the openness for learning and approaching new techniques. I really think Barb's comment regarding partnering with CFSAN and the entire food side of this.

You want large numbers of engagement that will curl your toes. I couldn't help but notice from the time you began to the time you ended I believe every one of the audience out there communicated with people. If you're not thinking in terms of social media and fully electronic ways to connect with patients then you're going to miss an incredible opportunity.

And then finally the comment regarding behavioral sciences is extraordinary. The science is pushing hard and really opening up all new avenues. And we certainly could contribute to ensure that you have a rich background to tap in terms of supporting your work there. Thank you so much. We appreciate the vision and sense of opportunity that you're presenting. We're very excited about this role in FDA.

MR. SHAIKH: Thank you. Appreciate it.

MS. FURIA-HELMS: Thank you so much.

MR. SHAIKH: So one quick comment. We will look to bolster this Board with some behavioral science expertise. I think that was a good call. So we will work on that immediately. And as Andrea said, you know, they will be coming to this -- they'll probably

be coming to the Science Board again in the future. I've given them an open invitation. It's a nascent initiative, so it's kind of refreshing for the Science Board to see something as it starts and to have some influence and provide some direction to help it succeed. So I know they look forward to working with you guys and it seems there's a lot of interest, so I'm glad it worked out.

DR. MCLELLAN: So Board we're on a formal break until the Commissioner's report at 11:30. So please be back by 11:25 at the latest. And we'll reconvene at that point. Thank you very much.

[Recess in proceeding.]

[Proceeding resumed.]

COMMISSIONER'S UPDATE AND OVERVIEW OF AFTERNOON DISCUSSION

DR. MCLELLAN: So I'll call the board meeting back to order and we'll proceed with our agenda as scheduled. We're very glad to have Commissioner Scott Gottlieb here to provide an update with the FDA's recent activities and his priorities and progress he's made in the term thus far. Dr. Gottlieb will also be

giving us some context behind the questions that we've received and, of course, the reading material that we've had to explore those. And if time permits before the lunch hour we'll actually start our discussion with question one if there's time. Commissioner, the floor is yours.

DR. GOTTLIEB: Thank you so much. It's a real delight to be back with this group. And I appreciate everything that you're doing to support the Agency and the dialog that we've had over the course of the year that I've been in this role.

I wanted to just use the opportunity to talk about some of the newer ideas that we're working on. I think line up and comport with some of the discussion that's going to happen later in the afternoon around the questions that have been put to the group. And I wanted to particularly focus on the FY-19 budget and some of the proposals that we put forward in that budget. Because they represent, first of all they represent I think broader foundational initiatives that we have an opportunity to put resources behind. They're in the President's budget. I'm testifying

tomorrow before the Senate Budget Committee, Senate Appropriations Committee. I testified last week before the House. And we've had good dialog with members on Capitol Hill about the ideas we put forward.

I think, number two, I think what we've tried to put forward this year with respect particularly to some of the databased initiatives, sort of the knowledge management and database initiatives are ideas where we could build out capabilities I think are foundational to the Agency. I think they have the potential to provide a transformative change to core components of how we function. They're the kinds of things that, you know, you're only able to do with an appropriation, a deliberate effort. I mean we can make -- when we do we make constant and incremental progress to how we approach or processes in the context of user fee agreements and just in the context of our normal course of policymaking and the efforts that we do every day. But I think this affords us the opportunity to think of sort of paradigm change. That might be overstating the impact, but from my vantage point it isn't overstating the impact. And finally I think it lines up closely

with what the kinds of questions that were put forward to the group and that I hope you're going to have the opportunity to discuss later today.

So the two biggest elements of the -- or the two biggest elements are the budget proposals that we've put forward that I think are foundational in many respects. And if people were to ask me, we put forward nine ideas, if they were to say, well, you know, talk about the two or three that you think are the most critical to the Agency, the two that would probably be the most critical to the Agency I think are what we put forward with respect to continuous manufacturing and what we put forward with respect to what I would say broadly speaking is data management and making better use of real world evidence and real world data. And I'll talk a little bit about the continuous manufacturing because it's less directly relevant to some of the questions. Although some of the questions that we put to the group touch on it. And then I'll focus a little bit more on the data management elements and then I'll pause for questions.

Continuous manufacturing I think we have long seen

and opportunity to see more of the industry convert towards continuous manufacturing platforms. And, you know, arguably one of the impediments is the uncertainty in the development space about how to do that and whether or not you're creating incremental risk and uncertainty in the course of a development program. In the element of the development program that should be the most derisked. I mean, you know, if you're a drug developer and you're taking a lot of clinical risk in terms of how you develop product the last thing you want to do is inject a whole lot of uncertainty at the end of the application process related to the CMC portion of the application and how you're going to be manufacturing it. That should be more routinized and predictable.

And so by asking sponsors to consider converting to continuous manufacturing we're also asking them arguably to inject a level of uncertainty into the portion of the development process that probably is the elements that they want to derisk the most. And so I think there is some onus on us to try to think about how we develop scientific principles that can derisk

that conversion if we think that this is an important public health goal. And we think it is. And so the proposal we put forward in the context of the budget was to start putting resources behind the development of public/private partnerships and other policy development that could more fundamentally derisk the conversion and see a more rapid migration towards continuous manufacturing.

I think a lot of the discussion around continuous manufacturing to date has been on the small molecule side. And you've seen companies developing small molecule products convert to continuous manufacturing platforms. I think there's four or five companies that have engaged this technology. I'm not sure of all the specifics of what's going on in the industry. There must be more behind it. And there's a lot of benefits from that from a public health standpoint in terms of lower costs, mitigating the risk for shortages, improving quality and reducing the opportunity for mistakes.

And also we put it forward in the context of redomesticating manufacturing. We think that if more

companies move towards smaller footprint, higher intellectual property continuous manufacturing platforms, those are precisely the kinds of manufacturing platforms that you wouldn't want offshore. You know, you might want to put that kind of a platform in downtown Boston. And while that's, well, you know, that's not one of our sort of explicit public health goals to try to redomesticate manufacturing, that's not within FDA's mandate and I would never put forward that that is or that's a rationale for us pursing it. It's certainly a mandate of the Administration to try to build out domestic manufacturing to the extent that, you know the Administration and Congress are considering how to allocate resources behind goals of trying to, you know, grow domestic manufacturing. I think this could line up very well.

But that's the small molecule side. I think when we start to talk about these technologies on the biologic side it takes on a whole different complexion. Where if you look at what's happening with respect to cell and gene based therapies, things like gene

therapy, CAR-T, the ability to introduce continuous manufacturing into that setting actually could be enabling to the technology going forward. I think that while it's very nice to have on the small molecule side of our house, it could very well end up being a must have when it comes to some of the technologies on the biologic side. And I think further elucidating that and developing the use case for that and understanding that is going to be very important as we think about how to take these things forward and build a compelling case for why we ought to.

And just on the vaccine manufacturing side, when we were going through some of the challenges we had, say with this years' flu vaccine. You know, a lot of the discussion was around trying to get towards a universal vaccine, which is obviously an important and laudable goal and hopefully we'll get there. But we'll probably get there in a good amount of time. You know, maybe we're a decade away from a universal vaccine, one that can be deployed. What we're much closer to achieving is the ability to develop flu vaccines in vecompetent [ph?] systems through a continuous

manufacturing process in a cellular environment where you could quite literally, you know, change the gene cassette in a continuous manufacturing platform and be able to scale up the production of a different vaccine in the matter of six weeks, as opposed to six months in chicken eggs. I mean the technology to do that is there.

There are some companies already manufacturing vecompetent vaccines in cell based systems. You know, developing a sort of replaceable gene cassette that could go into a continuous manufacturing platform. You're basically -- and to do that you're putting together parts of technologies that already exist. We could get there in a much shorter period of time and that would be I think a fundamental shift in our ability to move flu vaccine production in a direction that's going to assure a greater degree of confidence that we're going to have a properly matched vaccine to the circulating strain. And if not we can adjust mid-season or scale up a monovalent vaccine if we had to in the outbreak of, you know, some pandemic strain. So I think that this is sort of fundamental enabling

technology and it's why we put it forward in the context of the budget.

The other thing I'll just touch on and then I'll close is what we're trying to do with respect to data more generally. And under this bucket there's really two proposals we've put forward. One is for a knowledge management system here at FDA. And the other is to try to invest more heavily in our existing systems like Sentinel and NEST to move them further in the direction of more active surveillance by converting to a common data model and developing more interoperable data that where we can get data that is specifically tailored to answer healthcare questions or clinical questions related to the FDA regulatory process.

And we talk in the budget explicity about having the ability to interrogate EHR data on 10 million lives. But not just interrogate EHR data in 10 million lives, but do it in a way where we have a sort of common data standard that we can use and then we can make that resource available outside parties so others can also be interrogating off of the same data

backbone. And you can ultimately see the ability to do more clinical studies in a clinical care setting if we had such a system.

We right now do have the capability of doing active surveillance and we do have the capability of looking at EHR data. But we haven't consolidated enough data and collected it in a way that makes it highly effective for this purpose. And so part of the bigger vision of trying to invest resources in that is to develop that model and develop a more robust platform and move towards, you know, what has been arguably a little bit more of a passive surveillance system and that in many cases relied on claims data. And move more firmly in a direction of an active surveillance system that relies more heavily on properly collected clinical data. And a properly collected clinical data environment that we can actually do studies in that environment, in addition to interrogating data. Not to say we're not doing that now, we are. As part of our congressional mandate we do have an active surveillance tool within the context of Sentinel. But this would be to try to build on it

and really take it I think to another level.

And that can be obviously an enabling took for FDA to have because you could envision different clinical developing constructs and different regulatory constructs based on this where in settings where there are certain questions that we can't answer in any reasonably sized preapproval study, perhaps we could move some questions into a post-market data collection system, coupled with the right authorities where we could answer things with certainty in a clinical care setting.

On the first point, and I do think of these as sort of coupled, and I talked about this, the testimony I gave before the House budget hearing, the appropriations hearing, what we also want to develop simultaneous to this is a knowledge management system where we have the capacity at FDA to archive and interrogate the basis for our own decisions. Right now if someone was to come to me and say this is a very interesting, you know, use of a reliance on a certain biomarker construct or a certain clinical trial design in the context of this approval, where else have you

done that? I would, in answer that question, I would have to pull together all the reviewers that I thought could possibly have worked on something similar and ask them all. Or, you know, maybe got Bob Temple in the room because he remembers more than most of us, and maybe he can bite off 70 percent of it. And then for the other 30 percent I'd have too query the rest of the Agency. We don't have a good way to both archive the basis for our decision-making and be able to query it. And that becomes very important for establishing and understanding precedent. It becomes very important for policy formulation.

And so I talked about when I gave the testimony of the House hearing that if we had such a system in place it would help facilitate the more rapid development of guidance across different disease areas. And we've committed to a process where we're going to be developing many more disease focused guidance documents, hundreds of them in a new construct that we've created within the Office of New Drugs once it's fully operational. But having a knowledge management system where we can query, collect and query the basis

for our decisions would greatly facilitate that.

So I just wanted to leave the group today with these two sort of big buckets of ideas. I think that we do have the opportunity, you know, with what the Administration has put forward with a big plus up in our budget. And hopefully, you know, we'll be able to work with Congress and some of those resources will flow to the Agency behind what I feel are opportunities to put in place, foundational elements that could pay dividends for many years.

We have these sort of inflection points from time to time. I've been in and out of the Agency now this is my third time here. And I've seen opportunities before come where we've had the ability to make some foundational change in how we do our work that had a distributed impact across the Agency. And I do feel that these two, you know, big buckets trying to move towards continuous manufacturing and trying to move towards a broader data management enterprise building on what we've done with Sentinel and NEST. We've obviously done a lot already, but building on it and trying to take it into a new realm I think that it

could be foundational and transformative for many years to come. So I'll pause there. And I'm very grateful for the time. I hope I didn't talk too long. Thank you.

DR. MCLELLAN: Thanks Commissioner. Hopefully you'll stay for some questions.

DR. GOTTLIEB: Absolutely.

DR. MCLELLAN: Board, the floor is open. Please indicate with your flag. Barbara.

DR. KOWAKCYK: Thank you. So I have two questions for you. One is about data management. I'm a biostatistician and epidemiologist, so this is near and dear to my heart. I think that the data management initiatives that you described are really important and very much needed. I would encourage you to take a holistic view across the Agency and not just focus on drug development, but also focus on food as well.

You're probably not aware, but we had a committee of this Board a couple years ago. We looked at the FERN laboratory network. And one of the things that I think the committee was really struck us and was deeply concerning to us is when we did a site visit to one of

the premiere labs in the FERN network and they described how they got data to FDA. And what they did is they had no way to get data, so they would fax the data to FDA and FDA would reenter the data by hand into the system. And besides the whole data quality and management nightmare that that creates it's certainly not an efficient use of time and resources.

So that's on the CFSAN side of things and I would just strongly recommend that you take a holistic view across the Agency and think about how these data management systems can better operate and how you can better share data in a timely and efficient manner with your partner agencies, such as CDC, the state and local health departments and so forth. So --

DR. GOTTLIEB: No, look, I -- the point is well taken. And one of the questions put to the group was around just trying to address the computing environment. And I think some of this feeds into that. If we were building a system for data management across the Agency we would probably build something that looks a lot better than what we're operating with.

DR. KOWAKCYK: Right.

DR. GOTTLIEB: And the truth of the matter is that a lot of the emphasis and resources have been put in the medical product side over the years in terms of trying to build out some of these capabilities. And, you know, we get into a situation where we have have and have nots across the Agency and that's deeply concerning to me. I just spent the morning talking about that in the hiring context as well. Where some of the new hiring authorities they give us more ability to direct resources to key hires, as well as streamline certain hiring processes, again, have been directed more towards the medical product side of the house. And we're going to look at how we can redirect that now towards every element of the Agency so we don't have these inequities.

But, you know, I would put it back to the group as you have discussions, if there is ways to, now that we've grown up the system that we have, to retrospectively try to fit an architecture on top of that as we build out some of things on the medical product side that addresses, you know, some of the other challenges. That's certainly something we would

want to do.

DR. KOWAKCYK: Okay. If I may, my second question.

DR. GOTTLIEB: Oh, I'm sorry. Yeah, please.

DR. KOWAKCYK: Which feeds in very nicely to that is, you know, I was very interested, you mentioned that there is some equity at the Agency. And so FDA is charged with regulating about 80 percent of the food supply. And I was wondering if you could comment on your priorities on the food safety side of FDA's responsibilities.

DR. GOTTLIEB: Yeah. Well, we've done -- so on food safety in particular, because we've obviously been trying to advance a lot of proposals and some new proposals with respect to nutrition, trying to use diet and labeling, our regulation of certain aspects of labeling as a way to try to reduce the burden of chronic disease. You know, I think on the food safety side a lot of what we're doing is focused around continued implementation of FSMA.

FSMA was a fundamental transformation in how we approach food safety towards a system of preventative

controls. And, you know, we have gone a long way towards implementation. Peggy Hamburg, Rob Califf did a lot of work towards implementation. But there are still elements that haven't been implemented. There's elements where implementation was delayed. There's elements where the implementation is now coming into focus, like intentional adulteration. And some of the issues that were delayed were delayed because they were the hard issues to try to resolve, either from a policy standpoint or from a scientific standpoint. You know, issues with like agricultural, water, which is obviously a primary source of or a common source of problems. We also don't have all the tools and policies that we need at this point to try to implement that. And so we've gone back and we're now relooking at our approach towards that.

There's other challenges. I think we're going to, you know, continue to have to work towards the optimal framework in working with the states. We're going to be very dependent on the states and our state partners for the success of this framework and for implementation of this law. And I think we've done a

lot to try to, you know, partner with NASDA and the other state organizations, the state agricultural commissioners. I think there's more we have to do. There's more I'm committed to doing. So that's a big area of policymaking, focusing a big area of my attention and focus right now is trying to see how to even better leverage those relationships. Because this law won't be successful unless we're working very cooperatively with the states and are able to leverage their expertise and resources on a state by state basis.

So, you know, the answer to the question about what we're doing on food safety is trying to make FSMA work. And I think we've gone a long way towards implementing this law. But I think that there's still unfinished business. And some of the things that are the sort of residual elements that we still need to do are some of the harder questions. That doesn't mean we're not going to solve them, but some things have been pushed off because they're hard. And we're grappling with those now.

DR. MCLELLAN: Thank you, Barb. Minnie.

DR. SARWAL: Yes, thank you so much. I was actually -- I found it quite exciting that actually one of the main missions that you talked today is also about creating a data management and a knowledge management system at the FDA to query past data, past trial data, et cetera. But I think this will rely to a great extent on capturing like user conversations, user behavior all through perhaps social media. Some of those feeds will be coming through that. So do you feel that the FDA would have to do any additional, jump through any additional hoops with Congress or how do you see approaching that, especially with the recent things with Facebook and Cambridge Analytica. I mean is this something going forward? How should we best approach this so that it's really effective for what you need to do without the kind of burden of what we're seeing if it doesn't get happened properly?

DR. GOTTLIEB: Yeah. I have to confess I've never contemplated how we could use data that's available in a consumer environment as a way to try to capture maybe safety information, what people might be saying about products. How they might be discussing it online as a

tool where we might be able to use that as like an early warning system.

I mean, you know, we've talked about things like looking at Google search trends for certain key words as harbingers of, you know, flu outbreak, right, I mean we've seen some sophisticated tools for doing that, or looking at sales of OTC products as a way to get an early indicator of epidemics. I haven't really contemplated how we would use social medial in this context.

To be perfectly blunt, in the context of, you know, just all the concerns about people being, you know, looked at by the government I'm not sure I'd really want to step into this so vigorously. I think there would be a lot of privacy concerns around any government agency trying to track this information or trying to make assessments of it. And so I think we'd want to make sure that we could validate that it's a really important public health tool before we stepped into it. And I suspect that this is going to be well validated by the private sector before the government adopts these kinds of tools. But, yeah, I just have

not at any realm contemplated this or heard it contemplated at the FDA, at least at my level. It's an interesting thought though.

DR. SARWAL: Thank you.

DR. MCLELLAN: Thank you. Lynn.

DR. GOLDMAN: Hi. Yeah, thank you very much, Scott, for being with us here today. And I really have appreciated the way you have continued the focus on science at the Agency. And we noticed in the things that we're looking at. So I just wanted to say that.

In terms of the initiatives, I can't say I really understand enough about this continuous manufacturing to say anything about it. But on the data management side that actually does connect to an earlier discussion that we had today. And I have a couple of comments. And one is that in terms of the EHR commentated standard, if you find a way to do that we in academe would like to be able to help look at those data. We spent a lot of money on hiring consultants to put together EHR platforms so that we can do our research. I'm just going to say that. I mean it's just a lot of effort.

We have a cohort in DC called the DC Aids Cohort, all the people with HIV Aids. And they are seen at 30 different healthcare institutions and they use multiple platforms. And we have to have a, you know, part of our funds for our research has to just pay a consultant who can help us to put the EHR data together. It's a huge obstacle to a lot of efforts.

And, you know, at the end of the day the government is paying for it, by the way, because that's paid for by our NIH grant. And so, you know, so we've done and we're doing it, but I think it's very important that the FDA can do this. Otherwise, you know, your cherry picking from systems where it's easier to get the data and you're not going to get a full picture of the spectrum of what's going on out there.

The other thing that I was really excited about, like Minnie, is the knowledge management system idea. Bob Temple, you mentioned my last name Goldman, and the Goldman family, he will tell you a story about my family and me. He probably doesn't realize it's the same Goldman, but that, you know, we have a family

member who's had an adverse experience with one of the medications you regulate. And one of the things that -- and we actually got the Agency to change the label, so that was pretty amazing. That was back before the days of, you know, official patient participation.

So but rather than tell you that whole story, but what I learned from that is that, you know, life threatening complications are considered idiopathic, you know, by the FDA, are dealt with in vastly different ways for different medications. And I think that KMS can be incredibly important for achieving not only consistency in policies about how the FDA manages those risk, because the risk management we found, you know, is all over the map, but also when the day comes when the effect is no longer idiopathic, but it's actually understood because there are genes involved and there are probably more personalized ways of managing that. You know, precision approaches that can be used rather than a label that impacts everybody. Then if you had a KMS you could implement that. But it's very difficult, you know, to find that kind of information, you know, across, you know, multiple

drugs.

And so I think that that's exciting because I think that it could be not only a boost forward for patient safety, but also, you know, some of the things that are done for patient safety actually, you know, inhibit the freedom and life choices of patients as well, you know. Like multiple sticks, you know, if you're looking for neutropenia.

And then the other thing that I wanted to mention is, again, that issue about the use of broader data, social media data and other data. I mean if you're trying to get more input from patients to find ways to do that without getting down into their personal lives. But most patients aren't members of patient advocacy groups. And there's a lot about patient experience that we can learn through behavioral science.

And one thing that occurred to me after our conversation this morning is that that is another area where you could think about maybe doing an initiative just to bring people together across the Agency who are involved in behavioral science, but also involved in patient engagement, to bring a little bit more of a

lens of social science onto that and a little more depth to the approach. And there are databases that some of them are using that are not necessarily available on all the centers. Just like where we were with genomics a few years ago. There might be an opportunity here to make -- get more bang for your buck with the resources there. So --

DR. GOTTLIEB: It would be interesting to know if there is also outside third parties that are doing this, particularly things in a public health context where we might be able to partner with them to look at those capabilities. You know, because there might be -- if we were to look at that as a tool for trying to inform decision-making or, you know, glean information about how patients were experiencing products, particularly looking for safety issues, you know, it might be something that we can pilot with a third party in a narrow context, particular diseases, particular patient, cohort, to think about. Now, and it might be going on at FDA and I'm just unaware, but I've never seen --

DR. GOLDMAN: I think that's a good idea. You

know, and there are other agencies like PCORI and others that fund research like that. Maybe even NIH you might be able to somehow engage some resources.

DR. GOTTLIEB: I will say, you know, on the first question or your comments about, you know, having the data accessible. I think one of the long term goals would be to try to build a system. We spend the most money on the purchase of the data and then cleaning the data in a way that it can be consolidated and interoperable. That's where we spend the most money on things like Sentinel. And that's an enormous investment. And if we're going to be able to create a repository like that that is, you know, highly valuable in which we're making important regulatory decisions, ultimately we'd want to make that accessible. Not just to academic groups, but also to industry. I mean if we're making decisions based on a dataset I do believe that dataset should be subject to public interrogation.

And so that is absolutely the long term vision. And I think it could become helpful not just to third parties who want to assess important public health questions, but even to the industry that might be able

to use the same data to help facilitate development.

I do worry, getting to something you mentioned, I think you were eluding to this, I do worry that we're entering an environment where the data itself is so ubiquitous and cheap to obtain that everyone who is contemplating on trying to build a decision-making tool says, oh, I'll just do it on my own. Because, you know, the data is easy to get and we have it, so we'll just build it separately. And what we're ending up with is multiple silos or multiple systems and tools for trying to assess clinical data and make decisions on the basis of it. And I think FDA has a unique opportunity to try to bring a long of those stakeholders together and build a better system, if you will, a better mousetrap, you know, with the proper resources and focus.

DR. GOLDMAN: I was eluding that, Scott, and that is a big problem that, you know, that we're all going to have to address. In that it's easy to acquire the data and easy to make numbers from it, but that doesn't mean that they have epidemiology skills or other, you know, other skills.

DR. GOTTLIEB: Right. Thank you.

DR. MCLELLAN: Sean.

DR. KHOZIN: Thank you, Mr. Commissioner. Your talk is very inspiring, you know. I just want to bring some of my personal experience and also some thought. I have a center funded by NIH. I'm the Director and the PI. It's called Center for Excellence for Computational Drug Abuse Research. And with those we have occurring a lot of the data, including all the data we publish in nature and [inaudible] and for specific, including for cardiovascular chemical genomic knowledge base and Alzheimer chemical genomic knowledge base. And the stem cell and the drug abuse research. So those are including chemical and drug and clinical phase I, phase II molecule, small molecule to protein to gene and the pathway, all the [inaudible] will integrate together.

So our experience is that we find even if we buy data from insurance company or we access the data from Alzheimer clinical research center, a lot of the data is not carried well. It's a lot of risk to using those junk data. I think I agree with Barbara and Lynn is if

the partner was academic we can curate it and benchmark data published will make your data more valuable. And that's just something I can [inaudible].

We have consulting with FDA building an allergen projection and database we published. Our prediction is better the experiment data too.

DR. GOTTLIEB: Yeah.

DR. KHOZIN: Yeah. So those are things that we can do. Second, if you allow me to ask a second question. I remember last November or something we came here for the meeting, you mentioned about alternative to animal study. Because animal less than ten percent accuracy transformed to the human data. I don't know anything FDA have created initiative for that? Because all [inaudible] creating a virtual animal for the last seven years.

DR. GOTTLIEB: So on the second question, we laid out our toxicology roadmap probably about six months ago, five months ago.

UNIDENTIFIED SPEAKER: Yeah. Six months ago.

DR. GOTTLIEB: Which I --

UNIDENTIFIED SPEAKER: Predictive toxicology,

yeah.

DR. GOTTLIEB: Yeah. Which predictive toxicology roadmap, which outlined, you know, the various policy initiatives that we're undertaking to try to pursue better tools that could be complimentary to and ultimately supplant some of the animal testing. If we can develop a better predictive model that's a cell based assay rather than doing something in animals, ultimately we'd want to do that. I think in the long run it would be cost savings. Maybe in the short term it might cost more because some of these predictive models are proprietary and expensive. But in the long term it would be probably cost saving and help facilitate lower cost development. Obviously it has the important benefit of not exposing animals unnecessarily to testing and, you know, the issues associated with that, which we are acutely sensitive to here at the Agency. So that is a goal.

I would just comment on the first -- your first points. And your points are well received. I think one of the goals that we would want to do with this initiative that we've put forward in the budget, in the

FY-19 budget, is try to get more data collected in a way where it was being collected for the purpose for which we're using it. Right now a lot of the data that we use is data that's collected for other purposes and we spend a lot of time trying to annotate it and, you know, massage it into a form in which it can be applicable to the purpose for which we're using it. But if we were more proactive and had the resources and capabilities to do it we could actually be proactively collecting data for the purposes in which we're ultimately going to be using it. And that would be part of the long term vision. And these aren't hard things to do. I mean the tools for doing this and the expertise for doing this is fully achievable.

DR. KHOZIN: Thank you.

DR. MCLELLAN: Scott.

DR. STEELE: First, thank you for comments and taking time to join us. I was on the internal knowledge management system, I was just curious if you saw any alignment with Open FDA and other parts of what Office of Health Informatics is doing. I know we've heard from in the past, but I didn't know how you --

what their role would be or what --

DR. GOTTLIEB: Yeah. Okay. So is she here from Open FDA?

UNIDENTIFIED SPEAKER: Yes, Elaine Johanson.

DR. GOTTLIEB: Do you want -- do you have a comment? I don't want to put you on the spot. Sorry. Come to the table. He just thought you had a lot of activity going on in that space if that can contribute to this.

MS. JOHANSON: Yes. Actually, yeah, we have a lot of information that we've been pulling from all over the Agency and making public through Open FDA. And we're also developing some widgets that can be used in external applications to pull data directly from say patient advocacy groups or people like that. So we're doing a lot of work in that area. We want to be able to collect the identify data, not with the, you know, privacy data included because that isn't as critical to us. But we do need to know the patient preferences information. And the other aspect of that is being able to provide a large amount of data to them.

So right now the Open FDA data we do curate some

of it and we do provide some metadata, et cetera. But what we don't do is we provide it externally for other organizations to develop tools to consume it. What we're trying to do now is be able to develop some tools where we can actually present that data from our perspective, but do it by leveraging other applications.

So that's what we're busy working on, so that could certainly tie very well into what the Commissioner is talking about. It fits very neatly into that idea. And we are working on questionnaire processes and things like that with different groups throughout FDA. Is that helpful?

DR. MCLELLAN: Cynthia.

DR. AFSHARI: So one comment. And certainly I benefit from all of the comments of the other Board Members ahead of me and express ethusiasm for what we heard today. You know, one of the things you mentioned is you just came from talking about future workforce and how you develop the workforce and the FDA. And I think that's something the Science Board can help with, in particular as you talk about the knowledge

management system. Because I know for those of us who have a lot of experience a lot of times you say, well, this is deja vu. And if you don't have a Bob Temple or somebody to benefit from that knowledge management system and thinking about how to capture the cases of what was done for future students to study and learn and so that they can iterate faster as you see an increased workload coming as technology advances, has huge value.

And so I think some of the members around the table and on the Science Board certainly are thinking about future ways of educating students beyond the textbooks and thinking about how they may serve to leverage that kind of knowledge system in terms of future education could be a benefit to solve future workforce challenges.

DR. GOTTLIEB: Yeah, just to build on that. I think it's becoming a greater challenge to have a capability like this as the scope of our program continues to grow. I mean we're going to be developing as part of the reform of the Office of New Drugs, many more divisions, therapeutic divisions to have more

finite focused areas of drug review. And, you know, our medical product review programs have gotten a lot bigger. The diversity of what we're seeing has increased. We're processing more applications and so it's no longer as easy to get everyone in a room anymore or to query across the center. So having this kind of a architecture to facilitate, you know, cross-division and cross-function decision-making is going to be even more important.

DR. MCLELLAN: Tony.

DR. BAHINSKI: Sure. I just want to reiterate again, thank you for, you know, highlighting some of the key initiatives you want to work on. I think that the continuous manufacturing one is a very interesting one and one that I think, you know, we're going to be forward in the industry a lot.

I think you highlighted some of the key benefits. And one of the ones that I also thought about was, you know, the distribution, increasing distribution to regional areas. You can have localized manufacturing plans.

DR. GOTTLIEB: Right.

DR. BAHINSKI: Especially in, you know, areas of low economic or even developing nations. And also, you know, potentially reducing costs. You know, for the -- really the knowledge management, you know, like Cindy and others in the industry, you know, we suffer from the same issues, probably even more acutely than the government.

DR. GOTTLIEB: But you have the systems.

DR. BAHINSKI: We have the systems, but we don't always utilize them very well. And I'll be perfectly honest also, you know, we're not very good at interrogating our own data. And I think we're getting better at that and we're developing systems. It's often difficult to do that retrospectively. You know, building the systems going forward is going to be a lot easier than trying to interrogate the historical databases because often they're siloed and not talking to each other.

But I was very encouraged by that. Because I think, you know, as we move into trying to reduce cycle times in development and looking at adaptive, you know, clinical trial designs or things like Bazi analysis,

you know, as you pointed out understanding where those are applicable and where you can get the best benefit out of those is going to be really important I think in the future. So thanks.

DR. GOTTLIEB: And the example that I used when I testified last week, and it's not directly on point to what I'm discussing here, because what I'm discussing here is the ability to sort of interrogate some kind of system that allows us to know when we've made similar decisions where we would otherwise wouldn't know that we've made similar decisions, based on some sort of common principal, but I talked about what we're doing with respect to interrogating drugs for the risk of QT prolongation and the proarrythmic effects. Where we were able to by looking at drugs that didn't have that effect and trying to discern biological characteristics that either led a drug to or not to have that risk. We were able to develop an assay tool in collaboration with the industry that's going to be we think more predictive than the ECG approach that we're using now and fully replace it.

But it doesn't speak to a basic principal of being

able to collect information across a lot of different drug reviews and use it to do our own science more easily. We do that, but when we do it now it's a major project. We can't do it in a very efficient fashion. And so this I think will make it much more efficient. For some of even the smaller questions about maybe the applicability of a certain clinical trial design to try to develop a common guidance on that, it would make it much easier to do that.

Right now we see certain principals getting pioneered within the context of certain therapeutic divisions or certain drug context and it becomes hard to democratize those principals across the Agency because we don't have the ability say, oh, we're basically doing the same thing here, here and here. And so let's come up with a common guidance on how we approach it.

DR. MCLELLAN: I have a page of questions I could end with, but I'm instead going to pass it to Ted for one last question.

DR. REISS: The last question. Oh, boy, too much pressure. So thank you again, Scott, your thoughts are

very welcome and tremendous. So there has been a lot of discussion about sort of the knowledge management, it's been around safety. So I just want to go to the efficacy side just for a second because I think that's a little bit more tricky and perhaps a little more complex. It has to do with what you mentioned the real world data once or twice. Of course that can be a loaded question. But there's going to have to be some, if we're going to go in that direction, they'll have to be some policy choices. So I just wanted to probe you about sort of what your thinking is about that, about how if we can sort of realize this vision knowledge repository integrating data what would the future look like from your point of view from an efficacy side?

DR. GOTTLIEB: I think the optimal from an efficacy side would be to have a capability that's reliable and robust enough that we can do -- answer more clinical questions in a medical practice setting. And use that to also support supplemental indications on the efficacy side. Because the reality is that there are certain questions that it would be more appropriate to answer them in the context of clinical

care. You're going to get a better judgment about what the ultimate effectiveness is of a product when you're evaluating it in a real world setting versus a highly artificial and sort of contrived setting of a clinical trial where you're controlling for all the variables that actually do affect how patients experience products. So that would be the ultimate vision.

And I think this is a win-win. I think that if we had this kind of a capability I it would, you know, sharply enhance our ability to assure the safety of products, but also provide for an opportunity to expand commercial opportunities for products as well in a more efficient development platform. And I'm very happy with that kind of a win-win.

DR. MCLELLAN: Well, Commissioner, thank you for spending time. I was quite serious, we could easily use another hour of your time and have great fun with you. Thank you so much. We thoroughly enjoyed being here for you, with you as we move FDA forward. Appreciate it. Ladies and gentlemen, we're on a break for lunch. I know it seems like we've had a few breaks. We'll be around the corner in Room 1404 and

we'll be back here at 1:15 promptly.

[Lunch break.]

[Resume proceeding.]

DR. MCLELLAN: We're going to go ahead and call our Board meeting back into session in our afternoon discussion. And we've got four issues of discussion teed up, electronic health records, drug repurposing, FDA single secure computing environments and real world data. And as you might guess they're sort of there is an intuitive connection between electronic health records and real world data, so we may hybridize some of that discussion.

I am not sure how far we'll get today. We'll just sort of start in on it as go as far as the questions will go. We are looking for areas that might be of interest in terms of follow on work, areas that might need support via subcommittee is also welcome. But honestly we will ask our subject matter experts to give us a lot of that guidance as to where they may be scratching their head.

So let me at this point invite our subject matter experts to come to the table. We have quite a few open

seats here. So if Sean Khozin is on the phone, right?

UNIDENTIFIED SPEAKER: No. Vahan is on the phone.

DR. MCLELLAN: Oh, Vahan is, okay. So Vahan Simonyan is here. Okay. Gideon Blumenthal. Bakul Patel and Wi Dong Ton [ph?]

UNIDENTIFIED SPEAKER: Wi, are you on the --

MR. DONG TON: Yes.

UNIDENTIFIED SPEAKER: Okay.

DR. MCLELLAN: Good.

MR. DONG TON: Yes, on the call.

DR. MCLELLAN: Okay, great. Chardae Araojo here? Okay, great. And Elaine Johanson. Okay. And if you could come -- great. So the way I requested that this happen is that our subject matter experts would sort of kick off the conversation and tee it up. And then, of course, we're usually not shy of asking questions and chiming in. So --

UNIDENTIFIED SPEAKER: Or you can read the question and then have them [inaudible].

DR. MCLELLAN: Okay. Happy to do that too. So let me go ahead and I'll phrase the question and then we'll move from there. So the first one, lack of

interoperable EHRs are weak incentives for data sharing and concerns about patient privacy and cyber security are important barriers to the ability of providers and researchers to leverage predictive analytics to improve patient safety and enhance productivity across the medical research ecosystem. The questioned poised is how can the Agency work with other stakeholders to create a regulatory use case for high quality datasets that can provide market incentives to address and overcome these barriers? So --

DR. KHOZIN: I can get started. I'm Sean Khozin, I'm an thoracic oncologist by training and also a bioinformatician. So I think there's a lot of information packed into that one question. And depending on how much time we have hopefully we can dissect out the major themes.

Lack of interoperability in the electronic health records systems is widely recognized. And it doesn't necessarily relate to the idea that there are challenges with data sharing, such as patient privacy and, you know, figuring out how to share data.

DR. MCLELLAN: Let me ask, Ted, I think you're

maybe on the phone. Could you mute your phone?

DR. REISS: Sure. I sure will. I'm on the phone and I will go on mute.

DR. MCLELLAN: Thank you.

DR. KHOZIN: There we go. Okay. So basically --

DR. REISS: Good job, Mark.

DR. KHOZIN: -- thinking about it that way is that, you know, interoperability is a very important concept. But if we go through the hypothetical exercise, let's say there is interoperability among all the electronic health record systems starting today, still the FDA will not have access to a lot of the critical data elements that it needs in order to incorporate electronic health record data to regulatory decision-making.

And I'll give you a few examples. Currently the way electronic health record systems are designed is really based around billing needs. You know, these are essentially medical billing machines that create ICD codes, CPT codes, so the majority of structured data elements in EHRs are diagnostic codes and codes that are required to support billing activities at the point

of care. And what has been left out, unfortunately, now at the FDA now that we're extracting electronic health record data we recognize this first hand, that what has been left out are clinically important variables that are actually telling you something about the patient. Very basic information that is not available in a structured fashion in electronic health records systems.

For example, if we look at in the world of oncology almost all of our product approvals are based on tumor based end points. For example, overall response rate or progression free survival, and also survival, overall survival is an important end point we've used in approving oncology drugs. However, that information is very hard to get from electronic health records. We need to know, for example, is the tumor size at each visit growing or shrinking. Something very simple as that is not part of the structured data elements that are currently in electronic health record systems.

Tumor size, for example, is still part of a radiology report that's scanned in most cases as a PDF

file into the electronic health record. So for us it's very important to understand what that tumor size is. And diagnostic codes don't necessarily give us any information about the patient, per se, because again, these diagnostic codes are part of these billing transactions that occur between the provider and the health plan. And a lot of times, you know, the provider sends let's say 50 billing codes for an episode of care. Half of them are denied and then the others are reimbursed. However, those codes remain in the electronic health record footprint. So interoperability is critical and important, but it's not going to solve all the issues.

So what do we need? I think we need to create incentives, and I think that's where the FDA can be very effective, to enable structuring clinically relevant information at the point of care. And what the FDA looks at when it makes its risk benefit determinations, it's around a concept called clinical benefit. And we need to understand if a drug enters a market that it has demonstrated clinical benefit. And we do that in variety of different ways, typically

through the approval process with well controlled studies.

And that idea of clinical benefit is something that is now also becoming very important to health plans. It's the idea of creating paying for value. And also it's always been very important to clinicians at the point of care. Because clinicians when they treat their patient, when they actually go back to read the information that's been entered into the EHR they're not reading what has been sent to the health plan, for example, they're not reading billing codes. They're reading the last note that they wrote on the patient, that one paragraph. And that's actually, that one paragraph tells you everything you know about the patient in that clinical context. And that's actually the information that we need and we've applied, for example, national language processing and other ways of structuring that information.

So the clinician also at the point of care is thinking about clinical benefit. And I think that concept can be a point of convergence to create the incentives that are required to develop better

electronic health record systems to streamline clinical workflows at the point of care. And to also provide data that's relevant to the FDA, but also to payers as we move towards a more value driven healthcare system.

DR. MCLELLAN: Okay. Vahan.

DR. SIMONYAN: Okay. Maybe this is Vahan Simonyan. I am a data scientist and bioinformatician from CBER, FDA. So I can provide more maybe perspective from a technological viewpoint. First of all let me say that there is no lack of interoperability frameworks for EHRs. For example, FHIR can integrate more than 90 percent of all of EHRs. But so it's not about technology, it's about incentives to this. But I think one of the biggest barriers is not the security, it's not the interoperability, it's lack of incentives to do anything about it.

And perhaps one of the reasons, and this may be arguable for some people, is the patient's disconnectedness from data. Data ownership does not belong to the patient. And living in a world, a regulated world of HIPPA and the common rule, and when

the only person who can give a permission for freely integrate all these data sources and do analysis of all types of data is the patient, but patient doesn't own the data.

If you compare with financial examples, like imagine if you say data has a value and this compared with financial markets money had a value. So our data universe is like a [inaudible] key, not a capitalistic free market they exist in, because the ownership is detached form the patient. Imagine what kind of financial market it would have if it wouldn't have people owning their money? I think that's where we are, patients are detached, they cannot be incentivized because they do not own the data.

Believe it or not we can come up with incentives for every single stakeholders, for payers, for FDA, for clinician network, for clinical trial enterprises, for EMRs once the patient's own the data and once the data can be reused multiple times. By the way, this is the statistics, 85 percent of all clinical trial data has never been used twice. That's siloed in some kind of hard drive in some kind of companies in the warehouses.

96 percent of EMR data has never been researched after the primary use. It's just a siloed place somewhere in somebody's hard drive. One of the major reasons is not the technology, it's the inability for the patient to participate in the decision-making process.

Where are they to go? We cannot link the data. And why only EHR? There are different types of data. We live in a world of precision medicine where novel drugs are coming with specifics to patient, to disease, to time point and we are talking only about EHR. How about I link the [inaudible] here, or wellness data? Isn't it cheaper to take care of a person while he's healthy instead of making him healthy after he's sick? Perhaps some of the data we should be looking is also wellness data. And we cannot link this data. One of the reasons is, again, detachment of the patient from its own data.

So the technology is not the problem. The lack of incentives is. And I think blockchain based technologies which allow you to build processes, not just transfer data from point A to point B. Data doesn't have a value if there's no vehicles extracting

the knowledge out of the data. And today [inaudible] of technology it's like block and chain and the smart contracts, et cetera, we can actually build processes. Let's forget about data. EHR is just a data point. It's just bits and bytes. Unless you build processes which are extracting that information, that knowledge and connecting back to the healthcare, back to patient's situation we are not going to succeed.

So my recommendation would be for FDA to look at the whole picture, not just EHR, not omics, not just clinical trial. To build this virtual continuous trials sample, pilots, a few of them. I'm trying to answer how can the Agency work with stakeholders to build something useful. To completely revisit the way we are doing this stage process of healthcare development from pre-clinical, clinical, post-market, et cetera.

So perhaps we should be looking saying, well, 50 years has passed since we designed the first ones. Let's just look at it from a completely new perspective. Let's say we have all of these wonderful technologies, all of the interoperability platforms,

all the high performance computing platforms, let's completely design the novel approach for one study as a pilot model if you can look at the whole same person. That would be my recommendation. Thank you.

UNIDENTIFIED SPEAKER: Mark, may I ask a question? Please just clarify, when you started you said that I think something like 90 percent of the EHRs can be transformed by or connected by something. I didn't hear what that something was.

DR. SIMONYAN: No. No, no, FHIR platform, it's coming from -- there's a whole consortium and FHIR and FHIR genomics. These is the interoperability platform for linking electronic medical record data. And now there's a FHIR genomics platform also, which is doing the same thing for genomic space, which will be allowing us to move to the precision that it's in really.

DR. MCLELLAN: Minnie.

DR. SARWAL: Yes. Thank you so much. I think I completely agree with you. And thank you for bringing this up. This is incredibly topical. To be from the Science Board I'd just like to -- I'd really like to

encourage how we can actually develop these partnerships more, especially with the strength of the FDA.

So I think one of the questions is how can the Agency work with other stakeholders? I would put it to you that there is a great stakeholder that the FDA could currently go work with. And I don't have any stock or any bias here, but I'm just mentioning this like the Human Longevity consortia, which Craig Venter is doing all sorts of sequencing and micro bio and EHR data and then giving some kind of an eventual report back to, well, currently only the really wealthy person who can afford to do that at a really premium cost. But that is also generating an inordinate amount of data.

Is that something that the FDA potentially, that kind of mechanism, can the FDA actually work with that kind of stakeholder to set the system in place? I guess that's the first question. And the second question is how do we deal with the whole, you know, economic incentives that are coming out of this kind of -- I mean you're absolute question is how do we deal

with the whole, you know, economic incentives that are coming out of this kind of -- I mean you're absolutely right, the patient is not owning their data, even though this is all coming from them. So how do we work with the economic structure of this? Like who are the beneficiaries first of information? Of course, it's the patient. But who is the beneficiary of the dollars and how do you play that?

DR. SIMONYAN: Well, I mean can just have --

DR. MCLELLAN: Before we go further, just caution us all to stay away from specific product descriptions and --

DR. SARWAL: Yes, sorry.

DR. MCLELLAN: Okay.

DR. SARWAL: That's purely an example, only an example.

DR. SIMONYAN: Yes. Well, I can bring you, I mean, example of my discussions with maybe payers who are saying that two-third of all of the payments, I'm answering the second question first, so two-thirds of all of the payments insurance companies are making are usually the terminal stages of human life, cancers and

chronic diseases. Which are most of the time are still terminated by death. So and out of that, but let's say take cancer, two-thirds of all of the costs mostly goes to cancer like disease. And out of that about 50 to 70 percent of treatments are off target. Which means companies are paying, patients are taking the medication. They're very expensive. But 50 to 70 percent of the time that does not help the patients. Why companies cannot do better management of who takes what drugs, their alternatives and things, because there is a lack of data access to profiles.

I mean we know that some of the oncology there we know who are no responders and responders are. Some of the new human oncology drugs have very clear targets. But the lack of access to human genome data does not allow the companies to make a better judgment of what drugs should be taken or is the person within the responder group or not, or what diagnostic should be used to determine that. Now, imagine now if the payers can get access to that type of data. Imagine 50 percent of the two-thirds of the cost can be saved out of it. Do you think that's enough incentive for the

company to promote that type of a data use patent? I think it is. And it's just one type of a use case.

At the clinical trial, I mean, I'm afraid if you start discussing this this will be hours of very interesting and dynamic discussions. So perhaps on can stop on this and maybe later we can have this wonderful discussion. Different stakeholders' perspectives from patient advocacy groups, from payers, from clinical trial enterprise, from clinician networks and from patient's perspective itself.

Maybe, I mean, and the longevity, about longevity project and there are longevity project and other similar projects actually who are producing immense amount of beautiful data. At some point we actually tried to work with longevity process, but it was just an initiation stage and we did not succeed in the clarity of understanding who does our analytics and who actually gets what data, who drives the analysis.

Also security of the data came to be an issue. Because we want to run our own analysis from the data which is hosted somewhere else, that was one of the bottlenecks, I think. And because, again, patients do

not own the data, they couldn't clearly communicate with us that we have access to the data. We only had access to a particular type of questions to the analysis. And that pretty much stopped the collaboration.

DR. MCLELLAN: Sean.

MR. DONG-TON: So, hi. This Wi Dong Ton in CTR. Just make a quick comment. Actually, I'd like to come back to Sean's, you know, comment about ERHs has really developed to put a very different purpose. And so what questions FDA tried to ask is not necessarily innate in the EHR problems. And we have a couple experience and by working with the VA in the EHR systems and to manage addressed issues related to the drug and use delivery. Particularly try to find out why do women more successful to [inaudible] compared to male. So even that simple questions and [inaudible] in formatting the data and to bring the [inaudible] to the high quality data to address these questions.

So I would like to take a step back and instead of to convert EHR in such a model of all database, you can ask all kinds of different questions, whatever the

question you wanted to ask, rather and to turn the attention on what specific questions are relevant to the FDA. And then we're going to ask EHR to reconfigure in such a way these sort of information available for the FDA for use.

DR. MCLELLAN: Thank you. Sean.

DR. XIE: Mohamed, is that right?

DR. SIMONYAN: No, Vahan Simonyan.

DR. XIE: That's a very interesting plan and also I like this you try to build an enterprise structure from pre-clinical and post-marketing, the virtual trial. My question is I engage in research since 1995. So a lot of people [inaudible]. So are you going to take an off shelf software to safe site to using the software like FDA combined software, or are you going to build your own? You said you do de novo design. Or you hire somebody like Patel? He already have some experience, I know him in the past.

So it's kind of the reason I mention this is because Popcaan is a database, Steven Bryant built at NIH. It's too big, a lot of people started complaining about difficult to use. This is one question. The

reason I mention this is because a lot of lab, including my lab we build a machine in [inaudible] and GP [inaudible] computing online, resource already tested by a lot of people. We can work with you in collaboration to support some of the technology we developed.

DR. SIMONYAN: Well, thank you for --

DR. XIE: And that goes to the last question. The question I tried to ask because you mention a lot of technique. And could you elaborate how you're going to use a blockchain on this concept?

DR. SIMONYAN: Yes. So first of all thank you for mentioning Popcaan. I was one of the four people who started it. I'm not part of it, so it's too big. So, okay, so, well, I mean there is no one recipe who should be doing the development. We at the FDA are accumulating immense amount of expertise, so we can do some part of it. But obviously intelligence is spread across the nation. So it's not like we have one recipe where it should be conducted. I think it should be accumulative collaboration for our experts and outside experts. Just we should leverage the best expertise

wherever.

So I mean the first question where should it be done? I think everywhere. I think we should be collaborating with everybody. Well, funding is always going to be an issue, contingent issue. And whatever ways that are available if you can leverage and we can have support from leadership to support different types of finding for funding for internal and external collaborations I think that would be wonderful.

So as for software development and type of software, we at FDA, I don't know how familiar you are, we have one of the top four platforms for big data analytics. We started from genomics, but now we are doing all type of analytics, high performance computing. We can crunch petabytes of data using thousands of thousands of computers in a very compliant and prominent manner. That's what we call HIVE and we are supporting that platform. Thankfully our leaders are very understanding the need of the Agency in such a platform and we are succeeding. But there are many other types of developments in FDA, we kind of connect all of them together.

So software development I don't think there is ready software off of the shelf for types of analytics sometimes what we need. You can take apart good software which works very well with small datasets, produces valid outcomes. You take the same good software in a much bigger dataset the outcome does not necessarily need to be valid. So it's a continuous development needed. So and we are trying to keep up with the technology with as much resources as we have. But there is always a need to develop new as much resources as we have. But there is always a need to develop new type of software. And AI is one side, big data and analytic approaches in multi-dimensional occur within our universe is a different type. And I can name you areas of science which are still in need of development with relation to the software.

And the third question about blockchain, well, blockchain is a transactional history keeping distributed database. So what it is best at is keeping history of what happens. It's not the big data platform. Neither it is a good fast database. It's a wonderful way to keep the provenance information. And

if you are running processes from data to knowledge I think the blockchain is perfect to maintain the entire chain of events which have driven your final outcome from the original data. So the block, you cannot run the computations on the blockchain. Let's be clear about it. Blockchain is not designed for it. So but linking the blockchain as a provenance framework with the high performance computing technologies in a site chain I think that has a significant amount of future.

And believe it or not every time I go to a conference I get about 20, 30 pharma representatives, technology representatives coming to us and saying we are doing this wonderful type of analysis and studies. What does FDA think about it? Can FDA be involved with us? And we have our own development with blockchain and data exchange sharing. So but I think it is very ripe and we have to pay significant attention to the blockchain and all of the developments as a provenance framework.

Maybe I can give you a perspective. Do you remember when internet appeared how wonderful it was and how it changed the world? I think the next

internet is called blockchain. We have to pay very clear attention to what is happening.

DR. KHOZIN: I just had a quick -- so Vahan and I have a blockchain effort where we basically have developed a decentralized framework for exchanging of data at scale. And the first data that we exchanged happened to be your son's genomic germ line mutation data. And essentially anyone can participate in this framework. The idea is to create a, again, decentralized, that's sort of the key phrase, framework that can accommodate data exchange at scale. Including, you know, if the data belongs to the patient, which ultimately I think that's where we should be and we are as industry moves in that direction, patients, individuals should have a mechanism for sharing that information with appropriate entities. Clinicians, research institutions, also the FDA. If we decide to interrogate patient generated data, including data coming from centers, for example, for making regulatory decisions.

So I think having that decentralized framework, again, this is not necessarily about computation, it's

about data exchange and data access, focusing on the individual patient and the rightful owner of the data, whoever it is. In some cases it's an institution and in other cases it's maybe a small sort of a clinical study that has bulk data available to them and they can provide that data and allow it to be reused on blockchain.

And also just a very general comment, I think, you know, in terms of, you know, the stakeholders, you know, who are the stakeholders? I think it's very important for us to identify actually who those stakeholders are. For example, in the area of electronic health records it's a multi-stakeholder kind of milieu. We have HL7 FHIR whose developed very interesting standards that can essentially be used to create certain profiles to meet certain use cases on an operating system that's harmonized. An analogy would be, for example, the App Store for Android or IOS that has a modular approach to developing applications. There are different entities developing these applications, however, it's based on common standards. And FHIR and HL7 and these HR standard can accommodate

that. However, the bottleneck has been that some of the decisions that have been made to encourage adoption of electronic health record systems haven't taken that into consideration.

However, we have a great window of opportunity to move forward and to do new things, as long as the right stakeholders are at the table. I think the Office of the National Coordinator is one of those stakeholders that essentially determines and distributes through rulemaking their regulatory authority how these electric health record systems should be designed and how they should be able to communicate. And I think by identifying who the right stakeholders are so we can bring them to the table is as important as thinking about what are the use cases that we need to test on these systems.

DR. SIMONYAN: That's good. Thank you.

DR. MCLELLAN: Let me just interject here. I, you know, there are two things I hope we can really go into quite in depth. One is this concept of incentive. And I'd really like you to explore that further as we get in. The other as we just talked through a bit here on

the blockchain. And I presume ultimately you were saying that's where a patient could own data from birth to death and everything. You know, and that although it may not be a computational rich environment, you may have to move that, still you would have your ownership of data there. Am I following your concept?

DR. SIMONYAN: Yes, you are absolutely following right. And isn't it surprising we in this country created blockchain, we created high performance computing, but Estonia is the first one who is doing all of their healthcare in a blockchain. And we are not benefiting from this technology as much as they are. Now there are multiple different nations considering doing the same. Actually, I was just back in Armenia in my country, they are considering switching to the blockchain entirely, their e-health for [inaudible] patients, longitudinal. It's all of the provenance, all of the trace maintained in a blockchain. You go to a diagnostics company it's attached to your identity. You record your wellness data from your mobile phone, it's attached to your identity. You go to doctor it's attached to identity.

You buy a drug it's attached to your identity. And I think this will solve multiple questions. This technology allows you to keep histories immutable. That means nobody can treat you later. That's the very important value here. DR. MCLELLAN: Cynthy.

DR. AFSHARI: Yes. I think you addressed the question, one of the questions I was going to ask, which was you were describing what your pilot was and the blockchain. Is that the work that we got a preread around your two-year agreement with IBM?

DR. KHOZIN: Yeah, exactly. So that's -- and then we're testing the utility of the framework. You know, there are scenarios including exchanging genomic information. And again, this is about facilitating data exchange at scale in a way that's decentralized. Because the focus has always been on creating data repositories and aggregating data into siloes with its own provenance and authority.

Whereas, blockchain is really a grid, we can think of it that way where the transactions are validated. There is always an audit trail, there's transparency. However, no one actually owns the data and the rightful

owner of the data decides what to share, when to share it and how to share it. So as a framework I think there are -- conceptually it's something that has a lot of potential.

And also there are more immediate opportunities available to us to use the existing frameworks on resources to enable data sharing. And when it comes to the FDA, you know, authority is different than NIH, for example, NIH being a research organization. For us big data is important, however, it has to be pragmatic and practical. And, you know, combining genomic data, proteomic data, data from the microbiome, there are a lot of interesting resource questions that you can answer. However, when it comes to the FDA it's really about understanding the patient experience. How does the microbiome and the proteome and the genome influence patient's response to therapies? That's a completely different question than resources questions that typically occur in the academic setting, NIH funded studies. And under the NIH is a mandate, public health mandate which is more research based. We're much more translational and we really have to start to

think about how we can use the existing resources, incubate ideas that can take us where we're not today, where we can be tomorrow, for example, blockchain, but also how to maximize the use of the existing resources.

And there's a lot more than can be done. As an example, you know, EKG data right now it's still the way it's interpreted is the same old way, how I learned it in medical school, human visual inspection. So here's a digital asset that we have, for some reason we convert it into an analog format for human visual inspection. And that's something that can change using very basic neuro network AI driven modalities to classify arrhythmias with a much higher accuracy than what humans can do. So we've incubated some projects and that arena.

We're also looking at imaging, CT scans. For example, in oncology we have a classification scheme called Resist, which is a very coarse way of measuring tumor response. And the reason it's coarse is because we call anything that grows more than 20 percent disease progression and any lesion that shrinks more than 30 percent response. That 20/30 percent margin of

error is because the human eye, the human visual kind of inspection inaccuracies.

So what we did actually as part of an attempt in oncology to create a data knowledge management solution to start aggregating data and looking at what is actually occurring currently today in clinical trials, we aggregated 12 clinical trials in lung cancer. Looked at the assessment of lesions per the investigator and also the FDA has made a requirement that an independent review committee should take another look, an independent look at the images to come up with an assessment of response. So we get data from the investigator and also the independent review committee. And the discordance between the two is 30 percent. And that's based on classification according to the resist criteria, which already has a 50 percent margin of error built into it. If we look at tumor size the discordance is much higher.

So that's, for example, one of those areas is a low hanging for AI. So we're looking at AI methods and algorithms to assess not only classify the lesions into Resist, which would be a low hanging fruit, but to come

up with a bulk assessment of if you look at the head or whole body CT scan of a patient, Resist you can only pick five lesions. But if you look at a whole body CT scan what is that tumor index, that holistic tumor index? That's what we're interested in. Is the tumor growing or shrinking? And that's a completely different approach. So these are the translational opportunities that would be very relevant to the FDA.

And so the challenges, for example, it really goes back to the ability to aggregate the data to create this knowledge management solution. I know that's another question that's coming up, but they're all interrelated, that can allow the FDA to do these exercise and regulatory science research activities that can inform not only policy decisions, but also provide new ways of streamlining development programs and also developing drug development tools that can be very useful, not just to the FDA, but the entire ecosystem.

DR. MCLELLAN: I've got Scott, Laura and then over to Sean.

DR. AFSHARI: Yeah, I just --

DR. MCLELLAN: Do you need a follow up?

DR. AFSHARI: Well, my -- it was a yes/no question. But I guess what I haven't heard, and maybe this will come out in the other questions, is just, you know, you can have data and you're talking about how you would use it, but ultimately you also have to assure kind of the quality and integrity of the data, otherwise it's, you know, the rest of it downstream isn't worthwhile. And I guess I was interested if that's part of your framework as you're thinking about this, are you focusing on those aspects?

DR. KHOZIN: Well, I can quickly just talk about, and others please chime in. So in terms of data integrity we're -- when it comes to electronic health record data and also data from digital health devices, and if these datasets are used as part of formal submissions for right decision-making. We already have a framework to validate data. And it's very interesting when you think about the existing framework. So that requires us to step back and think about how do we validate data coming from traditional clinical trials? There are no mathematical techniques

or any statistical techniques and there are no sophisticated tools or technologies when it comes to validating data from, you know, well conducted randomized clinical study.

It is a logical framework, as we call it, and we deploy, for example, the Office of Scientific Investigations who do site inspections and what they do, the do source document verification. We have good clinical practice guidelines and sponsors have to attest to having conducted the study based on the requirements of explicitly stated in good clinical practice guidelines, so there's that attestation to conducting the studies in a formal fashion.

However, we do find discrepancies all the time. We do find protocol deviations. And that assessment, again, is made in a logical fashion that at one point protocol deviations that occur in every clinical study reach a point that it compromises data integrity. And I think we can apply the same framework to assessing data coming from electronic health records or digital health devices. In fact, those tools may allow us a much more pragmatic and accurate way of assessing data

integrity because these are electronic data systems that can leave audit trails. And we can do a much better job when it comes to verifying the source document.

And do when we look at the processes that are built in into the Office of Science Investigations the red flags are always fraud. And because even in the best conducted randomized clinical study there are discrepancies you notice with the source document. There are protocol deviations, even clinical trials just the like the point of routine care. It's a messy world. Obviously we put experimental control conditions to control that, but these are all procedural solutions. And we can kind of translate those procedural solutions and apply them to novel high points of data, such as electronic health record data.

DR. SIMONYAN: Maybe I can add the perspective to this. Recently I was in a conference and somebody mentioned there are more than 60 types of fraud and falsification in clinical trials. Somebody has [inaudible] apparently. So and there are some which are intentional, some unintentional. But imagine if

you can record every single event again in the chain which is immutable and cannot be altered and modified. Again, even during the clinical trial when a sample is sent to diagnostics company to take the measurement diagnostics company without knowledge of what is the trial records it on patient's behalf. And even if the value is altered later and we have seen in a few cases it will always be caught very quickly because there's an immutable trail of every medical event on behalf of the patient.

So they're actually from cherry picking for falsification to alteration of different types of data and all of the sub-cohorting. There are many different attempts today by pharma companies themselves and CROs and technology companies to build new frameworks using the blockchain to address some of these issues. In fact, I am going to be inviting a few of them in the row to give us their perspective how blockchain can be leveraged to provide the complete provenance of the clinical trial process.

The same can be said for the drug supply chain that can be addressed using an [inaudible] technology.

Every single transaction of every single drug can be recorded in the blockchain, like immutable databased. And every single change of hands can be recorded forever. So that's another kind of a technology which -- another kind of application which we can use for the blockchain. So this point I know some major areas of the blockchain used in healthcare which we should I think pay very close attention, supply chains, trial provenance and compliance and data exchanges. I think all three are worth very big considerations for the Chair. They are going to be [inaudible] the entire ecosystem. And companies are onboard with this.

Another aspect I want to mention is because the data is so large is it's getting better and we have learned to accumulate data so fast we didn't yet learn to interpret it quickly. Our human intelligence has limits. So unless we start relying on artificial intelligence soon we'll be incapable of making the real good decisions. So what these new technologies allow you to do it put compliance framework on softwares, software made decisions. Once we let artificial intelligence browse the data eventually we will come to

that because our own intelligence has certain limits. The blockchain based provenance technologies are a very good way of controlling the access partners and permissions partners for the softwares themselves. Blockchain allows you to build processes. And if some of these processes of decision-making are AI processes, that's a very good synergy between two technologies.

I think by understanding we learn to observe faster than you learn to understand. That creates this condition we have to eventually switch to artificial intelligence for a majority of our human decisions. And that's where the blockchain like technologies can also help us to maintain the compliance of AI softwares.

UNIDENTIFIED SPEAKER: Yes, thank you. As you were describing the integration of the genomic proteomic and digital health data and collecting and sharing some of that, I was just curious how you're partnering with the All of Us initiative. It just seems that the [inaudible], you probably already are, but might be an interesting platform to, on a long term way, look at some of these issues. Is that something

you're -- because I know they're collecting many of those data sources and presumably --

DR. KHOZIN: So we've talked to all of us. And some of the digital health efforts has been coordinated through the Scripps Institute and Dr. Topol and so forth. So we've -- and we have a couple interagency initiatives. So in oncology we have a data science program called Information Exchange and Data Transformation. And part of what we do is we aggregate a lot of internal data and we do meta-analysis and we publish a lot of these meta-analysis. In fact the upcoming asco [ph?] we have I believe six or seven abstracts that speak to some of the meta-analysis that we've done.

But also we have -- we're doing foundational work around how to best organize censored data and what are the new end points that we need. And that is a collaboration we have with NCI where we're actually conducting an observational clinical study in patients with advance malignancies where we are incorporating sensor solutions into their process of care. And we're trying to come up with an objective digital biomarker,

if you will, to assess the patient's functional status. Currently, as many of you know, we use the ECOG performance status, which is very subjective. And if you look at how to provide as clinicians assess ECOG performance status or discrepancies.

And digital devices, and Bakul is here, he can chime in, can basically provide us more objective means of assessing that. So the FDA does two things. You know, obviously we regulate, and I'm sure Bakul is going to talk about this, digital health devices. But we also can use these devices in a proactive fashion to develop new biomarkers and digital biomarks. And in fact, that's in the 21st Century Cures Act that the FDA is required to design and develop drug development tools. And part of that are algorithms that can be derived from digital health devices. And all of us program, you know, is very much based on those ethos.

We haven't been able to formalize a specific relationship with them, but we have been engaging with them. And as I mentioned we do have joint programs with NIH and NCI where we're designing and qualifying new biomarkers, digital biomarkers in this case.

UNIDENTIFIED SPEAKER: Yeah, just you're giving the scale of that cohort it could really be --

DR. KHOZIN: Right.

UNIDENTIFIED SPEAKER: -- hopefully useful to address some of the questions in that.

DR. KHOZIN: Right.

DR. MCLELLAN: Laura.

DR. TOSI: Thank you. I'm an orthopedic surgeon, so I have been very influenced by the whole issue of bisphosphonates. And I'm not sure that will mean anything to you. But many years after we started giving bisphosphonates we've discovered a quite significance incidence of A-typical femur fractures. And everything you've said has sounded wonderful from the clinical trial standpoint.

But to a large extent most of the problems I've ever seen haven't been because you haven't been running the trial right, but have been that problems occurred down the road and the BIPS don't come up, aren't reported enough.

And I don't see your system discovering a typical femur factures unless we all give up every sense of

personal privacy that we ever had. And I don't see how you make this work. Are we going to 1984 here?

DR. SIMONYAN: Well, maybe here Bakul can actually give an answer to the [inaudible]. But I mean but we do receive post-market data to a certain degree and we do monitor and but it's more of the CDRH domain in this particular case most probably. If you have input.

DR. PATEL: Yeah. Hi. Sorry, I'm a bit late and I'm trying to catch a plane also right after this. But I can answer to this, I think what we're trying to set up going forward with the precertification program and the focus on real world experience of use of devices so to speak. And even actually perhaps even other medical products that we regulate with the whole aspect of in this connected world we can get data that can actually get to the A-typical scenarios. But in order to A-typical something we have to collect things that actually differentiate between normal and A-typical. So that's the infrastructure we are trying to set up.

I'll be the first one to admit that what we have today in terms of what we get from either from the manufacturers or from practitioners or even from MDR

reporting may not necessarily be that level of details that we seek to sort of have at this time. So how can FDA move to a system that we can actually collect that data? And you mentioned privacy. But I think it's beyond sort of not even get to the level of privacy, but it's about the performance of the product itself and how can you sort of anonymize it so that you can actually learn about the medical product as opposed to learn about the patient or the use of that patent or that product.

So we are not there yet. I think there is a big need in this day and age of information that we need to sort of get there and I think that's where we are heading towards. And then some of the stuff that Sean's working on in terms of digital biomarkers is actually information that we would have had, but collected very manually in the past. How do you automate that we actually can take it to the next level of granularity that we really all seek? I don't know what that looks like.

And just understanding sort of what that means in terms of, you know, having something continuously

collected or long periods of time has a completely different sort of set of information that can be gleaned from, as opposed to a periodic set of information that's manually collected. So that's the transition we are in today.

DR. TOSI: It's just tough to imagine everybody in America who's on a drug sort of reporting into you guys all the time. And where is the middle, the middle ground that's productive?

DR. KHOZIN: Well, I think, you know, also the existing systems we have in place are working. Let's also recognize that. For example, when it came to the osteonecrosis of the jaw with the diphosphonates we started to see those signals in the data that we're getting through FAERS, the post-market [inaudible] system that we have. However, by moving into a world where we can proactively interrogate data coming from sensors and [inaudible] health records systems we can be much more agile in picking up these signals. Because even the largest study will not in some cases show us these rare safety signals and also efficacy signals. I mean maybe populations who can benefit

either more or less from a certain therapy. And that's important to know.

So I think we are moving in that direction. And the percent program that Bakul mentioned that to me when I look at it as a non-CDRH person it does accomplish two things. It encourages, it provides a framework, a path for these devices to enter the market, which is very important. We need a path for these new tools and technologies in a way that they're deemed safe and effective to enter the point of care, the market. And once they enter then the FDA can actually benefit from the data that these tools and systems generate. So it kind of accomplishes two different tasks. And obviously that's consistent with the demand that we have, which is assurance of safety and effectiveness of medical products.

DR. SIMONYAN: Maybe I can add a technology perspective to this. The platform we are building allows you to share not only data, but also derived information of data. For example, let's say I have genomic data and somebody asks me to count the genomic data access. I might say no, but I can give you access

to particular biomarker that can be computed on per request on the genomic data.

So when you mention like unless everybody gives up 98 percent of all of the data all of the time you don't need to do that. Because imagine an ecosystem which can run intelligent processes. And that's what smart contracts are. You can have a software which is compliant running on the data without sharing the information, receiving the signals and then sharing the signal, not the data. So we are designing that into our technology. And to be honest I never thought of your use case, but I think that's wonderful much.

You know, we had other use cases in mine, so this is important. Because when in our discussions a lot of time patients are saying we are not going to share our genomics data with insurance companies because they're afraid of lack of coverage in the future. But you don't need to share your genomic data. You can only share the markers which are relevant for current disease condition. And I think that's a key functionality which any exchange ecosystem should have. And your case is another wonderful example of that.

UNIDENTIFIED SPEAKER: I'd like to add to that if I might. I want to take it from a little bit different perspective. Because we want to talk about incentives and I wanted to get to that a little bit. So when I think of, you know, we need certain data I think about where do we need that from? We need that from the patients, that's where we need the data from. And who do the patients trust? They trust their clinicians. That's that trust relationship.

So those are our partners. Those are the people we need to work with. We need to have partnerships with advocacy groups and with organizations, healthcare organizations. And to do that we have to think to when you build a partnership, when you build a relationship you want to give something, you want to receive something. You want that sort of, you know, two-way street. What does FDA have that these people want? And one of the things that we have is we have a tremendous amount of very valuable health information, which is very difficult to find.

So for me I'm a caregiver for my father and when I'm looking for information to help him it's

difficult. I can imagine what it's like for a clinician. You know, they're always trying to find this information, look for it. Maybe you can find it about CDER or CBER or, you know, different areas in the Agency. But how do you find it crosscutting like disease related? And, you know, some of the areas like your area, Sean, where you're looking across is one of the reasons those things are propping up, cropping up.

But what if we actually would use technology to help us build that relationship with the patient? Now, the first reaction to that is, oh, my goodness, if we do that it's going to cost a whole lot of money, it's going to be really difficult, all of us is already doing it. So we're taking a little bit different approach. What we're saying is work with the partners. Develop, as I said before, applications, apps that work on mobile phones that work within their existing tools that they have that they can go to a safe place, they can get these tools, pull them down and that would pull the FDA data. Now, we have this data and it's all in Open FDA. It's public data, we're adding to it regularly. So there's a huge amount of data that we

can leverage for this purpose.

In addition if you think about that now we have a trusted relationship. They're getting trusted information from FDA. Now there's an opportunity for us to collect information. And maybe that information is deidentified at first, maybe later, that becomes something more. But you're leveraging your capability in FDA by taking advantage of all those partnerships.

And so we're not trying to build a portal to solve all the problems of the world. We're trying to engage with other portals like all of us, like your healthcare providers have. When I got to the doctor I have -- every doctor I go to has some different type of unique thing they're using. I can put my widgets, my applications into their tool, with their permission or the advocacy group. We can use questionnaires through that tool, we've developed that capability. We can pull data. This is a very powerful way for us to get large amounts of data directly from the source, which I think is really where we want to get it from. And also provides information back. So as a patient I can go in and I can say I'm interested in breast cancer. I want

to know everything that FDA has about that. This could expand beyond just FDA to other health service agencies as well. But I can just pull all the data related to that cross biologics, I can do therapies, I can do drugs, et cetera. So I'm getting some very valuable information here.

Also, the next time the application allows you the next time you go in to say, oh, I remember your patient preferences and I remember what you came in and asked about. Do you want to add anything to that? But here's updated information and here's a clinical trial that's going on because we're pulling the NLM data as well. So what I'm saying is, is that we need to think from the perspective of the source of data, not just from the perspective of what we need and how we're going to collect it. Because the source of the data has to trust us in order to provide that data. And to trust us we need to build a relationship with them and a relationship of trust.

We also can leverage all of these clinicians who are already working with these patients, provide them data that they can query on. They don't have that

today. When, you know, you go to -- there's great pockets of FDA information along specific lines, but not a lot of crosscutting. And it is difficult to find that information. And even if you do find it what you're doing is you're looking at it in a static form. You have to bookmark it, you have to go back, you have to find it again. This way it's constantly coming to you. Clinicians can search for it. Patients can get it. And we're leveraging already the capability that already exists all over the United States.

DR. MCLELLAN: Lynn.

DR. GOLDMAN: Actually, my first comment kind of follows onto what you just said. Because I think one of the things that we see when we are trying to bring together data that's from EHRs that is a very important element is that the owners of the data feel that they're getting something out of that. That they are somehow participating in that, that it's something of added value for them. And often it's that it's not all that easy for them to analyze and interpret their own data the way that, you know, the EHR data are collected it's primarily, as you know, you know, for

administrative purposes. And yet, you know, they have a lot of other needs. And so that helps a lot because it's a lot of trouble for them frankly to work with you on that.

And I think that patients probably could benefit too, although we haven't done that in the approaches that we've used for epidemiology. But I do know as a patient myself that I'm always completely annoyed when I go online and look at my own medical record because it's full of stuff that isn't right. And I'm sure that people, you know, would like that ability to kind of be able to interact with that.

I mean I don't know what people are going to think, you know. They sometime look at my online record. I've gone to the ER and, well, what about that hangnail that she had in 1979. I mean still it's a problem still, you know. So it's going to be a problem forever. Well, I'm just making that up, but you know, that's just how it is. Any problem you've ever had just stays there.

You know, I do see, you know, some very large practical issues that I'm sure you're well aware of,

but something we confront all the time in doing research with these data. And one has -- so acronym called DUA, you know, data use agreements that have bureaucracy around that and legal issues around this is astounding. You know, you just have no concept of how difficult it is. And we, you know, we have one project where we have 30 institutions together and getting those DUAs together took a lot of time. And the other three-letter acronym is IRP and similar issue, you know. And just depending on the institutions and whether they have their own or not and all of that.

And but behind that, and this is something that is going to manifest some ignorance that I have about blockchain. I mean I really like blockchain and the idea of blockchain. I've never worked with blockchain, but there are things that I wonder about it, such as, and I think that Laura eluded to this, you know, could that become, you know, my blockchained together medical record could be the most valuable thing I own. I mean it sounds to me like that could contain every little bit of data that comprises my identity. And that if somebody got that they would completely steal my

identity. I mean I just, you know, over time what you divulge, you administratively for billing and all kinds of ways. So I'm wondering, you know, can you get the private stuff out of there? Because it looks like something where it's hard to do that.

And then the other thing, and of course, and you can't do a DUA, by the way, if you can't do that. You're not, you know, the IRBs aren't going to prove you can't do DUAs, nobody's going to give it to you. But the other thing is that there are, in my world, my world we don't have very many Kaiser patients here on the east coast, very many people in single systems. We have people that just see all kinds of providers in all kinds of settings. And so if we got a cohort that is bringing in together people we have multiple instances of the same person, you know, with different providers in different systems. And then we have to be able to deal with that.

And we make mistakes. The machines also make mistakes. People make mistakes and the machines make mistakes. And the wrong people get slapped together or people who are -- someone or a person ends up in a

system twice as two people. And you don't want either of those things to happen. You want to maintain the individual identity of individuals. And so, you know, they'll come together and then you realize they're not the same. You take it apart because the machine put it together and they're not together. And I don't understand blockchain well enough to understand like what happens when that happens, you know. Can you deal with that?

This isn't like another encounter in the same institution in a national health system. This is like, you know, they're 30 miles away and they walked into an urgent care clinic and got seen and their name was spelled somewhat differently or, you know, there's a tiny error in the birth date or, you know, something like that happens. You know, these things just happen all the time. Or somebody else's scan got appended to their record and it's not theirs and you have to get it out. We have a system that has errors in it in many, many, many levels. And, you know, you clean and clean and clean the data to make them better, but I don't know how that works with something like blockchain. Do

you ever get that out? You know, are you stuck with all the errors? And then, you know, then how do you ever at the end of the day actually analyze the data in blockchain?

Anyway, so that was -- it may be a little bit of advice, but also some questions. I mean I do think that it's important, you know, a lot of your questions are around, you know, should we do this? How can we do this? And I do think some of these critical questions about the security of the information, the data, you know, being able to use data, shared data are some of the most important questions. As well as the fact that we don't actually have a healthcare system, you know, just understand that. We don't actually have a healthcare system. So it's very complicated to try to, you know, look at data across multiple providers because the same people are in many different systems.

DR. SIMONYAN: Maybe -- thank you for the comments. And I agree with most of them and maybe I can address the question about what does blockchain provide? Today your data is already in different

sources, except you are not connected to it. And most of the data because you go to hospitals for billing and payments, they get your social security number. So most probably it's easier to link together today than it will be with blockchain ever.

So identity of the person can be detached from blockchain healthcare identity of the person. That can be done. In fact, we are discussing this. How do you create a unique blockchain identity of the person? So as far as we are concerned the new system should be much better than the previous one. Instead of hacking few systems of the hospitals where you attended as a patient and linking social security now, now they need to hack 30,000 computers distributed across the United States or all of the other countries to link so your identity all of the healthcare data.

There are in the computer cyber security we all know there are no 100 percent systems and they can never exist. But as far as we are concerned if the new system is so much more expensive to hack that it does make economical value I think that's what we are going to strive for. To create a system which is better than

the existing one and detach the patient's identity from patients healthcare identifier, which is assigned to a blockchain.

And some of the key functions which we are designing the new technology after is the banking system. I, in consulting with the people who are designing software and the protocols for the banking system, we all kind of learn to trust the banking system to maintain some of the most valuable things we have, our assets. We are trying to design that healthcare data is protected with same level of security and same level of privacy as the financial instruments are. And again, I want to make it clear there are no 100 percent secure system. But the software and the ideas for providing the security and privacy we are borrowing from some of the banking system and making it better than it ever was before.

DR. GOLDMAN: I mean just to follow up. I understand no system is 100 percent secure. I get that. A lot of my data were in the Office of Personnel management system, which is true for a lot of people in this room. But and, of course, and we got a nice

letter saying that it was just the government that got it, not criminals. So you can take it for what it's worth.

But there are these people in all of our institutions called lawyers, you know, who are operating under regulations. And I don't think that you can -- I agree with everything you said, but if the Agency is to move in this direction it must deal with the regulatory environment and it must find a way to make a case at a higher level, you know, because it's --I mean some of this comes from rules out of HHS itself, but some of it comes from rules from other government agencies who don't necessarily, you know, care, you know, that, you know, about the mission that we have and why we think it's so important to have this data.

DR. SIMONYAN: Yeah, I agree. And I think, again, maybe some of you heard me saying this, is when it comes to technology you are either around the table or on the menu. So I would rather have us all around the table working with technology and then thinking of developing the policies which is supported by the

technology and can be created, implemented and sustained. I think I completely agree with you, policies have to follow with the technological development, otherwise technology can do nothing and policy will hit the wall.

DR. MCLELLAN: I assure you we do not want to be on the menu. Sean.

DR. XIE: I read Sean, Dr. Sean Khozin's article, this one, records you sent to me published [inaudible]. And I read the last year 2017. That one is From Big Data to Smart Data. I like that article. In this article I understand that you try to emphasize decentralize the data. Actually, we build [inaudible] information database. We call it self-sustainable system. People can input data. But we found out after two years very massive, difficult to manage. We centralized.

So I'm pretty sure you have a way to managing this decentralized data. Allow patients, MD, neuro, entering data. So you have something to quickly share with us how you managing the decentralize?

DR. KHOZIN: Well, I think some of the concepts

we're working on in terms of blockchain is that ultimate decentralization of data exchange. But in terms of some of the things that you mentioned, there are different ways of doing that. Obviously some of the datasets we work with, for example, going from, you know, big data to smart data, highly protected proprietary data. So that's the data that is coming to us from sponsors of clinical trials. And we have that data available to us.

However, sitting in internal siloes, which we are breaking, and because just having data by itself doesn't really help. What you do with the data obviously is what we need to work on. So and there are different levels of data in terms of protection of data privacy. We probably have the most valuable data in the world at the FDA. No other regulatory agency actually gets clinical trial data. And we do when we approve drugs. So over the years we've accumulated a lot of data. And then there are other more experimental data sources that now we're acquiring through sensors and variables and genomic data and so forth.

So there are ways to master it. I want to go

through the technical nuances. So we've created protected sandbox. And I think like the first article you mentioned was about Informed and that's an incubator essentially. And we credential data scientists. They go through a background investigation and then we expose them to the data. And that's how we conduct a lot of our analysis. We also have a lot of data scientists actually already at the FDA that do product reviews. And if you give them a sandbox you really empower them to do amazing things. A lot of our pharmacometricians that were actually trained in neural networks and in AI. And that's a revelation that we had after we launched this incubator and then provided appropriate data assets to reviewers at the FDA and also external folks that we brought in. And it was very interesting to be able to empower them to do very interesting things with the data.

And then to make it more decentralized then there are privacy preserving protocols that we're looking at that essentially allow others to interact with the data to run computations on the data without exposing the data itself. So that would be one way that we can

decentralize our critical and our highly IP protected data assets. And there are other data assets that are not as sensitive and they can actually be exposed to a larger cohort.

For example, we're working with a group, a non-profit entity called Project Yedisphere [ph?] and we are encouraging companies to essentially donate data to his decentralized open access platform. And this is completely open access. You can actually go there and download the data yourself. And we've done a couple of interesting experiments with this open access data repository. We had it was a dream challenge, a crowd source challenge that essentially developed a very sophisticated model, a prognostic model for patients with prostate cancer. And this was completely crowd sourced. The data was there, it was in the public domain, it was open access, completely decentralized. And a challenge, well, we organized a crowd source challenge, and it was very interesting to see that a lot of solvers were -- some of them came from the financial sectors, others were -- we had high school students who actually started to interact with the

data. A variety of different folks who came to the table. And the model that was developed, the algorithm actually beat the performance of the existing model that we use for prostate cancer prognosis.

So those are the different ways that I believe you can decentralize and liberate data. And it has to be a very formal organized approach. And again, I'd like to highlight a formal on organize. I think there has to be new organizational constructs that can allow every institution, including the FDA, to engage in these types of activities. And that's an integrated approach that would have to be a little horizontal. I think every institution deals and battles with breaking their own vertical silo, especially when it comes to data. And obviously the FDA being a large organization is not immune to that. So we have to think about more horizontal frameworks. And I think other institutions have been thinking about that to kind of liberate these data assets. And then there are different ways that you can decentralize them.

DR. MCLELLAN: I have Barb, Scott, Minnie and Sean still. So Barb.

DR. KOWAKCYK: Thank you. I found the conversation interesting. I have a couple of comments. One is, and this is going to echo some of the themes I had earlier today, is that I would encourage you to engage CFSAN in this discussion. In the food safety arena blockchain technology is being used extensively for traceability issues. And I think coordination there would be very good.

Also, you know, I want to follow up on the last comment that you made. And, you know, coming back to the question that we have is how can the Agency work together with stakeholders to create regulatory use cases. One thing I think would be a good place to start is just improve data sharing within the Agency and across agencies, both at the federal and the state and local level. I mean we know that at least on the food safety side of things, which is where I work, there is a lot of data sharing issues just within and between agencies. So that’s a good place to start.

But I did wonder if you’ve engaged in any sort of stakeholder engagement activities where -- and whether or not you’ve considered public/private partnerships as

a way to at least advance the conversation about how to do this effectively.

DR. KHOZIN: We haven't. And depending on how you define a public/private partnership, we have a number of resource collaborations with the private sector where we're doing foundational work on addressing some of the issues that we've been talking about. And I think in order to consolidate all these efforts into a harmonized strategy that speaks to meeting the regulatory mandate and the directives that are given to the FDA is probably something that we're, you know, we're all talking about. That how can we consolidate all these very interesting efforts that are happening within the Agency, but also across HHS into a holistic, I believe you mentioned the word holistic when Gottlieb was speaking, we need that holistic strategy that can start to address some of these issues in a very -- in a concerted effort. Because I think a lot of the challenges that we have are not unique to the FDA. There's a lot of innovation that's occurring within the FDA in the different centers, different divisions. There's a lot of innovation that's occurring across

HHS. And also there's innovation in the private sector, which speaks to the need that there has to be a mechanism to do these public/private engagements.

The Department of Energy has a great track record of doing this. They have the national labs and there's been a lot of great successes that have emerged from that. And I believe something similar, and there are different ways of looking at this at HHS, but even at the FDA can really help. All these efforts, like Open FDA, for example, is a very unique effort that can be leveraged more. And those dots should be connected to some of the efforts that, for example, Vahan mentioned and I've mentioned. And that requires a new organizational construct.

DR. SIMONYAN: Maybe I can briefly comment on this too. You know, we all have successes we like to talk about saying what a collaboration we had done and things. But the reality is that a lot of time communication with stakeholders ends up having a problem, which is like network connectivity cables, who is managing the cable box or something. Or IRBs. I mean I'm getting the data from NIH, it took me about

four months to get the data. And we are, FDA, they are NIH and the data was public.

You know, and unfortunately we can do much, you know, although we can do much more, unfortunately there are no good frameworks for doing collaborative works. We are all bound. I completely agree with Dr. Lynn Goldman how difficult it is to come up with the IRBs and DUAs and mangle that. And plus you add network cables and connectivity and the peaks of internet tools and others, we can do so much more because here and outside we have the brain potential. Here and outside we have the idea and we have the willingness and devotion to the mission. But what we are lacking is that strong voice saying that everything else should be changed because the mission is more important. I think, well, I also can come up and talk about the good success stories. But unfortunately the reality is that we are sometimes struggling through completely unnecessary small things. I'm being realistic.

DR. KOWAKCYK: Pardon, I have a follow up not really question, but suggestion. So one of the ways that this -- I mean I understand where you're coming

from and all the challenges of bringing various stakeholders together. And in the area of work that I'm in one way that we have done that is have built stakeholder engaged -- stakeholders groups that basically spend a couple of years sitting together in a room hashing out what they can and can't live with.

So for example, I was on the meat and poultry dialog group that was -- and that's online, which is why I'm going to send you there. And that was collaboration between Pew Charitable Trusts and Cargill to see how we might be able to modernize meat and poultry inspection. I'm getting to where I'm going. But we spent two years sitting in a room and there were stakeholders from across the system. And we were educating each other about our challenges and also talking through some of these really tough issues. And at the end of the day saying where can we agree and where can we not disagree and where can we get some movement? And I think it might be worth considering that type of stakeholder engagement model.

Now, we were criticized. Government was not invited to the table and that was because it made

things a lot more difficult, but in terms of getting people to speak openly. But I think at some level to get this going you're going to have to sit down with the major players and say, okay, here's the problem and here's our different perspectives. And if nothing else you'll walk away with a better understanding of where the other stakeholders are coming from. I've participated in two or three of these types of things and I found them very informative. And while it moved the needle a little bit that's really the best you can hope for in a complex situation like this.

UNIDENTIFIED SPEAKER: I'd like to mention that we were talking about sharing data internally across HHS agencies. And the Chief Data Officer for HHS is working on an initiative right now regarding that. Because it is difficult to even share within FDA across centers, but across the Agency. So there's a big initiative under way right now exactly like what you're talking about. And I know you were talking about it more broadly, but within HHS there is actually an activity.

DR. MCLELLAN: Scott.

DR. KHOZIN: Just a very quick comment regarding that. Even at the level of the FDA I think if we connect our critical data assets, it speaks to what Dr. Gottlieb mentioned earlier, then it's hard to overemphasize the impact of that. It could be transformational. And we don't have to deal with IRBs or, you know, some of the nuances of working with other data systems aren't involved. But just the critical data assets of the FDA, if we figure out a new organization construct that can enable connecting these data assets just from a technical perspective is easy to do. It just requires a new organizational approach.

DR. KOWAKCYK: I think that would be an excellent starting point.

DR. GOTTLIEB: Just related to all the public/private partnerships piece, I was curious if you've looked at or considered to initiate or pilot something with CPATH, with Reagan-Udall, or one of the groups that FDA, you know, has consistently worked with in forming or initiating a partnership like this might be one mechanism.

DR. KHOZIN: We have a program around expanded

access with Reagan-Udall that has been very effective. With the biomarkers consortium, which is part of the foundation at NIH, there has been a couple of interesting projects around large genomic datasets. However, I think we can do better and we need new mechanisms that can support public/private partnerships and collaborations.

And I go back to, again, the national laboratories and how they've been able to do great work in that arena. And I think if we had a vehicle like that available to us within HHS it could be quite transformative.

DR. MCLELLAN: Minnie.

DR. SARWAL: Yes, thank you. As a clinician I'm kind of putting on the other -- that hat. I mean I think this -- all these discussions are incredibly interesting and I think completely the right direction we want to be going as a field scientifically. And I think listening to all of the discussions we would actually get fabulous use out of being able to take this kind of data modeling, integrating it with omics or looking at it longitudinally in all of the ways that

we've just talked about. And look at data trends, look at high risk populations, look at responders, non-responders, et cetera.

But I actually wanted to talk about something different is how do we actually get this back to the patient to change care? So currently if you actually have a new biomarker to actually get that to a patient to change a drug or select them in or out of a trial or increase, you know, and have their risk for a disease be predicted such that you come in and do something, requires that to go through perspective validation, perspective trials, which of course are extremely expensive, as we all know, and funds are limited. And then it goes through the regulatory part of maybe LDT or basically go 510K. And then if you have a device I mean, of course, it's even more stringent, you go through a PMA.

So I just want to come back to something like this because you're going to come up with an amazing, you know, gamut of wonderful associations. Some of them are going to be positive predictive, some are going to be negative predictive. And these all we want to get

them to patients fast. So what would be that part do you see when you find out something like this from these associations of different snips with omics or the microbiome, or whatever, how do we actually get this to the patient? Do we still have to then stop, go through the pathway of the perspective clinical trial, get that then again through a 510K? I mean then that's, again, that's the very clunky part of the process. Can we be -- are you already thinking of ways to make that more nimble so we're getting that to patients faster?

DR. PATEL: Let me address that. I think you hit upon something that we worry about as well. Like I think from a device perspective or 510K and PMA and the world of diagnostics where I've lived we've been thinking about this all along. And how do you get these technologies and the solutions to patients fast, as fast as we can? Our mandate is to still maintain the bar of safety and effectiveness, because you don't want stuff that is meaningless. Like you want stuff out there, two patients, two clinicians, two [inaudible], two caregivers, it has some meaning to it and has some confidence behind that.

So last July we launched a pilot program on what I mentioned earlier is the precertification. So moving away from a product by product review to an organization review is what we are looking at. And when you look at that the analogy, the easiest to understand analogy is like the precertification or precheck that you go through the airport. You trust the people going through the 510K process or the regulatory review process, you can actually trust them to do certain things much more streamlined so you have confidence in the people making the product. And then when it's required for FDA to review some of the stuff we can look at it at a different way to get products to the market. It doesn't just end there. We have to couple that --

DR. SARWAL: You're talking about like specific labs, like the New York -- like a lab, lab system that you have confidence in that they are doing things the right way.

DR. PATEL: Exactly. So I'm --

DR. SARWAL: Yeah.

DR. PATEL: -- generalizing that to any

organization making a medical product or software or digital health tools that can be relied upon and trusted upon to make those products in the right way. So it has a regular -- the people, the leadership, the culture to make -- to be used in the space. Because where I was going with this, like you have the organizational sort of confidence and you have the product confidence. But you have to couple that with the real world aspects, the learning aspects of how is a product performing? It could be a piece of software. It could be, you know, the combination that you just mentioned, and anything around that.

If you don't have that information that feeds into the knowledge and the trust that we can then say that even though it went through a process, let's just pick 510K, as we have currently, what's lacking or missing is, what I was mentioning earlier, is that real time know or real role knowledge of how the product actually works. That's what we're trying to set up in the coming year is trying to figure out a system that we can send products, we have organization confidence and in addition to product confidence that can then afford

people to have the trusted products in the marketplace.

DR. SARWAL: So you would potentially be able to allow real use, but kind of retrospective data. You know, not -- I mean change the mechanism in which we are currently, you know, taking these things through validation. Because we're always told you have to have the perspective clinical trial, you have to have it randomized, you have to have the biomarker or no biomarker issue, the efficacy. I mean that bar is pretty high. But I think if you have a trusted source that is actually measuring the assay and if they've been doing it as off label, or whatever, are you -- is that what you're envisioning?

DR. PATEL: Yeah. So --

DR. SARWAL: How do you accelerate that?

DR. PATEL: So we are trying to accelerate people. I mean the thing look at what we're trying to do is we are trying to separate the rigor that goes into making products from the products itself. And then if you take the rigor that goes into making products and delivering products it's not just about making products, right, it's about making, delivering,

maintaining and managing it throughout the life cycle. And that entire life cycle is what we're looking at. But that's just a big component of how products perform in the marketplace. Can they evolve, can they change, can they be maintained? In addition to that first time, you know, gate of review that can happen in certain types of products. So that's what we are trying to shift the paradigm towards is going from a product base to adding to that is organizational based with the real world sort of aspects of access to that data. And how we get there I think that's to be seen. But we are starting with this very, I wouldn't say narrow, but probably very broad base of software that is just the medical device and taking that.

I do want to touch upon the part about the bar that you were mentioning. The concept that we are trying to explore is like it's about what you say as a claim for the product versus what evidence you have in your study, right. And usually that's where the tension is. So the hope is for this vision and the product is if you could start with a low level and be in the marketplace, collect real world information that

can then feed it back into taking it to the next level of claim is really what the mechanism looks like. That's why it cannot be just about the product, just about the organization or just about real world. It has to be a combination of those three things. It will allow more access to patients as you mentioned.

DR. SARWAL: Yeah, well, that's fabulous. So that's more like an adaptive design in a way. You're coming in and collecting data on the go and then adapting the claim. That's great, thanks.

DR. MCLELLAN: Any questions? So let me then expound just a little bit. Because I actually have more -- I'm curious what questions you have of us, rather than us of you. We've got an interesting mix of individuals here. We even have an orthopedic surgeon here or two, right. And we would love to be responsive. I think much of what you've teed up is exciting, of interest. Obviously many different questions coming from our point of view. But actually not at a 10,000-foot level. But I'm curious if you can use the advisory, the Science Board and any of the component pieces that you're looking at to be effective

as a tool for you. And you may not have that answer right here and now. I guess I'm also proposing that as a possible future discussion if you'd like to come back to us.

DR. PATEL: I have a question, if you don't mind.

DR. MCLELLAN: Okay, yeah.

DR. PATEL: And one of the things that I always thinking about as we are creating this paradigm I just described, is how can we leverage the knowledge that's going to keep on growing either in the clinical world, the technical world and other data science world as we -- as things go on, is who do we tap into it? And once the collaborative communities can be set up that can leverage, can be leveraged. So it's not about just, you know, having everything at FDA, it's how do you sort of tap into those recourses? Actually, I should stop saying resources. It's just knowledge based.

And I think it goes in line with what Sean was mentioning in terms of not just data streams and evidence, but also knowledge in general in terms of information, evidence, technical progress and growth that's happening in the space. Looking at blockchain

2.0 if there such a thing. And AI maybe too. It's like how do you sort of get that confidence going back to our mandate of providing products to patients as fast as we can, but also with the high confidence? How we maintain that high confidence? I think that would be interesting, you know, if you guys have thoughts on that that will be good to sort of hear.

DR. KHOZIN: And just I think a lot of challenges arise from the fact that traditionally we've looked at delivering care as a completely different activity than generating knowledge in clinical trials. And I think now we have entered a world where the lines are not as clear. The markations are not as clear anymore. However, we have a health delivery system, although some may argue it is not a system, and a clinical trial enterprise that is completely based on different cultural norms. The good thing is that the legal construct us really the same. And it's just a cultural norms that are different. So how do you view really starting to exercise and create new incentives and new exercises, collaborative partnerships to start to bring those two worlds together? And payers obviously would

be involved in that. But more importantly it's the clinicians and patients who have to be at the table.

DR. MCLELLAN: Lynn and then we'll go to Cynthy

DR. GOLDMAN: You know, a couple of thoughts about the what I would say the problem and kind of it's a translational problem. It's going to be a problem of moving I think these approaches into actual real world application and acceptance. And I mentioned some things about, you know, policymakers. I thought that the point that Barbara made was a really good point too about bringing industry and advocacy people together to start to, you know, dissect the processes that are under way and how they can be made better and begin to get buy in.

I also think that those involved in the middle of the technologies have to realize that probably, you know, they'll continue to need to be human interfaced and there may be more than you think is necessary, you know, maybe for longer than you think is necessary to make patients and other people feel better about it. And sometimes technology is wrong. You know, so we thought self-driving cars would be an easier technology

I think to move into the world than it has been. All cars are going to have accidents. Self-driving cars are going to hit people that run in front of them, we get that. But people are going to make a much bigger issue out of that one person hit by a self-driving car than the thousands of people that are hit by cars driven by people. And that's just, that is a reality. And there's going to need to be somebody sitting there behind the wheel for a long time before people are comfortable when there isn't anybody sitting there, right.

And I think the same thing is true, you know, in principal more broadly for some of these things in terms of I think the public and probably politicians needing to feel that there's somebody looking and making sure that there's a check, you know. That you don't hand things over to AI, you know, without humans actually being in the loop until the society is ready for that.

DR. KHOZIN: And just that's a very great point and that really speaks to the core of the essence of what we're talking about. And also some of the

misconceptions and people have different views on this. As a clinician the way I think about it is that there are a lot of things that I as a clinician have had to do that I would rather a machine take over. For example, reading EKGs. In medical school it was not one of my favorite activities, or even reading CT scans as an oncologist. I want to sit with the patient face to face, spend as much face to face time as possible. However, that face to face time because of all the mechanics that have been imposed and have been created for a variety of different reasons has been taken away.

So I think technology can actually take us back to how we used to practice medicine back in the old days, you know, country docs. That holistic view of the patient, that holistic view can come from data. And that's exactly in a way we say when we say we want to merge the microbiome, the proteome and the genome. These are very technical concepts. However, at the end of the day we want to put the patient back together. Because in the past century or so because of the need to hyper specialize, you know, we've taken disease and the individual and have broken everything down into

silo individual units. So there's been hyper specialization and we've lost that holistic approach to treating patients. And we don't have much time to spend seeing patients and treating patients.

And in a way to think about the way that at least I think about AI and technology is to streamline the mechanics so we can go back to that essence of care, which is that therapeutic relationship. And also digital health can empower individuals that -- and return some agency back to them. Because, you know, when you interact with the healthcare system at the very best, you know, you have these fragmented 15, 20-minute conversations with a healthcare provider. The rest of the time you're on your own. So we can also do a lot using these technologies to empower the patient. But at the end of the day it's about streamlining the mechanics so we can go back to that holistic approach to care.

DR. MCLELLAN: Cynthy.

DR. REISS: Mark, this is Ted Reiss. I just want to make one point also going back to the --

DR. MCLELLAN: Go ahead, Ted.

DR. REISS: -- discussion a minute or two ago about innovation. I just wanted to point out also that the entire sort of innovation translational process, you know, that would be the consequence of this approach in technology would change. You know, being a pharma person, you know, there's a certain way of sort of thinking about innovation, how you bring something from discovery into, you know, what I call innovation to bring something to the real world. So we're changing the paradigm here and so that's going to be -- that will need to be reconsidered and rethought about in detail.

DR. MCLELLAN: Thank you. Cynthy.

DR. AFSHARI: Yeah, just a little advice on you question and then maybe how you could go about it. So we've heard a lot of really fantastic ideas. And actually your comments just there articulated a vision. And I always like to think, start with the end in mind. And so what is that ultimate vision that you're trying to achieve? And I think thinking about, you know, the return on investment and the metrics are going to be your guideposts along the way. I mean Minnie talked

about saying you're going to build this, but in the end practicality of you don't bring something you're not going to realize that return on investments. And so, you know, she was suggesting the path there needs to be policy around devices and biomarker and things.

But I think that there needs to be a really clearly defined framework of what you're trying to build that's anchored in that vision. And then you think backwards around the what are those places you'd look for those sweet spots of the return on investment. And so it's not trivial to build that. But once you have that map so to speak, and FDA has done that, right, roadmaps, that becomes your guidepost for all the people you're going to need to bring to the table. Because it's going to be like the elephant, right, where everybody's going to see a different part or be working on a different part.

So I know one mechanism that may work here, if you wanted to leverage the Science Board in this way, is I'm thinking about how National Academy of Science reports go about. So there be a standing committee around a topic, but then they do deep dives in

different areas with the subteam of experts. And so the challenge is if you just talk to a lot of different experts it's not -- you don't have a core of kind of continuity and so that becomes a challenge. So if you could leverage the Science Board we're not necessarily the experts in this, but as a core of continuity that knows the Agency mission that's worked with all of you on various things, we could potentially be that core that then sits with you to help think about, you know, as you bring other experts in, being a neutral party, so to speak, and listening to it in a very neutral way to help you advise and structure that framework. It's just an idea and an approach I've seen work in other areas like this.

DR. MCLELLAN: Right. And just to add to that, the Board has the ability to bring in outside adjunct Board Members, you know, to bring any kind of strength to our discussions as needed. So great point, Cynthia. Barb.

DR. KOWAKCYK: So I wanted to back to something Lynn said and also something that Cynthia said. First of all I just, you know, I think that what your vision

is really great and I'd like to see something similar in food safety. In essence we're collecting huge amounts of data across a system and it's observational data. And we should do the best we can to leverage that information to find new trends and new information from there that can -- the best we're ever going to do is prove, is find associations, not prove causality. But, you know, that vision is really important and great. I think you have to take small steps and look for that.

And I think one of the biggest issues, and this is what Lynn eluded to, is trust. We're all scientists and we forget that the rest of the world doesn't know as much as we do. And you throw out some of these terms like artificial intelligent and blockchain to the rest of the public and, you know, people's eyes start to glaze over because they don't know what you're talking about. And my experience is if people don't understand it then they don't trust it.

DR. GOLDMAN: Actually, I think most people think you're talking about Bitcoin when you -- as soon as you say blockchain that's --

DR. KOWAKCYK: Yeah.

DR. GOLDMAN: They think they're talking about investments and money and something that's a little shady. It's got a bad connotation.

DR. KOWAKCYK: Right. But data science in general I think goes -- you know, there's not a lot of people. So I would encourage you to, one, figure out a way to articulate it in terms that your stakeholders can understand and trust and have engagement that way. And then I want to pick up on something that Cynthia said and that is articulating also the return on investment for each one of your stakeholder groups.

I'm going to draw on my own personal experience. I just recently moved from Chapel Hill, North Carolina to Columbus, Ohio and I have kids that see various specialist. And I was very fortunate that Chapel Hill Healthcare System, the UNC Healthcare System is on Epic and so is Ohio State's Healthcare System on Epic. And let me tell you how much time it saved me. I went into a doctor's office, the pulled up our last visit, it was seamless. I think communicating that experience and saying the return on investment to you isn't that

you're going to be contributing to research, it isn't going to be this, it isn't going to be that, it's that when you walk into a new doctor's office they can pull up your records and see. And I don't have to remember. I mean I remember I used to have a whole list of all the medications my children had taken in the past and when they had had surgery. I didn't have to do that this time and it was wonderful. That was the return on investment for me to being part of that system. And I would encourage the Agency to think about how you can articulate that for your various stakeholder groups, if you have not already done that.

DR. SIMONYAN: Yeah, thank you. And the clarity of communication is very important, I agree. But you are lucky that two Epic systems were talking to each other. Because we know that's always true.

DR. KOWAKCYK: I understand that.

DR. SIMONYAN: Yeah.

DR. KOWAKCYK: I was very lucky. But I think what you can do is draw on the benefit there.

DR. SIMONYAN: I know.

DR. KOWAKCYK: And say, you know, when this does

work right this is the benefit. And that's what we're trying to get the benefit for consumers to be, that they don't have to keep a whole log, that they get better healthcare. You can do it to clinicians. I didn't have to fill out paperwork to get records sent over. It didn't have to -- instead of focusing on the data science, which is what's --

DR. SIMONYAN: I agree.

DR. KOWAKCYK: -- driving us, it's the practical way of how it impacts your life when it works well.

DR. SIMONYAN: Maybe I can make a comment which will lead to my question. My father used to say it doesn't matter what you are good at, eventually you're going to be salesman of that thing. So unfortunately everything when it comes to reality it doesn't matter what projects we do it costs money, it costs funds. And the availability of those funds is sometimes critical. Not only -- I mean we have to work under very strained conditions, but sometimes we don't have funds actually for a PR of the good idea. But that is really necessary. If you are trying to sell a wonderful idea which millions will benefit, you still

need to have certain amount of investment resources to develop that message and make it clear and make it for different type of stakeholders.

And retaining of stuff is very important. And we are having a huge issue with that. I'm assuming Science Board has a certain leverage, they can communicate the message to Commissioner, to leadership on how funds should be distributed to some level, maybe, if I'm not wrong. So here's the question, can you help us to attract and retain our scientific expertise? We are losing people. We are getting fresh people out of college or [inaudible]. We are training them for three years and we are losing them to salaries twice as much as we can pay them. And this is a real pain. And you know how many evenings or nights we are spending working together across our computer and then the moment Google finds them or Amazon finds them they are gone.

So here is the big question. Our center needs expertise. In fact, if you think really truly FDA is the biggest data science organization. That patient is a patient for a doctor. It's a line of a table for us.

The disease of a fever is the real temperature we can feel with a patient in a hospital. For me it's a column of the table. So we are a data science organization. We are truly a machine taking the data in, giving the data out. But we can't keep our data scientists onboard. We need expertise and we need hardware. Hardware is a small part of it, that's not the big issue. But getting the students, training them, not just students, young professionals, training them and keeping them that's a humungous issue.

And every year I lose about three to four very well trained specialists and I have to get the new ones and train them and do this. Here we go. You are asking what questions I have. Can you help me, help me keep my staff, help me find my staff? And that unfortunately costs money. And please help me with funding to retain my scientists.

DR. KHOZIN: So just a quick follow up comment on that, that funding is critical. Obviously there are areas of let's say unmet need. However, as important is an organizational construct that can actually get an appropriate return on these new investments. A lot of

what we're talking about right now are emerging concepts, ideas and solutions that are going to take us to a much better future. And things that we can do today to get to the place that we all want to be. However, we also have to recognize the fact that the existing organization frameworks are no longer effective in some cases, especially when it comes to data science. And because what we're proposing is data science to enable a holistic view of the patient. And internally that holistic view would come from an organizational framework that can maximize the return on these internal investments that are made and are going to information technology solutions, data science solutions.

And I think to just be a little more clearer is that we have a very division based system that. And I believe Dr. Gottlieb eluded to the fact that we may even have more divisions after reorganization of OND, the Office of New Drugs. That is in a way trying to address an organizational need. However, it may actually take us farther from the ability to start to create and harmonize a horizontal management solution.

Not that reorganization is a bad thing. And these are necessary steps that have to be taken. However, when it comes to data that sort of it's like electricity, you know, it's that common motif that connects us all. And it has to power ideas and it has to be horizontal and fluid. And if we can create that fluidity, based on the recommendations that you may have from an organizational perspective, then I think we can maximize the potential of the new investment and the new funding that's coming to the FDA, but also to maximize the use of existing resources and investments in a fiscally responsible manner. Because we can do it and we just need organizational support.

DR. MCLELLAN: Okay. In the --

UNIDENTIFIED SPEAKER: [inaudible]

DR. MCLELLAN: I know. We have [inaudible]. We're going to keep going, but I really need to try to bridge to point number four. I don't know if we can rotate the screen here wherever that is. But remember I said at the beginning of this that we had a natural bridge to point four. And that's where we're looking at clinical trial data. It's still electronic health

records, but we're talking about essentially bridging two clinicians all the way to point of care, particularly in underrepresented communities, and trying to make a difference with these technologies. And I think, Captain, you have some comments maybe that could set the stage just a little bit here.

CAPTAIN ARAOJO: Right, sure. I'm Chardae Araojo, the Director of FDA's Office of Minority Health. And, you know, we all know that historically racial and ethnic minorities have been underrepresented in clinical trials. That's a long standing fact that we are all aware of. And the Office of Minority Health, along with others across the Agency, has been really working to try to address this issue.

For example, one of the many activities that we have ongoing is the Office of Minority Health has a minorities and clinical trials campaign. So that's one of the ways that we try to raise awareness through education, through multimedia, as well as through partnerships about the importance of minority participation in clinical trials. And I think, you know, providing some context to this question and for

this specific conversation when we talk about building platforms and we talk about new digital sources, EHRs, it's really important to minority health that we remember as we come up with these new innovative ways to obtain data that we think about making sure that we have that subpopulation data, that we have the subpopulation data specific to racial and ethnic minorities.

And I do want to circle back to one of the comments that was made earlier when we talk about a trusted relationship. So we know that one of the long standing reasons why minorities don't participate or have not participated in clinical trials is because of a trust issue. So as we continue to advance in this area building that trusted relationship I think will be very important. And we know that our minority populations also were very early uptakes, you know, as far as up taking with mobile devices, smart phones, we know that they use those phones. That's a way for us to obtain data. And they were really early adopters of that. So I think it's important as we have this conversation that we really remember that as that data

comes in that we have a way to really analyze the subpopulation data.

DR. SIMONYAN: The exchange platform which are building, in fact, we are designing it as one of the use cases, is patient recruitment, if the patient data is available. I think one of the potential reasons for the lack of minority representation in clinical trials may be the lack of data to let me say shop for patients during the recruitment. I think if this exchange platform can eventually become something which the public uses and all of the data is connected to the exchange for minorities, I think that's one of the solutions. How easily they can be discovered, discoverability of the minorities, I think, is an issue because of their underrepresentation in EHR available records. So I think that may help to move the cause in this case.

The second is that even after the drugs are licensed and they are being targeted for patients, again, discoverability of the patients of the licensed drug is also a big issue. Not just for clinical trials, but actually targeting after the drug has been

on the market. And I mean if the platform is symmetric whoever participates will be able to be found. And I think this is the way technology can uniform the availability of patients from different minority groups.

DR. KHOZIN: So as an oncologist this is topic that's very near and dear to my heart. Because when you look at the evidence generation system in clinical trials that we have, especially in oncology, the majority of oncology patients are underrepresented. At any given time if you took a cross-section of all the clinical trials that are occurring right now in the United States only about three to five percent of adult oncology patients are in clinical trials. And because of the conditions and the restrictions that exist today in eligibility criteria, for example, and other reasons that we may have an opportunity to discuss today, the majority of patients just don't have an opportunity to participate in clinical trials. And as we know it's not because they do not want access to experimental therapies, they actually do, it's just because participating in traditional clinical trials is very

difficult.

So what's happened is that, you know, we exclude, for example, patients in traditional oncology clinical trials that are essentially sick, you know, poor performance status we call it ECOG of two and above. We exclude patients who have brain metastases, for example, which is one of the most common conditions in advanced malignancies. We exclude patients who have HIV. We exclude patients who have an organ dysfunction. And these organ dysfunction parameters are very conservative. Most real world patients don't have kidney function and liver function that mirrors what we actually see in clinical trials.

So we've created this very artificial construct that gives us P values that we get excited about. However, so what that means from a mathematical perspective is that the existing traditional clinical trials in a lot of cases, specifically in adult oncology, we have studies that produce results with very robust internal validity. However, we've done that over the years at the expense of compromising the external validity of the results of traditional

clinical trials. And that external validity deficit is very important because that's actually what clinicians need to personalize treatment decisions at the point of care.

So how do we do that? And one way would be there's a lot we can do to increase clinical trial participation. And in oncology we have several efforts that are trying to address that. One is an effort we have with ASCO, a professional organization in oncology, to encourage sponsors to expand eligibility criteria. So that would be one way. But we also have to recognize that in a lot of cases just financial toxicity involved when it comes to participating in clinical trials. Most clinical trial centers are miles and miles away from where most patients are being treated. And most patients can't, a lot of patients can't afford to even go and have a consult for screening to see even if they would be eligible for a clinical study.

And there are other barriers. For example, after developing a therapeutic relationship with your physician, clinician, it's very hard to peel away from

that, especially in cases where you are facing a life threatening disease. And if you have to travel to participate in a clinical study, even if you are eligible, if you are lucky enough to be eligible, there are transportation issues. There is financial toxicity involved. And you have to break that therapeutic relationship with your primary clinician and in some cases you have to leave your family behind if you have to travel. So these are realities that make scaling and really increasing participation in traditional clinical trials very difficult.

An approach that can be enabled and supported by technology is to start to move clinical research to the point of care. And we need to dissect that out. You know, obviously to do early mechanistic studies, those finding studies. Very hard to do that at the point of routine care. But as many of us who've participated in clinical trials, especially late phase studies, realizes that the majority of, for example, phase three studies, these are not clinical studies really, it's just patient care. And this is something that wasn't, from a personal point of view, very obvious to me when

I was in private practice. And then when I started doing clinical studies at NCI that it's essentially just patient care when you reach the stage to where you're doing a registrational study, for example, a phase three study. And a lot of our clinicians in the United States are more than capable to conduct these studies at the point of care. They just need to be empowered. And that empowerment comes from giving them the right tools and technologies that they need to capture the data that the FDA considers for regulatory decision-making.

DR. MCLELLAN: I was just about to go over here for questions but they all disappeared.

DR. GOLDMAN: Well, you know, he said what I was going to say basically. But I do think that there's been a failure, you know, to use the technologies that we have to be able to have people enrolled in clinical trials remotely. But I think there are other structural problems too that weight any clinical trials that are stopped. Because they don't fully recruit because they have so many exclusions and they're only recruiting from people right in their area. And there

are way too many people who die without having a chance to go into a clinical trial because they can't afford to move to another city and get an apartment and live there. I mean how many people can do that? And so I mean it's not just minorities. It's people who just don't have much money.

I did want to point to one of my professors actually, Tom LaVeist actually did a national survey about the opinions and attitudes and knowledge among African Americans about clinical trials. And actually a lot of things that people believe are not true. I mean there was very little knowledge about things like the Tuskegee experiment and stuff. I mean people think everybody knows that. Everybody does not know that. That's not how -- apparently it's not a subject of household conversation. And I do think it would be something useful for the FDA to look at Tom's work, Tom LaVeist, because there are a lot of factors that are less obvious that I think are very, very important about how people are approached about getting involved with research. Clearly it's just not that clear that there is going to be a benefit to them. So but anyway,

but I agree with everything you said about the trials.

DR. SARWAL: Yeah, and I think we had the patient engagement discussion earlier. I think I would like to point out that the patient engagement piece for the minority groups is like almost completely lacking in almost everything that we're doing. I think we're just getting to terms with it and it's, yeah, I think a lot more attention has to be given to that. And I think it feeds to exactly what Lynn is saying. They don't see the benefit. They only see the pain point of it.

DR. MCLELLAN: Rhondee.

DR. BALDI: And, Mark, I'll add one thing really quick.

DR. MCLELLAN: Yes, go ahead.

DR. BALDI: A follow up comment. Dr. LaVeist is actually coming to present this Thursday for a minority health equity lecture and he's going to be talking about that. So I just wanted to make sure I mentioned that.

DR. GOLDMAN: That's a good ad.

DR. MCLELLAN: Rhondee.

DR. BALDI: I just wanted to add two comments.

One is there a way going back to incentives to think about how to get pharma engaged with engaging clinicians in the real world to conduct these trials? And whether FDA can provide the incentive structure to make that happen, at least in a regulatory way, approving faster that conditional approval. What can we do to really make that happen?

And the second thing it seems like from the conversation that clinicians aren't very organized, but they're a big stakeholder group. As a group we're a big stakeholder group, but we're not organized in a way. So thinking through that maybe the Science Board can help thinking about how do we engage that type of group over time. It's a very heterogeneous group. But how do we engage clinicians over time to bridge the gap between patient care, clinical research and patient outcomes? Because I think clinicians naturally want better outcomes and better experiences for patients. So how do we leverage that and create that stakeholder group, which is thinking about that and spreading that message? I mean diffusion in medicine and diffusion of ideas is also a big problem, but I think that's

probably a stakeholder group we can think about how to engage more concretely.

And then I feel like the cost saving incentive either for insurers, not only pharma, but for insurers, they want to save money. They don't want to spend money on drugs or treatments that don't work. So is there some way to leverage engaging people in trials in that way as well?

DR. KHOZIN: Yeah, that's exactly what we need to do. And you're absolutely right, we need better outreach. And I think we have a cadre of very capable, well qualified, well trained investigators at our community clinics and at the point of routine care. And how can we empower them and give them the tools they need to do clinical research? And I think there's a technical component to that, but that's the greatest challenge.

And already if we look at community medical centers the data collection needs and the community clinics and private practice of very complex. And the ratio of clinicians to ancillary staff has been increasing far beyond the ratio of clinical

investigator to their data managers or to -- because we've reached a point right now that to deliver routine care the data collection needs in some cases are actually more complex than the data collection needs in clinical trials. However, the intent is different, but the expertise is there. So we just have to reframe and really bring them, socialize with them the opportunity and then the mechanics can be scaled through new incentives, meaning new electronic health record systems that can meet that need.

You know, when after the passage of the High Tech Act when the incentives through meaningful use, the meaningful use criteria for adoption of electronic health records were put out there the industry responded very rapidly. You know, the High Tech Act was only, it was an act back in 2009 if I remember correctly. So the adoption increased. The health information technology sector responded accordingly. And these systems are actually designed how they were formulated to be designed. I know we complain about these systems not being optimal, but that was really the intent. These systems were designed around

administrative and billing activities.

However, we can now start to change the conversation and try to reframe the question in terms of what we actually need from electronic health records. So a task force I think would be a great idea. Payers would definitely have to be part of this conversation, specifically CMS. CMS is in it for a long term. In the private payer community, in some cases depending in which use case and disease that you're looking at, the average member doesn't stay with the health plan that long. So in terms of like investing in certain efforts and investigations it may pose special challenges.

There are different numbers that are thrown around. Four and a half year is what a prior health plan said at a recent meeting. I've even heard two and a half years that the average members stays with a private health plan. But I think they have to be also at the table because the data that's the collected at the point routine care can be used to treat the patient and also meet the needs of the payers and the FDA.

DR. MCLELLAN: We are, for those of you in the

public audience, we are delaying just a few minutes on our open hearing time so we can sort of complete some of our conversation here. One of the comments you made I guess, boy, it just jumped right out at me when you were talking about losing your highly trained individuals to the private sector. And one of the comments I think, Barb, you made it was is there room here for a private/public partnership? I wonder if this whole thing shouldn't be flipped in a way to say, you know, Google, Amazon, whoever you are, why not work with us? You know, embed some of your best scientist for a couple of years with us. You can have them back, technically trained and then we'll take your next newest one. In other words it sounds to me like we may be offer the most perfect platform, which appropriate guards and protections. But the most perfect platform for someone to really understand how to create integrated incredibly detailed knowledge system on a very complex basis. So something to think about.

There is a question I would like to float back to you. One of the comments that we've made here was the potential for patient total ownership of data possibly

in this blockchain. I guess a question I would throw back is what are the things, what are the elements that would push against that, would not want that to happen? And I'm not sure I fully understand, not being embedded as much. But I'd be curious about your opinions on what might block that, sort of delay it.

DR. SIMONYAN: Okay. Well, every time when I share this idea with somebody from industry, different stakeholders the first reaction is that why would we even give away our data to a patient, because we have it now, we use it now? But the moment you describe the way you can increase the reusability of the data if the patient owns it. And every time you ask for the permission of the patient, even if it's monetized inquiry, you add an incentive to the patient to share further. And then let's imagine two different scenarios. Today let's say a pharma company has hundreds of gigabytes of genomic data stored in some kind of a siloed warehouse and they cannot use it because the primary use is done and done. So for new types of studies sometimes they have to accumulate new types of data from newly recruited patients. In fact,

if they could engage the old patients, get the permission from the patients and use it again that would be a significant benefit to them.

So and then I can describe different schemes like this when I was discussing them. So at the beginning everybody says but it's our data, we spend money to generate. At the end when you explain how much they will save by reusing some of the data, control run data or some type of study arms can be reused, or the genomic data, which doesn't change for the life of a person. So they eventually recognize how valuable it is if the patient owns the data. I haven't heard a single story other than EMRs. There are EMR software companies who could have been consistently resisting the idea of the patient ownership being a good idea. EMRs are a different story obviously because interoperability means sharing the market in a different way. Perhaps increasing the mobility of the clinician networks moving between EMRs. That's the story which I haven't yet kind of made up a good story to convince them. But I think every other stakeholder is actually eventually convincible for that patient

ownership is that economical vehicle that is releasing the valuable, again, modeling from financial marketplace. We are releasing the valuable to move by allowing the -- putting the patient on a steering wheel. So the only -- so if that valuable is the healthcare data, is the genomic data, is EMR data, that creates actually free floating economy. When it comes to the EMRs that's the story which you can help me come of, you know.

DR. KHOZIN: And I think it really speaks to the fact that data portability is an issue right now. And any of us can ask for our medical records or even go to, if we were part of a clinical study, get our data, the would give it to us. But in most cases either it's printed out or, you know, it's put on a CD rom, let's say, or a flash drive. That's now used more frequently. That is not really portable data. That's information that can be emailed or faxed to someone and but that's not really data. So we need conduits and mechanisms and pipelines to be able to create data fluidity. That's really what it's about.

And the best way to do that, I don't believe

personally that it should be a top down approach. In cases where we've had data liquidity it's all been bottom up. It's been entrepreneurial. However, the incentives have been clear and there has been a way to get there. And again, goes back to the incentives have been in place. However, unfortunately when it comes to managing health data the incentives are misaligned. And we haven't been able to maximize and capitalize on the great success of clinical Silicon Valley in data management and entrepreneurship.

However, I think now we have an opportunity because everyone nowadays wants to disrupt healthcare, but they just don't know how to do it. So we could capitalize and leverage those investments. But more importantly talent and put them and challenge them and put them to the task of meeting and addressing some of the challenges that we have. And that's a more bottom up approach and it has to be brought to the table.

DR. MCLELLAN: Barb.

DR. KOWAKCYK: Can I just add though in the financial, and tell me if this -- I may be not thinking about this correctly. In the financial environment

although blockchain, Bitcoin, exist it's regulation that prevents it from overtaking the current financial system. And so it makes me think again maybe still one of the priorities had to be focused on the policy for regulation because that's the shift in some ways.

DR. KHOZIN: Absolutely. And the policy. Absolutely.

DR. KOWAKCYK: It should have already taken the financial system, but it hasn't because we have regulations in place that have protected the current banking system.

DR. KHOZIN: Absolutely. I think policy and rulemaking should be a critical part of that. But I think in terms of creating top down infrastructure it would be probably the wrong way to do it. However, policy framework that actually can guide innovators forward and to put in safeguard so that the patient data is not abused and misused is critical. And we actually have that scenario right now at full force when it comes to social media content. And one way to look at that is the great success of data science and big data analytics when data is available and fluid.

However, the appropriate policy framework probably wasn't there. And we could have been as policymakers a lot more proactive to put appropriate safeguards in place so that, you know, the data couldn't have been abused.

So I think those lessons learned, in fact, can inform what we need to do moving forward. Having an adaptable and flexible policy framework, but also creating the incentives to risk takers and entrepreneurs that can actually provide the technical backbone and the solutions that we need. And it can be done relatively quickly. If you look at, you know, all the social media platforms right now that are rivaling Fortune 500 companies they're not that old. They've been only around for a few years. However, they were able to scale very quickly. And we can bring the same type of infrastructure and framework to healthcare by bringing them to the table and having, as you said, smart policy and safeguards in place to guide them forward.

DR. SIMONYAN: Maybe a perspective I can share. So this is a tricycle. Yes, we have one wheel which is

the technology, one wheel which is the economy and incentives, and the wheel which is the policy. So if any one of these wheels misses usually you can topple down, especially at the early stage of a childhood of this technology. So then what I think is important to understand that when technology, sorry, when economy and policy go against each other economy usually wins. So it is very important for now to have a technology based guided economical model development and then develop a policy which does not contradict and does not prohibit that first two wheels of movement. So it should be technology guiding the economy, which means you're developing economical models for the stakeholders to be incentivized enough to do this. And then policy, watching and following and engaging in a harmonious way so that tricycle doesn't fall down.

DR. MCLELLAN: Barb.

DR. KOWAKCYK: So I wanted to follow up again on your question about training and retaining scientists and some of what Mark said. First of all I think, and I'm assuming that you're doing this, but just in case you're not, I assume you're doing things like exit

interviews and assessments when you're -- when these folks leave the Agency. And I would also encourage you to think about how to engage with academic institutions, I mentioned this earlier. And there is a plethora of data science programs popping up all over the country. And, you know, identifying the core competencies that the Agency needs and providing that feedback. Because I'm a little worried that everybody and their brother has a data science training program now. Even outside of the academic institutions. And are they providing the expertise that is actually needed? You know, do we have an alignment between what the training is and what the needs are?

And then I think also, you know, the people that are going to work in -- first of all I want to say I think movement between stakeholder groups is a good thing. It gives different people different perspectives. And so, you know, there's always I think some level of movement and that's to be expected. But I think too in thinking through and selling what the Agency has to offer. So, for example, I'm a very mission driven person. Money, it wouldn't matter to me

how much money Google or Amazon threw at me. That's not what drives me to go to work ever much money Google or Amazon threw at me. That's not what drives me to go to work every day. And I think that's true of the public health or of our federal agencies. And are you marketing yourselves appropriately to attract those people that are mission driven and that's why the want to be in this? And they won't leave just because more money. They'll probably, if that's what drives them, they're leaving for other reasons. And I would suggest that you look at that.

My husband's a data scientist. I'm a statistician. I can tell you that one of the challenges that I've seen is organization's inability to meet the needs of the Millennials and data scientists. You have lots and lots of options. And so is the work environment conducive to work/life balance, to flexibility? I think there's lots of training programs that could be implemented. IPAs with academia, that's another option, to bring the academics into the Agency. You know, we have programs where if you serve, you know, like Math for America, or Teach

for America and those kinds of things. Should we be thinking about some of those types of programs specifically for statistics and data science and epidemiology? And I could actually go on, because most of the public health arena is facing a workforce crisis. So can use some of those models to address this important need? And it's not just within here, but you know, from what I can tell a lot of people are willing to take on a lot of debt to get degrees in data science. And, you know, they recognize it's like the number one job right now. So how can we attract them and what incentives can we provide to them?

DR. KHOZIN: Those are all fantastic points. And you're absolutely right. So we have experimented with two programs. Just two weeks ago we launched a post-doctoral fellowship program in artificial intelligence and machine learning with Harvard. And we're definitely looking forward to that. Six months ago we launched a fellowship program with NCI in data science. And we just recruited our first candidate who happens to be a radiation oncologist. And they're going to be exposed to the data and the data science capabilities

we have internally. In the case of the Harvard fellowship program this will be a very -- the idea is to bring someone who has already been exposed to data science, is very capable in AI and actually learning. They don't have to necessarily know anything about healthcare or regulatory science. However, when we expose them to the data internally it could be a very interesting synergistic relationship. And we're developing a curriculum.

However, it's going to be very interesting to see how these two experiments scale because one of the bottlenecks would be data itself. And if our data internally is siloed and fractured there's so much that these folks can do. Because, you know, again, it goes back to the idea of having that horizontal framework where the critical data assets at the FDA are harmonized, organized, prepped in such a way that can support data science solutions and experiments.

DR. SIMONYAN: And the one thing is that, yes, I understand that flocks of the working force it's a normal thing you expected. That's one of the reasons we are training in order to release them to the

industry. But I think because these new technologies that you are working in are moving so fast, more and more companies are producing data. And we in the regulatory scope see more and more of the data. It's difficult to support horizontal and vertical scalability. When we started in the next generation sequencing data scope here at FDA we got one submission for the first half a year when we started. Today we have a few submissions a week. And then not only the size grows, but different types of analytics has to be kept out of it.

Two years ago in was in a conference where they mentioned that 88 percent of all pharmacogenomics styles are generating NGS data of different kinds, exome, RNAC, DNAC. Today I'm pretty sure that's much larger. And we started to see the brunt of the data coming to us. And we have to, as FDA, we have to be able to review the data, analyze the data. And sometimes because we are working on a cutting edge sometimes there are no tools which allow us to look at it. We have to develop it as we go. Sometimes we have to adapt tools from the industry that also is an

effort. So, yes, I agree that there should be certain level of mobility in the workforce. But sometimes because the workload increases and the number of projects increases we need to maintain horizontal and vertical, like how big, how many more and how many new types, scalability of the expertise. And that I think is a challenge, but we are to do our best. And I think up to this point we were successful, but we recognize that the brunt is only growing and we are going to get more and more of this. So I'm agreeing with you and at the same I'm saying the challenge is still there.

DR. MCLELLAN: Mike.

DR. YASZEMSKI: Hi. This is something that our presenters likely know, but I'll pass it on because it may be of use to anybody interested in this. About two or three months ago I listened to a presentation at NIH by the Director of the General Medical Sciences Institute who talked about the need for just what you're talking about, data portability and EHR interoperability. And said that that would be a major focus of the funding opportunity announcements from his institute later this year, I suspect. If you can

embellish it please do, but if you -- otherwise this is just an FYI comment.

DR. MCLELLAN: Minnie.

DR. SARWAL: Yes. You know, I think we're reaching the end of the afternoon, so I just wanted to come back to really how do we actually, again, make that difference to the patient? And I think based on what Dr. Gottlieb said and I think what came from that side of the room right in the beginning is that we actually want to create a better database that's not just capturing billing, but is actually capturing clinical identifiers. And we want to make this something that is uniform across every different provider that the patient goes to so that they can talk to each other. We don't have to just chance on an Epic that talks to another Epic, but that all of these data should talk to each other. And then there is the sustainability of how do you sustain this cost?

And so I just wanted to put some ideas out. And I don't know if -- but I think we should be looking, you know, we're looking at all of these things right now, but I think we should be looking like five years from

now how do we actually get this to a reality? And I think two points I just wanted to raise. The first is I think it's fabulous that we should be thinking of making our own customized, like what is that, what do we want the data queries to be, what should it look like? But I think we need to have then recognition that there has to be some kind of common data language. And I know there are different vendors and there are different commercial interest, but I think this is something that the FDA probably would have a lot of value, like really thinking about like what is it that you want as that language? Because if we still allow all these different databases to lurk around and then we have our data sciences people writing code to do normalization of data across all these data languages that's still very clunky.

And then the second thing I just wanted to say is how do you sustain this effort? So, yes, it could be that the FDA looks for more money and we look for money from Congress. But at the end of the day we're making a difference to patient's lives. And I think there needs to be an investment at the end user side too. So

I would really put this onus on insurance companies. I mean private, as well as other. Because I think this needs to be a way that we improve patient care. And if that's the case there needs to be a bottom line that needs to be tagged with this increased data delivery and patient quality improvement that comes with that kind of new way of delivering medical care. So I would just say that I think we should think of a, you know, cost sharing model where at the end user they're actually putting an investment into making that better.

DR. MCLELLAN: Scott.

DR. KHOZIN: You're absolutely right. And rather than a database I would rephrase that. We don't necessarily need more databases. I think we have just way too many databases. We need standards for data communication and data portability and interoperability. Because actually we want to move away from the idea of aggregating data and creating databases and more towards a framework where there is data fluidity. And I'm going to look into the NIH effort. And, Michael, thanks for bringing that up because those early investments, those investments can

go a long way. And I'm glad that NIH is really looking into this because the grant mechanism, the traditional grant mechanism hasn't been designed in a way they can address some of these issues. But it seems like NIH is looking at that and that's great to hear.

DR. SIMONYAN: And [inaudible] which we are working on with relation to standard, it's not just the standard of data and types, but standard of bioinformatics protocols which are communicated between stakeholders is very important. Today the data by itself, I might be repeating myself, doesn't mean much unless you can extract the knowledge. And there is a process between then. So we are also -- CBER started supporting biocomputer first. This is the attempt to harmonize by informatics protocols communication language. In order for stakeholders to at least be able to communicate this is how I did to the computation.

Believe it or not, and these are true data which are surprisingly scary, 70 percent of all big data by informatics computations are irreproducible. Well, I mean in the research domain if I do that and then I

find out it's not reproducible I sound -- I publish an oops paper. I'm sorry this errata and this is what I didn't do right. But in the clinical, in the regulatory domain you make a mistake the impact is so much larger. And I'm going to tell you another number which is even scarier. 65 percent of owned research in big data analytics is irreproducible. I mean that has to be addressed.

And that's what we tried to do. We have collaborated with George Washington University in development of the biocompute part of them where this is -- it sounds cooler than it really is, it's a language how you communicate your protocols of computation. Every single one of us who have ever been a student has done lump notebook. This is I added 20 grams of this substance and 50 grams of that substance. I kept half an hour boiling it under this temperature. And that's normal for us. But people what they don't recognize in a bioinformatics world, in a data science world the protocols need to be kept also. Because there are hundreds of alternative plot space how you can try to compute the outcome based on that data. And

we are also doing significant efforts on that one, developing the language framework.

DR. GOTTLIEB: I just wanted to go back to some of Barbara's comments on training, which I think were really helpful in considering further defining the core competencies and needs that the Agency sees. Because I feel like we've had similar discussions around regulatory science training. And I just wonder how much -- I presume there's a mixture, you know, maybe there's individuals you want to have really core data science and there's a number of data science program. But how much of the expertise is blending with having expertise, knowledge and on a specific product, you know, at the product center level?

So I mentioned you said a post-doc that's where you don't need to have some of the biological knowledge. But I mean how do you view that? Are you looking more for people who have the specialty area and you can bring in the data science expertise?

DR. KHOZIN: No, I think it's interesting. When I first came to the FDA I asked my colleagues what is regulatory science research? And, you know, I asked

ten people and I got ten different answers. All great thoughtful answer. But everyone views regulatory science research in a completely different way.

And I think perhaps as something that this Board can champion is construct, again, we go back to that organizational construct powered by data that also has a mandate that encourage and create solutions and definitions around regulatory science research. And I think some people, I'm sure if you ask Vahan, developing platforms and technologies and agile tech is part or regulatory science research. If you ask someone else it may be policy. And so there are many dimensions to regulatory science research which requires different skillsets. And I think it will be interesting to look at that in a much more -- in an organized -- under an organized framework.

DR. GOTTLIEB: Well, I was making the analogy to data science. So I think when we talk about regulatory science we usually say, well, that's certain sets of tools that you're bringing into a particular area. And so the data science, I mean, if you're looking at medical devices, isn't the data science training is

going to compliment the product that you're reviewing or --

DR. KHOZIN:

DR. GOTTLIEB: -- evaluating. So --

DR. KHOZIN: Absolutely. You know, the way we're looking at, for example, for the AI, ML fellowship program that we have a lot of data internally. And that actually in some cases that exceeds our ability to analyze the data. A lot of even large pharmaceutical companies are having the same issue. There's a lot of -- there's no shortage of next generation sequencing data or proteomic data or clinical trial data. However, our ability to really put it all together is not optimal. Because the way that traditionally we've reviewed data is in separate siloes. You know, we do our next generation sequencing analysis, we have platforms there and then it creates, it generates a report that we take and then it informs an action.

However, the idea here is to actually connect all these different data streams and that requires a completely different way of looking at data, analyzing data. And that's data science. And data science in

this situation would be regulatory science because what we're trying to find out through some of these exercises, we have a portfolio of research initiatives, but in some cases it's understanding patient variables, intrinsic and extrinsic that explains the response to therapies. Because not all patients respond the same.

If we look at the Kaplan-Meier curves are the backbone of FDA approvals they're average treatment effects. You know, we look at the median survivals and as always patients above and below the median. And we never look and there's no mechanism to start to dissect out, for example, exceptional responders who may be in the long tail and patients who may not be benefiting. And now we even are seeing Kaplan-Meier curves that are non-proportional, non-proportional hazards where they cross. All of those sort of average treatment effects tell a story that can be dissected out at the individual patient level through data science. So building those capabilities requires different approach. A different approach to human capital management, but also a completely different approach to organizing data and creating a knowledge management

solution that can support these efforts. So those mechanics wouldn't be the bottleneck.

DR. MCLELLAN: Tony, I think we're going to let you have the last question here and then we'll move into a little bit of activity. But go right ahead.

DR. BAHINSKI: More comment than question. So just to follow up, this was in my original comment. You know, the irreproducibility of the data and then you're correlating that with research. I mean Amgen did a really nice study a few years back of the reproducibility of academic data. And it does have an impact because it really sends us down wrong tracks. So there's a financial impact there.

But I wanted to go back to something that Minnie said. You know, really the whole goal of this is to get medicines to the patients faster, right, that's what we want to do. And I think you're, I hope you're aware of the Adam Initiative with NCI. You know, so the real goal there is this, you know, reducing aspirational goal of reducing the time pre-clinically from, you know, six years to say one year from target to clinical trial. And exactly as you pointed out,

it's to in parallel do that efficacy safety testing and mechanism testing all in Silico. And, you know, data is the currency there and it's really difficult to get that in.

So I think, you know, all these efforts that you talked about with blockchain and, you know, high performance computing, feeding into that I think is really going to energize those efforts. And I think that's -- it's not going to happen overnight, as we've talked about multiple times here. But I think it's something we need to aspire to in the future.

DR. MCLELLAN: My sense is that the Board had a plethora of questions here. And that it's worth us maybe considering a subgroup particularly answering some of the questions that have been raised regarding support of these directions. Maybe additionally adding other guidance, things to think about as a part of that. And, you know, a number of you indicated that there's quite a bit here. So I would propose that we do create a subcommittee and consider, not an extravagant review, but a report that reflects some of our discussion here, reflects a little further

interaction with our experts and some guidance, if you would, going forward. Is that an agreeable route? If so I would be interested in any folks that might want to support that.

Mike, we were just agreeing to set up a committee to do a brief report in reflection of what we've been working on here. Scott, I'm going to ask you, would you be willing to chair that?

DR. GOTTLIEB: Sure, I'd be happy to.

DR. MCLELLAN: Great. Are there others that will join Scott as a part of this effort? Rhondee, Barb, Mike and Sean. You have half the Board, how's that.

UNIDENTIFIED SPEAKER: I think Lynn [inaudible].

DR. MCLELLAN: Yes, Lynn, we caught her. That's right, she was --

UNIDENTIFIED SPEAKER: [inaudible]

DR. MCLELLAN: Very good. Captain and gentlemen, thank you so much for being here. It really has been most enlightening. And our reaction here will be primary at question one and tying it to question four. We understand we haven't even come to two and three. Next meeting. Next meeting.

DR. KHOZIN: Thank you.

DR. MCLELLAN: So we are now --

UNIDENTIFIED SPEAKER: Can we get your email so [inaudible]?

DR. MCLELLAN: Yes.

UNIDENTIFIED SPEAKER: I'll send them to you. I'll circulate it out.

DR. MCLELLAN: we are now at our open public hearing portion of today's meeting. Both the Food and Drugs Administration and the public believe in a transparent process for information gathering and decision-making. To ensure such a transparency at the open public meeting session of the Science Board meeting FDA believes that it's important to understand the context of an individual's presentation. So for this reason FDA encourages any speakers at the beginning of their oral statements to advise the Committee of their financial relationship they may have with a company or group that might be affected by today's meeting. If you choose to not the issue of financial relationship at the beginning of your statement it will not preclude you from speaking. As

of today there have been no requests to speak, but now is the time if there is any in the audience that would like to step forward and we'll allocate a five-minute segment to you.

[No response.}

DR. MCLELLAN: And it doesn't look like we have any. So just some final thoughts. This was a fun format. Partway through this afternoon I leaned over to Rakesh and I said "I hope the Commissioner is absorbing all this." There is just a ton happening. And that is exciting. But I think that's part of our voice back to the Commissioner that he should be paying attention to these things. And that is one of the strengths of the Board. It has been a grateful day, tiring day. I don't know about you guys, but tiring for me. And but I appreciate you all being here. And welcome back, it is great to see your smiling faces and be interacting with you. Rakesh, we will be meeting again the fall, correct?

MR. RAGHUWANSHI: October 22nd.

DR. MCLELLAN: October 22nd, mark your calendars, we need you here. And with that I'll take a motion to

adjourn. Barb. Second, Sean. And we are adjourned. Thank you very much folks.

[Whereupon, at 4:01 p.m., the SCIENCE BOARD meeting was adjourned.