

1                                   SCIENCE BOARD TO THE  
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10                                   9:00 a.m.

11                                   Monday, April 23, 2018  
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18                                   FDA White Oak Campus  
19                                   Building 31, The Great Room  
20                                   10903 New Hampshire Avenue  
21                                   Silver Spring, Maryland  
22

Alderson Court Reporting  
1-800-For-Depo

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1 P R O C E E D I N G S

2 [9:00 a.m.]

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

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

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

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

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

1 Immunology.

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

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

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

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

11 MR. RAGHUWANSHI: Hi, Rakesh Raghuvanshi,  
12 Designated Federal Officer for the Science Board.

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

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

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

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

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

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

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

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

18 CONFLICT OF INTEREST

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

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

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

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

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

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

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

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

22       Today's meeting the idea is not to have a



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

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

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

1 [No response.]

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

5 So our discussion today is sort of at a  
6 30,000-foot level as we get into that. And as Rakesh  
7 reminded us, we want to stay absolutely clear of  
8 specifics in terms of specific products so we are  
9 absolutely safe in terms of our conflict of interest.

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

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

20 CHIEF SCIENTIST'S UPDATE

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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



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

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

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

20 RADM HINTON: Okay. Well, thank you.

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

1 you introduce yourself?

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

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

13 MR. RAGHUWANSHI: Maybe not yet.

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

20 FINAL REPORT FROM THE CBER RESEARCH  
21 PROGRAM REVIEW SUBCOMMITTEE

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

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

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

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

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

1 hear you fine.

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

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

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

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

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

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

1 disease area.

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

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

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

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

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

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

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

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

9 DR. MCLELLAN: (Inaudible.)

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

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

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

6 DR. MCLELLAN: Go ahead, Scott.

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

18 DR. MCLELLAN: Sean.

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

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

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

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

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

6 DR. MCLELLAN: Great. Laura.

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

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



1 -

2 DR. MCLELLAN: Platelet rich plasma.

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

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

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

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

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

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

1 DR. MCLELLAN: Barb. Go ahead.

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

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

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

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

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

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

1 DR. MCLELLAN: Thank you. Barb.

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

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

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

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

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

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

6 DR. MCLELLAN: Mike, go ahead.

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

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

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

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



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

5 DR. MCLELLAN: Ted.

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

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

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

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

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

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

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

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

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

15 DR. MCLELLAN: Great. Sean.

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

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

21 DR. XIE: So something -- under -- it's under FDA  
22 21, Chapter 11 they just combines on the software of

1 the computing facility security.

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

8 DR. XIE: Yeah.

9 UNIDENTIFIED SPEAKER: Yes.

10 DR. XIE: Okay. Thank you.

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

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

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

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

1 work on other areas which have higher priority.

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

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

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

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

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

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

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



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

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

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

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

17 DR. MCLELLAN: Go ahead Scott.

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

1 that a work in progress?

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

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

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

16 DR. STEELE: Great. Thank you very much.

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

1 DR. BYRNE: So I so move.

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

5 (Multiple ayes.)

6 DR. MCLENNAN: Those against?

7 (No response.)

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

14 [Recess in conference.]

15 [Conference resumed.]

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

1 Furia, if I got that right.

2 MS. FURIA-HELMS: Andrea Furia-Helms.

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

6 PATIENT AFFAIRS INITIATIVE AT FDA

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

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

22 So as I mentioned the Patient Affairs staff was

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

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

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

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

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

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

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

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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



1 would like to congratulate you because that is so  
2 needed.

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

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

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

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

21 DR. MCLELLAN: Sean.

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

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

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

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

1 with you.

2 DR. MCLELLAN: Barb.

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

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

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

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

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

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

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

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

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

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

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

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

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

1 oranges.

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

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



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

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

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

20 DR. MCLELLAN: Cynthia.

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

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

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

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

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

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

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

7 DR. MCLELLAN: Lynn.

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

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

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

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

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

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

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

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

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

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

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

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

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

22         MS. FURIA-HELMS: Thank you for all those



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

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

1 work. Thank you.

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

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

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

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

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

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

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

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

20 MR. SHAIKH: Thank you. Rhondee.

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

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

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

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

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

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

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

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

16 MR. SHAIKH: Thank you. Appreciate it.

17 MS. FURIA-HELMS: Thank you so much.

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

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

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

13 [Recess in proceeding.]

14 [Proceeding resumed.]

15 COMMISSIONER'S UPDATE AND OVERVIEW  
16 OF AFTERNOON DISCUSSION

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



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

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

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

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

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

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

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

22         Continuous manufacturing I think we have long seen

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

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

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

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

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

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

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

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

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

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

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



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

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

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

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

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

1 and really take it I think to another level.

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

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

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

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

1 for our decisions would greatly facilitate that.

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

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

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

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

7 DR. GOTTLIEB: Absolutely.

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

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

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

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

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

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

22 DR. KOWAKCYK: Right.

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

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



1 want to do.

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

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

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

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

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

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

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

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

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

22 DR. MCLELLAN: Thank you, Barb. Minnie.

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

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

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

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

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

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

4 DR. SARWAL: Thank you.

5 DR. MCLELLAN: Thank you. Lynn.

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

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

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

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

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

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

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



1 drugs.

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

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

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

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

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

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

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

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

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

1 to use the same data to help facilitate development.

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

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

1 DR. GOTTLIEB: Right. Thank you.

2 DR. MCLELLAN: Sean.

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

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

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

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

7 DR. GOTTLIEB: Yeah.

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

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

20 UNIDENTIFIED SPEAKER: Yeah. Six months ago.

21 DR. GOTTLIEB: Which I --

22 UNIDENTIFIED SPEAKER: Predictive toxicology,

1 yeah.

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

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

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

15 DR. KHOZIN: Thank you.

16 DR. MCLELLAN: Scott.

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



1 what their role would be or what --

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

4 UNIDENTIFIED SPEAKER: Yes, Elaine Johanson.

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

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

22 So right now the Open FDA data we do curate some

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

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

14         DR. MCLELLAN: Cynthia.

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

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

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

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

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

10 DR. MCLELLAN: Tony.

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

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

22 DR. GOTTLIEB: Right.

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

8 DR. GOTTLIEB: But you have the systems.

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

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

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

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

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

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

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

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

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

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

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



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

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

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

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

2 [Lunch break.]

3 [Resume proceeding.]

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

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

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

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

2 UNIDENTIFIED SPEAKER: No. Vahan is on the phone.

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

6 UNIDENTIFIED SPEAKER: Wi, are you on the --

7 MR. DONG TON: Yes.

8 UNIDENTIFIED SPEAKER: Okay.

9 DR. MCLELLAN: Good.

10 MR. DONG TON: Yes, on the call.

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

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

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

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

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

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

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

1 maybe on the phone. Could you mute your phone?

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

4 DR. MCLELLAN: Thank you.

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

6 DR. REISS: Good job, Mark.

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

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

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

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

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

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

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

1 through the approval process with well controlled  
2 studies.

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

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



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

5 DR. MCLELLAN: Okay. Vahan.

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

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

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

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

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

1 96 percent of EMR data has never been researched after  
2 the primary use. It's just a siloed place somewhere in  
3 somebody's hard drive. One of the major reasons is not  
4 the technology, it's the inability for the patient to  
5 participate in the decision-making process.

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

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

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

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

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

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

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

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

18 DR. MCLELLAN: Minnie.

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

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

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

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

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

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

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

13 DR. SARWAL: Yes, sorry.

14 DR. MCLELLAN: Okay.

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

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

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

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



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

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

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

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

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

6 DR. MCLELLAN: Sean.

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

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

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

6 DR. MCLELLAN: Thank you. Sean.

7 DR. XIE: Mohamed, is that right?

8 DR. SIMONYAN: No, Vahan Simonyan.

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

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

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

7 DR. SIMONYAN: Well, thank you for --

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

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

1 wherever.

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

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

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

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

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

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

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

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

22       DR. AFSHARI: Yeah, I just --



1 DR. MCLELLAN: Do you need a follow up?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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



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

3 DR. KHOZIN: Right.

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

6 DR. KHOZIN: Right.

7 DR. MCLELLAN: Laura.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

3         So when you mention like unless everybody gives up  
4 98 percent of all of the data all of the time you don't  
5 need to do that. Because imagine an ecosystem which can  
6 run intelligent processes. And that's what smart  
7 contracts are. You can have a software which is  
8 compliant running on the data without sharing the  
9 information, receiving the signals and then sharing the  
10 signal, not the data. So we are designing that into  
11 our technology. And to be honest I never thought of  
12 your use case, but I think that's wonderful much.

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

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

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

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

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

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



1 can leverage for this purpose.

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

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

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

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

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

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

11 DR. MCLELLAN: Lynn.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

18

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



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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

22 DR. MCLELLAN: Scott.

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

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

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

22 DR. KHOZIN: We have a program around expanded

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

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

13         DR. MCLELLAN: Minnie.

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



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

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

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

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

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

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

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

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

21           DR. SARWAL: Yeah.

22           DR. PATEL: -- generalizing that to any

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

13       If you don't have that information that feeds into  
14 the knowledge and the trust that we can then say that  
15 even though it went through a process, let's just pick  
16 510K, as we have currently, what's lacking or missing  
17 is, what I was mentioning earlier, is that real time  
18 know or real role knowledge of how the product actually  
19 works. That's what we're trying to set up in the  
20 coming year is trying to figure out a system that we  
21 can send products, we have organization confidence and  
22 in addition to product confidence that can then afford

1 people to have the trusted products in the marketplace.

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

14 DR. PATEL: Yeah. So --

15 DR. SARWAL: How do you accelerate that?

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

1 maintaining and managing it throughout the life cycle.  
2 And that entire life cycle is what we're looking at.  
3 But that's just a big component of how products perform  
4 in the marketplace. Can they evolve, can they change,  
5 can they be maintained? In addition to that first  
6 time, you know, gate of review that can happen in  
7 certain types of products. So that's what we are  
8 trying to shift the paradigm towards is going from a  
9 product base to adding to that is organizational based  
10 with the real world sort of aspects of access to that  
11 data. And how we get there I think that's to be seen.

12 But we are starting with this very, I wouldn't say  
13 narrow, but probably very broad base of software that  
14 is just the medical device and taking that.

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

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

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

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

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

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

6 DR. MCLELLAN: Okay, yeah.

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

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



1 2.0 if there such a thing. And AI maybe too. It's  
2 like how do you sort of get that confidence going back  
3 to our mandate of providing products to patients as  
4 fast as we can, but also with the high confidence? How  
5 we maintain that high confidence? I think that would  
6 be interesting, you know, if you guys have thoughts on  
7 that that will be good to sort of hear.

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

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

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

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

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

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

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

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

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

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

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

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

19 DR. MCLELLAN: Cynthia.

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

22 DR. MCLELLAN: Go ahead, Ted.

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

13 DR. MCLELLAN: Thank you. Cynthia.

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

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

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

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

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

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

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



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

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

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

1 DR. KOWAKCYK: Yeah.

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

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

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

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

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

17 DR. KOWAKCYK: I understand that.

18 DR. SIMONYAN: Yeah.

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

21 DR. SIMONYAN: I know.

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

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

8 DR. SIMONYAN: I agree.

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

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

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

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

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

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

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

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

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

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

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

14 DR. MCLELLAN: Okay. In the --

15 UNIDENTIFIED SPEAKER: [inaudible]

16 DR. MCLELLAN: I know. We have [inaudible].

17 We're going to keep going, but I really need to try to  
18 bridge to point number four. I don't know if we can  
19 rotate the screen here wherever that is. But remember  
20 I said at the beginning of this that we had a natural  
21 bridge to point four. And that's where we're looking  
22 at clinical trial data. It's still electronic health



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

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

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

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

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

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

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

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

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

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

1 difficult.

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

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

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

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

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

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

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

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

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

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



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

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

1 but I agree with everything you said about the trials.

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

11 DR. MCLELLAN: Rhondee.

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

14 DR. MCLELLAN: Yes, go ahead.

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

20 DR. GOLDMAN: That's a good ad.

21 DR. MCLELLAN: Rhondee.

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

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

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

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

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

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

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

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

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

1 administrative and billing activities.

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

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

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

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

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

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

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



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

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

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

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

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

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

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

19       DR. MCLELLAN: Barb.

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

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

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

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

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

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

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

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

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

17 DR. MCLELLAN: Barb.

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

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

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

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

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



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

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

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

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

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

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

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

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

12 DR. MCLELLAN: Mike.

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

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

3 DR. MCLELLAN: Minnie.

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

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

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

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

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

11 DR. MCLELLAN: Scott.

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

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

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

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



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

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

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

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

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

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

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

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

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

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

3 DR. KHOZIN:

4 DR. GOTTLIEB: -- evaluating. So --

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

13 UNIDENTIFIED SPEAKER: I think Lynn [inaudible].

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

16 UNIDENTIFIED SPEAKER: [inaudible]

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



1 DR. KHOZIN: Thank you.

2 DR. MCLELLAN: So we are now --

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

5 DR. MCLELLAN: Yes.

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

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

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

5 [No response.]

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

20 MR. RAGHUWANSHI: October 22nd.

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

1 adjourn. Barb. Second, Sean. And we are adjourned.

2 Thank you very much folks.

3 [Whereupon, at 4:01 p.m., the SCIENCE BOARD

4 meeting was adjourned.

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