Wednesday, March 4, 2015
8:33 a.m.

FDA White Oak Campus
Building 31, Room 1503
10903 New Hampshire Avenue
Silver Spring, Maryland 20993
PARTICIPANTS

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FDA REPRESENTATIVES:

MARGARET A. HAMBURG, M.D., FDA COMMISSIONER (on telephone)

DANIEL ACOSTA, PH.D.

DAVID ASHLEY, M.D.

BERNADETTE DUNHAM, D.V.M, PH.D.

JAN JOHANNESSEN, PH.D.

CAROL LINDEN, PH.D.

MELINDA K. PLAISIER

STEVEN POLLACK, PH.D.

DAVID WHITE, PH.D.

CAROLYN WILSON, PH.D.

ADDITIONAL FDA ATTENDEES/SPEAKERS:

CHEKESHA CLINGMAN, PH.D., M.B.A.

NATHAN DOTY, J.D.

ROBERT FISHER, PH.D.

SAU (LARRY) LEE, PH.D.
PARTICIPANTS (CONTINUED)

ADDITIONAL FDA ATTENDEES/SPEAKERS (CONTINUED):

MARTIN MENDOZA, PH.D.
TOD MERKEL, PH.D.
PAMELA SCOTT, PH.D.
LESLIE WHEELOCK, R.N., M.S.

INVITED SPEAKER:
ROBERT MEYER, M.D.
PROCEEDINGS

CHAIRMAN FREIRE: Thank you for being here today. We have a packed agenda, and it's even going to be a little bit more packed because we're going to try and do this at a polka pace so that we can get people out before the snow hits.

It is a pleasure for me to be here. This is my first official chairing day. So let's see how it goes. Martha, I hope I don't get fired by the end of the day.

And people here lie. It says that we're starting at 9:00 a.m., but we're not. We're starting now at 8:30 a.m. And the traditional start of this group is to do a short introduction of everybody that is around the table.

I apologize ahead of time because I won't be able to figure out who's on first and second for questions. So Bruce is going to be my buddy here, helping me. So if I don't get you in the right order, it's all Bruce's fault.

But we do have six new members. Martha, is that right?
MS. MONSER: Mm-hmm.

CHAIRMAN FREIRE: And we're delighted to have new members here. This is a very interesting group and a very important committee. And I would like to open the meeting today and start with the introductions, if we could start, please?

DR. GIBBONS: Hi, I'm Chris Gibbons. I am on the faculty of medicine at Johns Hopkins, the Associate Director of their Urban Health Institute there.

DR. JENKINS: Good morning. I'm Annalisa Jenkins. I'm the CEO of Dimension Therapeutics, a gene therapy company in Boston, and previously global head of R&D at Merck Serono.

DR. MCLELLAN: Mark McLellan. I'm a food scientist. I'm also Vice President of Research and Dean of Graduate Studies at Utah State University.

DR. REISS: Hi, I'm Ted Reiss. I'm the clinical development head in the primary care franchise at Novartis Pharmaceuticals.

DR. AFSHARI: Good morning. I'm Cindy Afshari. I head up preclinical toxicology at Amgen.

DR. RUSSELL: Alan Russell. I direct the
Disruptive Health Technology Institute at Carnegie Mellon University.

DR. XIE: My name is Xiang-Qun Xie. I'm Associate Dean for Research Innovation and also Professor of Pharmaceutical Science and Drug Discovery Institute. My field is in the pharmaceutical chemistry and computational chemical genomics for drug screening, University of Pittsburgh.

DR. WEAVER: Good morning. I'm Connie Weaver, head of Nutrition Science at Purdue University.

DR. KOWALCYK: Barbara Kowalcyk. I'm an epidemiologist and biostatistician, and I am a senior scientist in the Risk Assessment Group at RTI International.

DR. SARWAL: Good morning. I'm Minnie Sarwal. I'm a professor of transplant surgery at the University of California, San Francisco and previously medical director of the kidney transplant program for children at Stanford University, professor of pediatrics and immunology.

Thank you.

DR. YASZEMSKI: I'm Mike Yaszemski. I'm a
spinal and oncology surgeon and a chemical engineer. I work at Mayo Clinic, Rochester, Minnesota.

DR. TOSI: I'm Laura Tosi. I'm a pediatric orthopedic surgeon, and I run the bone health program at Children's Hospital here in Washington.

DR. BAHINSKI: Tony Bahinski. Member of the Advanced Technology Team at the Wyss Institute for Biologically Inspired Engineering at Harvard University.

DR. LINDEN: Good morning. I'm Carol Linden, the new Director of the Office of Regulatory Science and Innovation in the Office of the Chief Scientist here at FDA.

MS. MONSER: Good morning. I'm Martha Monser. I'm the Designated Federal Official for the Science Board.

CHAIRMAN FREIRE: Good morning. I'm Maria Freire. I'm president of the Foundation for the NIH, and I'm chair of this board.

DR. PSATY: Bruce Psaty. I'm a professor of medicine and epidemiology at the University of Washington, and vice chair.
DR. ASHLEY: Dr. David Ashley. I am Director of the Office of Science in the Center for Tobacco Products.

DR. JOHANNESSEN: Jan Johannessen. I'm the Deputy Director for Science in the Office of Translational Sciences in the Center for Drug Evaluation and Research.

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

DR. ACOSTA: Dan Acosta, Deputy Director for Research, the National Center for Toxicological Research at Jefferson, Arkansas.

DR. POLLACK: I'm Steve Pollack. I'm the Director of the Office of Science and Engineering Laboratories in the Center for Devices and Radiological Health.

MS. PLAISIER: Good morning. Melinda Plaisier. I'm the Associate Commissioner for Regulatory Affairs, and I look forward next meeting to introducing you to my new Deputy for Regulatory Science, Dr. Paul Norris, who was just appointed and
 couldn't be here yet today.

DR. WHITE:  Good morning. My name is David White. I'm the Chief Science Officer and Research Director for the Office of Foods and Veterinary Medicine.

DR. DUNHAM:  Good morning. I'm Bernadette Dunham, Director for the Center for Veterinary Medicine.

CHAIRMAN FREIRE:  Thank you very much. I believe we may have one or two members of the board on the phone?

Bill, are you on the phone?

(No response.)

CHAIRMAN FREIRE:  What about Lisa?

DR. NOLAN:  (on telephone) Yes. I'm Lisa Nolan. I'm Dean of the College of Veterinary Medicine at Iowa State University.

CHAIRMAN FREIRE:  Thank you, Lisa.

Bill, are you on the phone?

DR. HAIT:  (on telephone) Yes, this is Bill Hait. I'm the global head of R&D at Janssen Pharmaceutical Companies of Johnson & Johnson.
CHAIRMAN FREIRE: Thank you very much.
Have I not recognized anyone?
(No response.)
CHAIRMAN FREIRE: Very well. Thank you very much.
Martha?
MS. MONSER: Okay. Good morning. Welcome, everyone, to the Science Board members, our FDA staff, and members who are -- sorry. And we'll start right off with that, a reminder that we need to have our microphones on when we speak and turn them off when we're not speaking and apparently get close to them as well, so that the transcriber can pick up everything that is being said when you speak.
I'm also going to ask, too, that please remember to silence your electronic devices. That will help minimize the disruptions.
Today, the Science Board will be provided with a follow-up on FDA's activities regarding the reintroduction of bovine heparin. This topic was previously discussed at the June 2014 Science Board meeting.
The board will be provided with an overview of FDA's public access policy and will hear progress reports from two subcommittees, the Commissioner's Fellowship Program Evaluation Subcommittee and the Science Looking Forward Subcommittee. FDA is seeking your input, the Science Board, regarding approaches to regulatory science training coordination.

The board will hear an overview of science-related activities from the Center for Tobacco Products, and also today the recipient of the 2014 Scientific Achievement Award for Excellent in Laboratory Science will provide an overview of the activities for which the award was given.

All members of this committee are special Government employees and are subject to Federal conflict of interest laws and regulations. The following information on the status of this committee's compliance with Federal ethics and conflict of interest laws covered by, but not limited to those found at 18 U.S.C. Section 208 is being provided to participants in today's meeting and to the public.

FDA has determined that the members of this
subcommittee are in compliance with Federal ethics and conflict of interest laws. Under 18 U.S.C. Section 206, Congress has authorized FDA to grant waivers to special Government employees and regular Federal employees serving on advisory committees who have potential financial conflicts when it is determined that the agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Related to the topics for today's meetings, members of this committee have been screened for potential financial conflict of interest of their own, as well as those imputed to them, including those of their spouses or minor children and, for purposes of 18 U.S.C. Section 208, their employers. These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment.

In addition, if any of the members have any interests that were not disclosed earlier, please state them at this time.
Based on the agenda for today's meeting and all financial interests reported by the committee members, no conflict of interest waivers have been issued in connection with this meeting.

We have one open public comment period scheduled for 1:30 p.m. this afternoon, and there have been no requests to speak. If anyone in the audience wishes to comment during this period, please announce yourself then. And if there are no speakers, we will move the agenda up accordingly.

And I have already mentioned about turning the microphones on and off and silencing your electronic devices. So I turn this back to Maria to move on with our agenda for today.

Thank you.

CHAIRMAN FREIRE: Thank you very much. Thank you, Martha, and thank you, everybody, for completing your conflict of interest forms. They will become very familiar to you.

The tradition of this board is to have a
presentation by the chief scientist. Today, Dr. 
Ostroff is on Capitol Hill. So we're delighted to have 
Dr. Linden here today -- She says she's newly minted. 
So we have to find out how newly that mint is -- to 
give us an update.

And she's going to focus, I understand, 
particularly on her group and her responsibilities.

DR. LINDEN: Thank you very much.

So, so my newness dates to January 12th, 
which is when I joined the FDA. So not quite two whole 
months here, and everybody, and particularly Dr. 
Ostroff, decided to be very kind to me and give me a 
pass on attempting to represent all of the activities 
going on in the Office of the Chief Scientist.

So I will be calling upon my colleagues to 
present their portions of this briefing and provide 
updates on the office -- on the activities in their 
particular offices.

Where do I point this to make it work? Up?

Okay.

So the agenda for this little portion of the 
meeting is this update to you. Leslie Wheelock will
provide an update on travel and conference attendance
for FDA scientists, and then I will lead off the update
for the Office of the Chief Scientist by giving you an
update on my office, the Office of Regulatory Science
and Innovation.

And then my colleagues from these other
offices listed here -- from OCET, the Office of
Counterterrorism and Emerging Threats -- will give an
update on the MCMi program, and then Dan will give an
update on the National Center for Toxicological
Research. And we will have updates from Women's
Health, Minority Health, and the Scientific and
Professional Development Program, and from Nathan Doty
for the Office of Scientific Integrity on public
access.

So I will dive into this with first a welcome
again to the new members of the board -- I feel like
I'm joining you in newness here -- to Cindy Afshari,
Tony Bahinski, Annalisa Jenkins, Minnie Sarwal, Connie
Weaver, and Sean Xie.

Thank Maria for being the chair this year and
Bruce for being the co-chair. And just I want to call

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to your attention that there is a Federal Register Notice that's open now, calling for nomination of new members. So if you have any colleagues or folks that you know who you would like to suggest nominating or encourage to self-nominate as new members of the board, please encourage them to do so. That closes March 24th this month.

So, with that, I'm going to turn this over to Leslie for a moment to give you an update on the issues surrounding travel for Federal scientists, Federal employees, and conference attendance.

MS. WHEELOCK: Thank you, Carol.

And I want to thank the Science Board for their interest in the FDA's travel and conference attendance, which you voiced last year. So this is an update in terms of where the agency is with travel and conference attendance.

And some of you may know that, originally, the restrictions and limitations around travel and conference originated with a Presidential Executive Order, which then became an OMB memo, which then became language into the appropriations bills.
So just to let you know that earlier this year, in 2015, the FDA did conduct an assessment, and we were really trying to determine the impact of the 2012 travel and conference attendance restriction policies on our scientific staff. Some of the questions we assessed were the importance of attending the conferences, the negative impact that these restrictions have on our scientists, and the denials that were occurring.

We surveyed 10,416 of our scientists, which is basically all of our scientists, out of the 16,000 FDA population, and we got a 33.4 percent response rate on it. And these are some of the results. These are just preliminary results.

In terms of the importance our scientists see attendance at conferences, you can see that collaboration and really keeping up with the science is very important to them. The negative impacts, as you can see from the second bullet, is that retention of our scientists, also the information that they have, that they don't have, it impacts on their ability to do research and review in their work, and also recruiting.
The way travel is approved in the agency is it begins at the local level and then advances up to the center level. So we did reach out to all the centers and ask them how many denials were actually occurring in the agency?

And from the centers, we found that in Fiscal Year 2014, there were 2,288 conference requests at the center level that were actually submitted, and of those, only 7 were denied. The approvers really tried to work with the centers in terms of trying to look at decreasing the cost in various ways so that they could approve the conference.

However, our results with the individual survey showed that there were denials at the local level, meaning from directly by a supervisor or director or -- a division director or an office director. And a lot of those were related to work responsibilities.

The good news that we have on the upcoming year is that in the current Fiscal Year 2015 appropriations bill, there is language that says that
the Federal agencies have flexibilities in how we implement these restrictions. And currently, right now, the FDA is participating with the department, HHS headquarters, as well as other OpDivs within the HHS, to really look at how we're going to implement those restrictions so that we can really support our scientists going to these conferences.

So this is just an overview of where we are, and we're still looking at the data that we received.

CHAIRMAN FREIRE: Thank you very much.

This board has expressed many times the concern that scientists need to be up to speed and part of the conversation at the highest scientific level. So we appreciate -- seven doesn't look like very much, but we don't know how many were triaged earlier. So I'm glad that there is money in the budget for that.

DR. LINDEN: Thank you.

I'm going to move on to the update from ORSI, and Maria is giving me the sort of virtual poke with a stick here. So I just want to -- I'll summarize the slides. I'm not going to read them to you.

For the Intramural Grant Programs across the
Office of the Chief Scientist, we've established mechanisms using SharePoint as a vehicle to sort of harmonize the process for intaking and managing all of these grant programs. In 2015, you can see on the right-hand side of the slide, the awards that have been made or are in the process of being made, and those include not only new awards, but also renewals or continuations into a second or third year of existing awards.

The Broad Agency Announcement is very popular. You can see here a summation of the number of white papers received, proposals reviewed, and awards that were made for Fiscal Year 2014, and I will just note that since the renewal of the Broad Agency Announcement, which aligns with the nine focus areas in the Advancing Regulatory Science Strategic Plan, we've received something like 45 quad charts and white papers already in response to the reposting of the Broad Agency Announcement.

We have four CERSIs, Centers of Excellence for Regulatory Science and Innovation, established in academic institutions, two that were established 4
years ago, the University of Maryland and Georgetown, and two new ones. The University of Maryland CERSI has done a lot of work collaborating primarily with CDER and CDRH and has a number of education and training activities that are ongoing.

I would also note, if you are interested in more details about any of the CERSI's, each one of them either has or is in the process of getting up their own Web sites. So there is a lot more detail available there on their Web sites, as well as, I think, through our Web site.

The Georgetown CERSI is also one of the original ones, and the projects that they are wrapping up right now are on vaccine information and safety, as well as a project that they're doing with the Office of Minority Health on triple negative breast cancer amongst minority women. And you can see the education and training activities listed here that are ongoing in that -- in that program.

We have the two new CERSI's, UCSF-Stanford and Hopkins, and the projects that they have initiated are listed here. For UCSF-Stanford, they have five
programs going on, again primarily in collaboration
with CDER and CDRH. They've established some
educational programs in the form of lectures,
roundtables, and integration into academic programs,
and they are also facilitating a CERSI network so that
the four academic organizations, institutions in the --
who have CERSIs can network together and cooperate more
effectively.

And the last one is the Hopkins CERSI.

Again, the first-year projects are listed here. I call
your attention to the second bullet there, eliciting
patient preferences to enhance regulatory science.
This is turning out to be a very interesting area to
delve into. And then below are listed some of their
education and training activities that they are
advancing.

An important focus this year in 2015 is to
stand up or fully establish a Technology Transfer
Program within FDA. Previously, we had a very small
staff here with much of the support to technology
transfer being provided to us by an interagency
agreement with the National Institutes of Health
Technology Transfer Office.

That office is being decentralized. So all of the entities, both at NIH and outside of NIH, that were being supported by that office now have to establish their own capabilities. So on the left of this slide, you see a summary of some of the activities that went on in Fiscal Year '14. The centers are very active, the scientists in the centers, in filing invention disclosures, many of which turn into patents.

We have a number of collaborations that are established through this office, and we also manage the royalties that come back into the FDA into the centers and to the scientists from their patent and licensing activities. So we are going to be expanding this office or attempting to expand this office by bringing in the personnel that we need to support all of the technology transfer activities that are going on within FDA.

I'm going to turn the podium over to Robert Fisher to give you an update on what's going on in the Office of Counterterrorism and Emerging Threats, specifically in the Medical Countermeasures Initiative.
DR. FISHER: All right. Good morning, everyone. Like Dr. Linden, I'm relatively new to this position. I started work actually last week. So please bear with me, and I'll look forward to working with you in the future.

But for now, we've been rather busy with a little bug you may have heard of called Ebola, and what the Office of Counterterrorism and Emerging Threats is involved in is really facilitating efforts across the FDA and also coordinating with our other U.S. Government partners. Specifically, we've been providing scientific and regulatory advice to developers and to other USG agencies to support product development in the Ebola mission space.

We've also worked with these sponsors, our international regulators in West Africa and the World Health Organization and NIH, to manage to launch clinical trials to evaluate Ebola vaccines, and this was done under a very accelerated timeline, as you can imagine. And it's also important to note that we're doing this in a manner that is scientifically justified.
in terms of looking at randomized clinical trials.

Likewise, the same thing applies to our collaboration with NIH to establish a common protocol to help evaluate investigational treatments for Ebola, not only vaccines. We've also been collaborating with our international partners to support their efforts to respond to Ebola. We've also been working with our partners in the centers, mainly CDER, CBER, and CDRH, to facilitate access to investigational medical products for patients to be treated -- to treat patients with Ebola when that's requested.

And a bullet point here. Our office doesn't do the regulation. We facilitate and coordinate, but with that said, we helped to authorize the use of seven diagnostic tests for Ebola virus under emergency use authorization authority.

Some additional bullet points here. The first clear waiver for a nucleic acid-based was granted for an influenza diagnostic. Rapivab was approved to treat influenza infection in adults. While we're focused on Ebola, we're also keeping an eye on MERS and influenza and a few other things.
We managed to work with CDRH to issue a guidance on radiation biodosimetry device. Now this is a draft guidance. It's not final. It's out for comment.

And finally, we've been working to avert product shortages for a nerve agent treatment. That's the DuoDote auto-injector, and we're doing this based on scientific data to extend the shelf life of these units while we work through manufacturing issues associated with the device itself.

With that, I'd be happy to answer any questions.

DR. LINDEN: Actually, we're going to save questions for the end.

DR. FISHER: Okay.

DR. LINDEN: And move on to a brief update from NCTR from Dan Acosta.

DR. ACOSTA: Well, good morning. I'm here representing the National Center for Toxicological Research. William Slikker is the Director. He could not be here.

So again, like some of the other individuals
here, I'm fairly new. I've been here just a little over 1 year. I've been told you're not considered an old FDA employee unless you've been here 5 years or more. So I'm still learning a little bit about all the different aspects of FDA.

However, for those who are new on the Science Board of FDA, NCTR -- and as many of you know, FDA is a regulatory agency. And so, most of the centers that are identified within FDA regulate a number of products that have a major impact on the American public.

However, NCTR does not have any regulatory functions. Its primary function is to provide major research assistance and support to these regulatory centers at FDA. So in terms of what we'll provide today is to give you an idea that NCTR works very closely with the different FDA centers to identify research that these centers feel are important to the regulation of their products.

So with the next slide, just to give you an idea, I can't give you all the various research projects we're doing. So these are selected examples, and Dr. Ashley will be talking about the relationship...
But very recently, CTP and NCTR have developed a nice collaborative effort on a number of projects that CTP finds very important for their regulation of tobacco products. As you can see, there are a number of at least 18 identified projects that CTP feels that are very important and which NCTR scientists can help provide research support.

NCTR has about over 500 individuals, scientists and staff personnel, located in Arkansas, the natural State of Arkansas. And for those who have never been there, we're in Jefferson, Arkansas, which is just outside of Little Rock and really located in an Eden-like setting in a major pine forest.

So those who do come to Arkansas may be quite surprised to find NCTR located really 40 miles from Little Rock. So it's we hope that many of you can come and visit NCTR.

So these projects that we are doing, especially with CTP, CDER, CBER, CDRH, CVM, the various centers, we have a number of projects that are ongoing right now. And the ones with CTP, you can read to see

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some of the active projects that are ongoing now.

Another important activity of NCTR is to promote a global coalition of FDA-like agencies around the world. So this coalition for regulatory science research was developed several years ago with the leadership of the Commissioner, Peggy Hamburg, and with a number of individuals at NCTR, Bill Slikker, and individuals from the other regulatory centers at FDA.

And so, we've been having meetings, global summits, to discuss various topics, and the last one was held in October -- excuse me, last November in Montreal, and the next one will be held in Parma, Italy, focusing on regulatory science research. So we have a number of individuals from around the world who have -- are very active in this particular activity.

Other types of projects that we're doing. You can see under quantitative assessment of genotoxicity data, we have the Division of Genetic and Molecular Toxicology, Dr. Bob Heflich. He's very active in the area of genetic toxicology. He serves as a representative for this global committee in the area of genotoxicity assessment of data. And he's been a
leader in promoting this type of global cooperation in genotoxicity assessment.

Another type of agreements that NCTR has, they're called interagency agreements, and a major one is with the National Toxicology Program, NTP, of the National Institute of Environmental Health Sciences. This group identifies, NTP identifies chemicals of interest that should be investigated in more detail toxicologically.

And you can see there, over the years, NTP and NCTR have collaborated on a number of activities in the areas of looking at such compounds as bisphenol A, retinyl palmitate, triclosan, melamine, et cetera. And so, these studies have been all documented and reported in technical reports, which provide very important information to the American public, as well as FDA, EPA, and NIH.

Another example of activities that NCTR is working on is in the area of sequence quality control, or identified as MAQC IV, a consortium of a number of scientists from around the world in which NCTR leads in developing next-gen sequencing technologies in the
regulatory arena.

So I know that I just briefly covered these projects. So, thank you.

CHAIRMAN FREIRE: Thank you very much. We appreciate all of that.

Now I'm sensitive to the time, but I'm always glad to welcome Dr. Scott. So, again, we're going to try and accomplish this in record time here.

Thank you. We'll take -- I already have two questions. So if you want to queue up for questions, let me know.

DR. SCOTT: Good morning. The advice and recommendations that you provided to us last year has been invaluable as we develop our women's health research roadmap. We are planning to release this, hopefully, in time for the Fiscal Year 2016 Office of Chief Scientist joint application process.

For Fiscal Year 2015, OWH is fulfilling its commitments to second-year funding for projects that we funded last year, and for this year, we're focusing in on funding research in two areas. We instituted a new research funding stream in which we are providing
supplemental grants to ongoing or planned center-level research in which we're providing supplemental grants to address sex and gender differences, as well as providing funds to the centers to support their activities in the implementation of FDASIA Section 907 action plan.

As part of the action plan, OWH's responsibilities as lead fall under the development of the research roadmap and also working with NIH's Office of Research and Women's Health and developing a clinical trials initiative to encourage diverse women to participate in clinical trials.

In addition to funding research, we also conduct research every year, and the three research projects that we're focusing in on this year focus in on a systematic review of pregnancy exposure registries, assessment of the inclusion of women in the conduct of sex analysis and select drug applications, and also the assessment of FDA's OWH's regulatory research program, the regulatory impact.

In terms of the pregnancy initiative, we also are revamping our pregnancy exposure registry Web site,
and also we are increasing our digital and print information dissemination.

OWH continues to conduct digital and print outreach to disseminate FDA health information and safety information to women's health stakeholders, including consumers, health professionals, affinity groups, and women's organizations. The Take Time To Care outreach program is currently collaborating with both Federal and private partners to disseminate OWH publications materials from CFSAN and the Office of Consumer Information.

The College Women's Campaign is expanding its digital and stakeholder outreach to help increase college women's access to FDA information, as well as OWH is continuing our social media outreach in terms of e-blasts to disseminate FDA risk communications and also our Twitter and Pinterest outreach.

Thank you.

CHAIRMAN FREIRE: Thank you so much. That was well done and quickly.

Dr. Mendoza? I think we have a microphone on back there. We may want to turn it off.
MS. MONSER: Annalisa? Yeah, thank you.

DR. MENDOZA: Good morning, everyone. My name is Martin Mendoza, from the Office of Minority Health, and this morning I just want to give you a quick update on what the office has been up to for the past couple of months.

So, as many of you are likely aware, in August of 2014, FDA released the FDASIA 907 actuary report, which is a plan to improve the quality and transparency of demographic subgroups, data reporting analysis, as well as address the participation of these subgroups in clinical trials.

Since then, the office has been hard at work at implementing this action plan. Specifically, next month, OMH will host a roundtable meeting jointly with the Institute of Medicine, entitled "Participation in Clinical Trials," that will attempt to address several of these subgroup questions.

And OMH has also been working closely with the inclusion governance board at NIH to learn what NIH has done as far as inclusion and sort of share best practices and see -- look for the areas that we can
Moving on to our research and collaborations program, last month OMH funded three projects with our FDA intramural program. The first with CDER, which looks at a molecular characterization of multiple myeloma in African Americans and European Americans. The second with NCTR that will conduct an EWA study of lupus also in African Americans and European Americans. And the final -- the third and final project that was funded is with CDER -- I'm sorry, with CBER, which seeks to develop a human cytomegalovirus assay to look at antibody responses in racial and ethnic minorities.

As was mentioned earlier, OMH also participates within the CERSI program, and we recently received the final reports from two health literacy projects, one each with Georgetown and the University of Maryland. And the office is currently reviewing those reports.

We are also developing projects, proposals with our two new CERSI sites, UCSF-Stanford and Hopkins, and hope to submit those proposals for consideration for funding later this summer.
Recently, OMH signed an MOU with the Satcher Institute at the Morehouse School of Medicine to fund two of their health policy research fellows. These projects will be in regulatory science with a focus in minority health.

And last week, OMH released a Federal Register Notice asking the public for input on our research agenda, and that closes on the 24th of next month.

Moving on to our communications and outreach program, OMH has been involved in several department-wide collaborative efforts. These include the commemoration of the 30th anniversary of the landmark Heckler report, the Million Hearts Initiative, and then also working with the Office of External Affairs to promote colorectal cancer screening awareness, as March is Colorectal Cancer Awareness Month.

Later this month, in March, OMH will host a webinar to assist the public with how to better communicate with FDA. Specifically, how to find and comment on FDA dockets. The office is also pleased to announce that we recently hired a new public health
adviser who will help coordinate the implementation for our office of the FDA Language Access Plan.

And then, as many of you know, next month marks Minority Health Month. So FDA -- I'm sorry, OMH has several activities planned to commemorate that or to promote it. These include displaying several research posters throughout the White Oak campus from several of our research fellows that we've hosted throughout the year, as well as hosting a joint scientific seminar with CDER that will host Dr. Joseph Wright from the Howard University College of Medicine. So we've been quite busy over the past couple of months, and we're looking forward to continuing that momentum.

Thank you.

CHAIRMAN FREIRE: Thank you, Dr. Mendoza. You have been busy, indeed. Congratulations.

All right. So moving on to the report from the Office of Science Professional Development update.

MS. WHEELOCK: Yes, and the Office of Scientific Professional Development coordinates agency-wide training programs, as well as work with the agency
to coordinate agency-wide training and development, as well as manage our agency-wide peer review, SBRS, and Scientific Achievement Award programs.

So some of the things that we've been doing since the last Science Board is that we've graduated 18 Commissioner's fellows in the fall, with 14 of them remaining at the agency. We're also actively in the process of announcing the recruitment for the eighth class to begin in October of 2015.

We also worked with the agency in helping them launch the FDA Fellows Association, which really is a nice forum to bring all the fellows together. And in terms of training, agency-wide training and development, we worked with the agency groups to implement genomics and medical countermeasures training. And we also support the CERSIs for training that's for the FDA staff.

And then in terms of bringing awareness to and supporting the STEM initiative, we host academic visits. So we had University of San Francisco and Duke come and visit us. And we also launched with the agency the STEM program, where we're now going to be
participating as an agency in conferences, such as the emerging researchers national conference that occurred in February.

And that's it for right now. Thank you.

CHAIRMAN FREIRE: Thank you all very much.

This has been a tour de force, and I know we haven't done justice to anyone who has presented today. So apologies for that, but we're very grateful for the bird's eye view. And I know that some of you have come before us in the past, and we, I'm sure, will ask you to come forth again.

We have some questions. I know that Dr. Hait, who is on the line, has a question and a comment.

Bill?

DR. HAIT: It is pronounced "hite," but you're not the first to mispronounce it.

So it's a comment. Great congratulations to the FDA in stepping up on the Ebola problem. Our subsidiary, Crucell, is working on a vaccine and has been very much involved with this. Here's my question. One of the problems that we face in the field is that the outbreak has at one point been decreasing
dramatically, although there's an uptick recently. And
with the dramatic decrease in number of cases, thank
goodness, it creates a problem for an efficacy trial
because the control arm would have no cases, or at
least very few.

This would lead to the question of whether or
not the FDA has -- is considering or has made an
opinion about an approach called the "animal rule." I
don't know that currently that's worth discussing, but
I just wanted to bring it up as a potential issue on
the ground in Africa, where our teams are busy setting
up the trials.

MS. MONSER: Robert, can you answer that for
us or have any information on that? Hold on, Bill.

DR. FISHER: Hello. Yes, actually, the FDA
has been engaged with several other Government
partners. We have what's called a thing which is a
working group to develop animal models for looking at
filovirus infections and therapeutics and vaccines.

So we are very much keeping the animal rule
on the table for the event, as the case may be, in case
the case rate goes down to the point where the clinical trials will be uninformative. So, yes, the animal rule is still very much in our minds.

DR. HAIT: Thank you very much.

CHAIRMAN FREIRE: Dr. Russell?

DR. RUSSELL: So I'm not sure if this is a question or a comment, and I'm also not sure whether I'm raising a red flag or a white flag of surrender because I've said the same thing a number of times.

As the agency drives forward in technology transfer activities and continues to seek licenses and all the things that come with that, that's very exciting for the inventors, and it seems like it's really good for the agency.

But I think it's a really dangerous road to go down because you get into a great deal of conflict of interest, not just institutional conflict of interest. But I think the center directors will begin to face real challenges finding the most experienced reviewers if those reviewers have been conflict of interested out of reviewing things that they've been filing patents on.
I know the agency has been thinking carefully about how to handle those conflicts of interest, but as I sort of saw the numbers of licenses and sort of pride about the amount of money coming in, I just want to again raise a real caution that doing tech transfer from Government in an agency that is responsible for reviewing technology I think bears really significant risk.

CHAIRMAN FREIRE: Dr. Linden, do you have any comment?

DR. LINDEN: I appreciate your sharing your concern, and I definitely will take note of that. And I know that Carolyn Wilson is going to comment on that, but I think the way the different centers manage their scientific research programs and their review functions -- and Carolyn can address this especially for CBER, which has the most integrated, I think, situation. But in the other centers, my understanding is that the reviewers and the researchers have somewhat of a separation between them.

But certainly, this is an issue that we need to address, I think, especially within those centers.
where the scientists execute both functions. And I
appreciate your concern.

DR. WILSON: So I just wanted to remind you
and the committee that it's actually a requirement of
the Bayh-Dole Act that we have to do this. We have to
protect our intellectual property. So it's not really
an option.

But the other thing is, is that we definitely
take conflict of interest very seriously, and we have
means to document that. And we're in the process,
actually, of developing a database so that it's more
integrated into the regulatory management of the
various regulatory applications and how they're filed
that we'll actually be getting flags coming up to say,
you know, certain reviewers may be involved.

But I also want to point out that not
everything that we are doing in the tech transfer space
is necessarily related to development of a product that
we regulate. Some of it may be development of
methodologies or other things that may not even be
within the domain of our regulatory portfolio.

So just because you see the numbers go up
doesn't necessarily mean that's also a huge red flag for conflict of interest.

DR. POLLACK: I'd also add -- this is Steve Pollack from CDRH -- that primarily the inventions that come out of our organization tend to be evaluative tools and not devices as such. So there, the conflict piece goes away.

CHAIRMAN FREIRE: Dr. Reiss?

DR. REISS: Just a brief follow-up question on that. How is the money from tech transfer used within the agency? How is that money applied?

DR. LINDEN: So the distribution of those royalties that come back in are dictated by the statutes that govern technology transfers. So I think a small percentage of it we can use for sort of operating the program. Some of it goes to the centers for supporting research in the centers, and then there is a prescribed amount that is allowed within a ceiling to go to the inventor themselves, the scientists.

CHAIRMAN FREIRE: I had the great honor of heading the Office of Technology Transfer at NIH, and FDA was one of the groups that we managed. NIH
actually has -- had historically the overarching responsibility for technology transfer and policy in this space. And that provided some buffer because the negotiations were happening at the NIH level, as opposed to the FDA level.

And with the restructuring at NIH, things are getting a little complicated. The agency can choose to protect or not to protect. There's no obligation to protect the technology. They have to evaluate internally if they want to protect the technology.

But I must remind you that there is very active science going on at the FDA, and there is some excellent technology that comes out of the FDA, and products have reached the market based on technology that was developed in this agency. And I can tell you that firsthand.

As has been said before, this is statutorily mandated, and the $150,000 cap for the scientists is true for all Federal agencies. So the concern I have more is one of simply how to get it done. This is not a simple process. It's a very complicated process, and the amount of money that you get at the other end, it

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has to be outweighed and balanced with the enormous investment that it takes to actually protect intellectual property.

So I'm sure that there are a lot of lessons that have been learned by others, and those of us around the table who might have some experience I know will be glad to be of help, if that would be important to the agency.

Any other comments or questions?

(No response.)

CHAIRMAN FREIRE: Very well. Thank you very much.

We now go to the heparin update. Let's remind the board and the particularly the new members of the board that this board was asked to weigh in on a discussion of heparin. And we face some interesting challenges in heparin, and I am -- the board asked for an update following the discussion that we had actually in June 2014.

So it's not quite a year, but it's several months down the road. So, thank you. Dr. Lee?

DR. LEE: Okay. Thank you very much.
First of all, good morning, everyone. I also want to thank for the opportunity for me to give an update on this very important initiative for CDER. Before I report our progress on this key initiative, let me first recap some of the main conclusions as well as recommendations that we received from the June 4, 2014, Science Board meeting. In that meeting, the Science Board agreed with CDER that diversifying the heparin supply chains is critical to help to ensure the continuous supply of high-quality heparin products in the United States. Specifically, the introduction of bovine heparin could be a viable option.

However, the Science Board emphasized that the CDER should further assess and address the potential risks associated with bovine heparin, particularly with respect to the potential exposure to BSE agent. We have received many good recommendations from you guys. Due to the time constraint we have today, I will only focus on the Science Board’s main recommendations, which suggested that CDER should further assess or explore a multiple step approach for...
minimizing the BSE risk in three key areas for bovine heparin.

These areas include quality of source animal by considering the prevalence of disease within the source country, slaughterhouse practices, and most importantly, capability of heparin manufacturer process to mitigate or eliminate the risk of BSE infectivity.

Following these recommendations, we have a Bovine Heparin Working Group currently working on these three key areas in order to address the potential risks associated with the use of bovine heparin. As you can see here, this working group includes the CDER heparin experts from the Office of Pharmaceutical Quality, Office of New Drugs, and Office of Compliance Office, which is not shown here -- my mistake -- as well as the CBER BSE experts from the Office of Blood Research and Review.

As you can see here, this working group represents a really wide spectrum of expertise that can cover chemistry, kinetic, as well as comprise aspect of heparin-related issues.

Let me first touch upon, a little bit upon
the first area. We are currently working on the BSE risk mitigation strategy to ensure a proper control of source animals. We have -- based on your recommendation, we have consulted with CVM, as well as USDA in this area.

We have considered manufacturers in controlling the BSE risk at source animal level. For example, these factors include criteria identified by world organization for animal health for the risk status of countries susceptible to the BSE, the type of tissues used for heparin production, age of cattle, as well as procedure utilized in USDA ante- and post mortem inspection for animal health.

By lowering the BSE through a proper control of source animal, for example, by using cattle or animals only from the countries with negligible BSE risk, we believe that this actually constitutes the first important step in our overall risk mitigation strategy.

We are also working on the strategy to avoid cross-contamination with specified risk materials, such as the cattle's brain tissue where the BSE agents may
be present. Based on our consultation with CVM and USDA, as well as based on our prior experience with porcine heparin, we have identified several areas to focus on with respect to the slaughterhouse practice as part of our overall risk mitigation strategy.

Let me just give you some example. We recognize that it is important to use a proper stunning method or device that will not spread the high-risk or specified risk materials to other tissues during the slaughtering of cattle.

For the purpose of application review, we will evaluate whether the slaughterhouse has a proper procedure or validation method for removal, segregation, and disposal of the specified risk materials, equipment cleaning, and traceability of crude bovine heparin materials that will be used for heparin production.

During the June 2014 Science Board meeting, although CDER indicated that the heparin manufacturing process has an intrinsic capability to reduce the risk of BSE infectivity, the Science Board suggested that it will be still important to systematically investigate
to what extent the heparin manufacturing process can reduce BSE risk through a well-designed study.

In line with this recommendation, I am happy to say that we have initiated a research project or research activity to investigate this key aspect of our overall risk mitigation strategy. We have made pretty good progress on this research study. Let me just briefly summarize what we have done.

We have developed a bench-scale manufacturing process to produce pure bovine heparin from the crude bovine heparin material. We have also tested the process steps of this manufacturing process with the crude bovine heparin material spiked with sheep TSE agent, and the infectivity test based on the animal assays are currently in progress for this phase of study.

And very soon, we will also test these process steps for their capability to reduce the BSE risk with the crude bovine heparin materials spiked with the BSE agent. And the removal of the BSE agent will be determined by using the traditional animal bioassays, which is based on the recovery of BSE.
infectivity, as well as the new in vitro method, the
so-called real-time, quick method that measures the
recovery of abnormal prion proteins, which is used as a
circuit for BSE infectivity.

We will look for -- we will look at these two
results and then to see whether they are correlated
with each other. I want to emphasize that this in
vitro assay, if validated in this study, can really
provide a very quick assessment of BSE infectivities in
only 2 to 3 days, as opposed to the traditional animal
bioassay, which takes about 1 year to find out.

So this will actually provide a real-time
monitoring of the quality of the heparin products with
respect to the BSE risk. We also reviewed the existing
validation methods of TSE or BSE clearance.

In addition to the activity I just described
from the previous slides, we also have completed or
initiated other FDA heparin-related activities, in part
based on your recommendations. Let me just briefly go
through this, and I'm not going to go into details.

These activities include analysis of global
distribution of pigs and cattle available for heparin
production, meeting with stakeholders to understand or to listen to their comments or input related to bovine and porcine heparin, structural characterization of bovine heparin and exploring the utility of animal models to assess HIT risk, and working with the USP to develop a monograph for bovine heparin.

With this, I would like to conclude my update. Once again, I would like to thank the Science Board for your very useful recommendations, and your recommendations really helped us to move this initiative forward.

Thank you.

CHAIRMAN FREIRE: Thank you very much, Dr. Lee.

I call for any clarification questions from anybody in the committee or on the phone. I will express my apologies because we're looking for questions that are clarification questions, not for comments, because we haven't really done -- we've extensively reviewed this, but we haven't done a clearance for conflict of interest in this particular issue.
So, Dr. Jenkins?

DR. JENKINS: Yes, and I apologize. It's my first meeting. So you may have already covered this in previous dialogue.

But I was just interested to understand potentially related to your bullet on stakeholders the collaboration of potential partners that you're working with to understand the feasibility at the end of the day of the operational implementation of the manufacture and supply chain of the product into the U.S. healthcare system that will be commercially viable.

And the reason behind my question is that I commend you for the robustness of the work that you're doing, but at the end of the day, there needs to be a process in place that is sustainable and scalable to meet the needs of the U.S. healthcare system.

DR. LEE: Yeah, that is a very good question. I think that actually brought up last Science Board meeting, and we -- one of the things we actually engage a lot of our stakeholders to understand the landscape of the heparin market currently. And we actually just
for bovine heparin is -- other countries, actually, does have a market for the bovine heparin.

So the visibility of manufacturing bovine heparin, based on our understanding, is there. And then we are talking to some of the stakeholders about this. So, so far, I think the most challenging thing -- so let me -- my answer to your question is that we know the visibility is there.

There are some infrastructure which would support this initiative, and right now, we are still working with the stakeholders and also try to talk with them to understand a little bit more. But to your question, yes, the visibility is there.

CHAIRMAN FREIRE: Thank you very much.

Any other questions or comments? Dr. Xie?

DR. XIE: To follow Annalisa, you mentioned about the country providing, I had a chance 2 or 3 years ago visiting Tianjin and Guangzhou about some of the production in bovine. I'm not sure they're updated. Is that the major supply, the bovine, this heparin?

DR. LEE: No. Right now, we don't have
bovine heparin in the United States. They are still in
other country, probably Brazil and Argentina or India.
And right now, the major source of heparin product in
the United States is derived from the porcine, and the
major supplier will be from China. It's the major
supplier for porcine heparin is from China.

CHAIRMAN FREIRE: Thank you.

One of the concerns of this board was, of
course, to ensure the uninterrupted supply of high-
quality heparin, and I think I speak for the entire
board to thank you for all your efforts. This is
critically important for public health.

DR. LEE: Yeah, thank you very much.

CHAIRMAN FREIRE: Thank you.

DR. LEE: Thank you.

CHAIRMAN FREIRE: All right. Any other
questions?

(No response.)

CHAIRMAN FREIRE: Then we shall move forward
to the FDA's public access policy. Again, this is a
topic that has been put on the agenda because of
interest from members of this board. And believe that
today we have Dr. Noty? Did I pronounce that --

MR. DOTY: Doty.


Look at that, I have a typo.

MR. DOTY: Good morning, and I get this a lot. It's not Dr. Doty. I'm just a lawyer. I'm probably the only lawyer that you'll be hearing from today. So I will try to keep this as engaging as possible. As a lawyer, I know that can be challenging in listening to lawyers speak.

So I'll be covering a couple of topics today. One is to provide the Office of Scientific Integrity update to the presentations earlier from the various components of the Office of the Chief Scientist. But the vast majority of my talk today will be about this issue of access to FDA research and the agency's work in complying with an initiative from the Office of Science and Technology Policy around public access to research.

So a little bit of background about the Office of Scientific Integrity.

CHAIRMAN FREIRE: Yes, if we could get you a
little louder here?

MR. DOTY: It covers --

CHAIRMAN FREIRE: They know you're a lawyer.

They tend to speak much more loudly than that.

MR. DOTY: It covers -- my office, the Office of Scientific Integrity covers quite a number of different agency functions. It's quite an amalgamation, frankly. And as I was starting in this position, some themes began to emerge that I undertook as sort of the mission of the Office of Scientific Integrity.

So in my office, we have the agency IRB. We're responsible for investigating allegations of research misconduct. We have an Office of Appeals that resolves disputes of agency decision-making, both primarily external agency -- disputes of agency decision-making.

We house the Office of the Ombudsman, and we also do a whole variety of science culture and science policy issues for the agency. And that last category there, fostering a culture of scientific integrity, is a category that I think covers much of what I'm going
to talk about today.

So in terms of an update of some of the important work that my office has been doing in the last couple of years, we've been handling a couple of initiatives from the Office of Science and Technology Policy. One relates to the management of scientific -- institutional scientific collections. That's actual collections of specimens that the agency maintains.

And we were asked by OSTP in March of 2014 to develop draft policies for the management of and access to agency scientific collections, and I'm very proud, actually, to report that we were in a very short timeframe -- in just 6 months, as required by OSTP, we were able to put together a comprehensive draft policy and submit that to OSTP in September and in January received a green light from them that we had put together a policy that was in line with what they had in mind.

And I'm very happy to say that they are actually consider this, our policy to be a model for what other agencies might be doing in this area.

CHAIRMAN FREIRE: May I interrupt briefly?
MR. DOTY: Yes.

CHAIRMAN FREIRE: Could you please define what FDA research means in this context?

MR. DOTY: In the context of scientific collections?

CHAIRMAN FREIRE: Yes.

MR. DOTY: I don't know that "research" is necessarily what we need to define when we're talking about scientific collections. We're talking here about actual scientific, physical scientific resources that the agency maintains for the purposes of maintaining a scientific collection.

So we're not here necessarily talking about, you know, for instance, cell cultures or tissues, samples related to a specific study, but rather if the agency were maintaining a specific set of cell lines or reference materials that were useful in a broader context and the agency had interest in maintaining those for scientific purposes, those would be covered by our scientific collections policy.

So the other large item is the public access to research results, and I will talk much more about
this. But this has been going on since early 2013, and you know, we've done an extreme -- we've really done a lot of hard work on this particular topic. This is not something that the agency has been heavily engaged in before embarking on this initiative.

And so, we've had -- we've had to do the best we can to get ourselves caught up and up to speed on the issues and learn as much as we can and try to get ourselves into a position to be making as much agency research available as possible.

So why am I here? In November, there was some brief discussion of this topic by Dr. Ostroff, and there were a number of questions that came out of that -- out of that presentation and discussion. Excuse me.

So, for example, there was a question from Dr. McLellan noting that this issue of public access to research was a hot topic. It was controversial and that there were particular concerns about how we make access to the underlying data behind publications available. Could not agree more. These are complicated, challenging issues.

There was also a question from Dr. Goldman.
about -- again about the data issue and some anxiety about how an initiative like this would be funded, whether this would be an unfunded mandate, and also an identification of the real challenges about long-term preservation of and access to datasets and how useful that long-term preservation may or may not be in a particular context.

And I think, wisely, Dr. Ostroff was kind enough to offer that I come and speak and start a discussion about this topic, and so that's what I'm here to do today. I will say I'm going to try and give a very high-level overview so that we have a little bit of time to actually have a conversation and I can hear feedback from the board because these are -- these are really challenging issues.

We've crossed some important milestones at this point, but there's a lot of work to be done still. And we are very much in a position where policies still need to be developed, and we would -- we would welcome any input learning -- thoughts, comments, concerns -- that come up as we go through here. So the OSTP memo from February 2013,
Increasing Access to Results of Government-Funded Scientific Research, has two components from OSTP. This memo is asking agencies to put together their plans for how they will provide access to research. I want to highlight here that we're talking about Government-funded scientific research. So this applies both to research where FDA or other Government agencies are funding extramural research, but it also applies to intramural researchers at FDA or at other agencies that are covered by this memo.

As I said, this is asking agencies to develop plans for providing public access, and that was our first step was to put together a plan. And I'll talk in a little bit about where we are in that process. But it's we are not yet at the stage of actually putting together the completed policy. We were asked to put together plans, and the implementation is still to come.

So the first component is providing free digital access to federally funded peer-reviewed articles after an embargo period. I would suspect that many of you are familiar with these sorts of
requirements based upon NIH's public access -- existing public access policies, PubMed Central, and perhaps many of you have actually interacted with PubMed Central or put manuscripts or articles into PubMed Central. So this is a relatively familiar requirement.

And the second item here is maximizing free public access to digital data from federally funded research, and I think, based on the questions from the last meeting and based on the work that we've done as an agency and in cross-agency collaborations, this is where a lot of the challenges are. I would just note that the memo here talks about maximizing free public access to digital data.

There is -- it's simply the case that the issues regarding access to data are still developing. We need to be doing the best we can to make as much of that data available as possible. But we are less prescriptive in our plan about precisely how we will be -- how and what data will be made affirmatively available to the public and when, and that will be an evolving and -- an evolving issue and one that I think deserves serious ongoing attention.
So I apologize for the overlapping text here. Apparently, my font was not transferred over. But at the very least, this is the -- I want to talk about the FDA's specific plan. I want to focus first here on the fact that this was developed through significant interagency collaboration and collaboration throughout FDA.

So we put together an agency-wide working group. I want to thank everyone who participated in that working group. Several of them are here today. Thank you. This was a very challenging, extensive process, and people donated a significant amount of time to making this work.

There were HHS-wide working groups that we participated in to do the best we can to coordinate the various public access plans across the department. There was a Government-wide working group that was hosted by the Office of Science and Technology Policy, again to try to make sure that we're being as consistent as possible Government wide in the way in which we create these plans and implement the public access requirements.
And there was a public meeting and there may be future public meetings on these topics, and you know, stay tuned for those, but we've certainly had a significant amount of input from in particular the publishing community, but also the scientific community on these issues. And you know, meetings like this are also opportunities for us to be hearing as much as possible from the public.

The plan that we developed was actually published last Friday. I feel great about that. It was a -- it was a, you know, almost 2 years in the making, and you can see it here on the FDA Web site. There is also an HHS Office of the Secretary cover memo and letter accompanying that, as well as public access plans for other HHS operating divisions.

So I encourage you, to the extent you're interesting in looking at those or maybe the research that you do is actually more likely covered by plans from other HHS operating divisions, to certainly give those a look. I would emphasize that this is FDA's plan. While we tried to be as consistent as possible in doing the collaborations around public access, each
plan is somewhat different.

Each agency has its own sets of challenges.

Each agency was at different stages in the actual development or existing public access policies were different from agency to agency, and so there was not an HHS-wide, one size fits all type of policy that could be developed here.

And as with the OSTP initiative, there are two main components to the FDA plan, the publication access and the data access components.

So publication access, first of all, articles will be stored in PubMed Central. And I don't know if everyone is, I suspect most here in the room are familiar, but for those who may not be familiar, there are two services that are run out of NIH National Library of Medicine. One is PubMed Central, and one is PubMed.

PubMed is essentially an index of biomedical research, if you've ever spent -- I'm sure all of you have. But if you ever spend time in PubMed, that gives you an opportunity to search through article metadata and their abstracts, and then at the top of those
pages, you would see links to the actual full text of those articles, either on the journal's Web site, or if this was an article that was subject to the NIH public access plan, there may be a link to PubMed Central, where the full text of the article is stored.

So PubMed Central is where full text of manuscripts or final published articles are stored, and that's the crux of what FDA is engaged in here. We will be ensuring that -- that FDA-funded Federal research which results in a peer-reviewed published article, that that peer-reviewed published article, the full text of that article will be stored in PubMed Central. It will be searchable, retrievable. It will be machine readable insofar it's in XML. It will be 508 compliant.

We will essentially be aligning ourselves with the way in which NIH's public access policy works so that full text of articles appear in PubMed Central.

I want to emphasize here also that we'll be using NIH's infrastructure for the intake of those articles, and that's key here because that's an important existing infrastructure that researchers are
familiar with. It's also the case that NIH has done a significant amount of work over -- over years now of engaging with the publishing community and coming up with arrangements for receiving articles directly from publishers to eliminate or reduce burdens on researchers in depositing their manuscripts into PubMed Central.

And so, that's -- we're very happy to say that we'll be using that same infrastructure, and this should be a relatively seamless process for those researchers that are already familiar with using PubMed Central.

And then we'll be using a 1-year embargo period. So in the 1 year after publication, we would expect researchers to have their articles deposited into PubMed Central, either by the publisher itself or by the researcher. And NIH will know the publication date and will be able to flip a switch and have the full text of that article freely available to the public after 1 year.

Okay. Data access. As I've said, this is where all the challenges come in and where we want to
be as thoughtful as possible going forward about how to implement this. The big component of the data access plan, both FDA's plan and the memo from the Office of Science and Technology Policy, relates to data management plans.

And it -- the OSTP memo requires and, therefore, our FDA plan requires that data management plans be submitted with requests for funding. And this goes for both intramural and extramural requests for research funding.

So a data management plan should be addressing, and certainly as we develop more formal policies on this, there will be additional detail as to what would be included in a data management plan, and it's very possible that some of you are familiar already with developing data management plans for your research. But we would be asking for a description of the data that's being collected, how it will be maintained, whether it ought to be preserved, whether there should be public access to that data.

And I think one of the most important components that we will be looking for in our data
management plans is, is that the researcher, in
submitting their data management plans with their
request for funding, make an attempt to balance the
costs and benefits of preservation and access to data
at the commencement of their research.

That means that if you are doing research
where the preservation of a particular dataset is going
to be extremely expensive and may not have benefits in
the long run, we need to know that, and that should be
considered in the creation of your data management
plan. And the agency will be considering the merits of
that data management plan in considering the request
for funding.

That's -- really, to me, that's key. And
given some of the comments from the last meeting about
the -- about what value there may be in preserving
datasets for 30 years and some datasets may or may not
be valuable and how you store those datasets for
decades is useful to think about in terms of being able
to actually retrieve that data. Those are the kinds of
issues that need to be addressed in data management
plans.
And if it turns out that we believe that or that a researcher believes that a preservation of or access to data for the long term is an important component of their research and a valuable tool and outcome of their research, then it's also the case, based on the OSTP memo and FDA's plan, that that researcher can request funding from the agency as part of their request for funding for that data management, for that long-term preservation.

And so, you know, there are certainly costs to this, but the key here is that we're not asking researchers to bear those costs on their own and that those should be incorporated as costs of actually doing the research that's being contemplated.

The third component here is that we will be asking that data that supports a published peer-reviewed article be made publicly accessible. We will be asking that researchers commit to that in their data management plans, and that is a fairly direct requirement. And it is something that I think will be, you know, somewhat new in terms of what the agency has required of researchers in the past.
So when will we be finalizing these policies? When will all of this be coming down the road? This summer, we anticipate that we will have the publication access and data access policies completed for the agency. That feels very soon to me right now, given that we've just completed our plan. But we have already been working on this while the issues have been worked out in collaborations with OSTP over our plan. So, you know, we have -- we have taken some steps forward on this front, and I do think we can meet the summer 2015 projection. In October of 2015, that's the beginning of Fiscal Year 2016, we should have FDA's version of the -- it's the same PubMed Central repository. But FDA researchers will be able to deposit articles into PubMed Central.

And starting in January of 2016, we would expect that awards of funding, subject to the data management plan requirements, would start going out.

So I think one thing I just want to highlight here is that certainly in conversations that we've had in the agency and with -- and with some researchers outside the agency, I think there is a lot of concern
about the idea that this is a new set of public access burdensome requirements that are being imposed by the Federal Government on researchers. I would just really highlight here that there is a significant trend toward public access coming out of the scientific community, coming from journals, coming from other private funding sources, and that if FDA were not pursuing this and other Government agencies were not pursuing this, we would actually be the odd man out here.

And we could -- you know, I could probably spend some time up here waxing poetic about how important public access is, but I think the more important thing in my mind is that this is where science and research and scientific community is going in terms of preserving data, making sure that data underlying articles is publicly available, making sure that full text of articles is freely available to the public.

And I'm very excited that FDA is coming into line with that trend, and you know, this is -- this is something that we're seeing from, for instance, the Gates Foundation late last year, I believe, came out
with their public access policies, where they would require full text of articles to be freely available to the public and that the data underlying those articles be available to -- freely available to the public. We're seeing more and more journals focus on making sure that the data underlying publications, all publications be -- be made publicly available upon publication. That's been the case for some certain scientific disciplines, genomic data, for instance, and for many journals. But that's becoming more and more true.

And I'm just really glad to see that FDA will be -- will be coming into line with that trend, and I expect that trend to be expanding significantly. And I think that trend is actually what's going to be driving much of researchers' work and agencies and funding sources and journals' work regarding public access in the future much more than FDA's specific plan.

So questions, concerns?

CHAIRMAN FREIRE: Thank you, Mr. Doty.

MR. DOTY: Yes.

CHAIRMAN FREIRE: Quite a -- quite an
impressive amount of work, I must say, and an important issue at that. And of course, you're not going to go away without having a whole slew of questions.

So right now, I have Dr. Hait, Dr. McLellan, Dr. Sarwal, and Dr. Psaty. If anybody else has a question, please use the universal U.N. system, and then we need to -- because I am challenged, you need to put it back down, or I'll call on you twice.

So, thank you.

MR. DOTY: I was hoping to run before the questions came in.

CHAIRMAN FREIRE: No, sorry. No such luck.

MR. DOTY: No, I'm happy to --

CHAIRMAN FREIRE: I'm going to give the floor to Dr. Hait, who's on the phone.

DR. HAIT: Yeah, thank you so much.

Just a question about the people that you've been collaborating with. I didn't see on the list, maybe I missed it, the Institute of Medicine. Their report on clinical trials data transparency, I was impressed that it included both industry and academia.

So it would include federally funded research.
I wonder if there has been an alignment or at least a discussion with the Institute of Medicine on this?

CHAIRMAN FREIRE: Did you understand the question?

MR. DOTY: I think so. So I am aware of the recent Institute of Medicine report on sharing clinical trial data. That's been, as far as I'm aware and from FDA's perspective, that's been a separate endeavor from the work that we've been doing specifically here regarding public access.

I agree that seems like quite a comprehensive report that considered clinical trial data from many different sources, you know, industry, academia, Government. You know, we have a bit of a narrower focus on this particular topic. As I said, there have been -- the National Academy of Science hosted a public meeting on this that FDA and HHS and other Government agencies participated in. There have been Government-wide working groups on this topic.

We have heard extensively from the publishing community. As you can imagine, they have a lot of
interest in how this all will work. But this is a bit of a narrower focus in terms of dealing with access to federally funded research. So we don't have quite the same scope that the IOM report had.

DR. HAIT: The only reason I would even stress it a little more is that potential problems -- I don't know that they will arise -- would be reanalysis of clinical data when all data is made available that disagrees with the FDA conclusion. So it's certainly a "watch out," and we could go offline and talk about how J&J is handling it.

MR. DOTY: I don't know if I got all that question.

MS. MONSER: Bill, could you maybe -- would you email me? This is Martha. The audio is rather garbled. If you'll email me your comment, and I can relay that to Nathan so that we're sure that we understand it.

Thank you.

DR. HAIT: Yeah, very good. I will do that.

MS. MONSER: Thanks, Bill.

CHAIRMAN FREIRE: Thank you, Dr. Hait. And I
will recognize you as soon as we get that question.

Dr. McLellan, who started this.

DR. MCLELLAN: Yes, indeed. Forgive me for being one of the culprits, I guess, in this.

Let me first start, Nathan, by congratulating you on the PubMed focus for publications. I think that's a slam dunk, and you're absolutely on the right path there.

My question really is more regarding, of course, the devil in the details regarding data management. The data perspective is where all of the controversy and challenge is. I found it fascinating that you were interpreting the word "maximize." And I almost detected a sense that it gave you flexibility, be that as it may.

It's interesting because you are probably one of the first people talking about a cost-benefit analysis of whether data should or should not be made publicly available. And I find that challenging in light of at least the overall verbiage of the OSTP guidance on this.

Of course, I think one of the important
things becomes who makes that cost-benefit analysis?
And I think your interpretation might be that you leave
that with the individual researcher, and that may or
may not be right.
I will tell you there are universities
standing in line, including my own, that would love to
have that perspective and have that control, be able to
make a cost-benefit analysis and determine if the data
should or should not be made available.
The other is a question of the lens by which
you view this, and it relates to the idea of who is
doing this determination of whether the data should be
made public. Because there are many that argue that,
you know, that a lens of 2015 would not at all shine
and identify critical issues of available data and
value of available data, as opposed to one 30 years
from now, 50 years from now, even 100 years from now.
Just go back to the 1918 flu, and you know,
there's lots of perspectives, one might say, if we only
had the data. So I'd be curious more of comments
regarding this issue of cost-benefit analysis in
particular from the perspective of, as you can imagine,
extramural funding is very critical on us. And I guess one follow-on is as you determine that a cost-benefit analysis and, therefore, data or no data is made public, how is that imply -- how do those rules apply to universities that are also bound by these Federal rules.

So thanks for your comments.

MR. DOTY: Okay. We covered a lot of ground there, and I'll try to give some general comments about this topic. So, you know, I think it's fair and I will say this is somewhat of my interpretation of the OSTP memo. But I think it's fair, as you've characterized it, that the -- that I do see a bit of flexibility in the approach that the OSTP memo makes regarding maximizing access to data.

Obviously, I think there is a big push in the OSTP memo, in associated memos from the White House and OMB regarding -- and executive orders from the White House regarding open data to be making as much data available to the public as possible, as quickly as possible, as machine readable as possible. And that absolutely should be a focus here.
But I will say that I'm not coming up with this cost-benefit analysis out of the blue. That cost-benefit analysis language is identified in the OSTP memo. I think, to me, it is a critical component of this project. I think that there are undoubtedly priorities that have to be set regarding access to data.

It is perhaps in the long run, you know, all data being made available in very usable, transparent ways is the goal and is achievable. But I think until that point, we need to be thoughtful about how we devote our resources to making the most important datasets publicly available. So I do think that the cost-benefit analysis is a crucial component.

I would note that we are focused on making sure that the data that underlies actual published peer-reviewed articles be made available to the public, preferably in a publicly accessible repository that's related to that scientific discipline. We think that does improve -- you know, does help to address issues around reproducibility of data.

It's just an important component of our plan,
and it does, hopefully, expand the number of -- expand
the research projects that are disclosing and making
publicly available data. You know, it expands that
waterfront beyond simply those where there's been a
cost-benefit analysis at the outset of research.

Regarding who makes the decision about this
cost-benefit analysis, it's my view that at least as we
start out, there will be some deference to researchers
and absolutely deference to scientific communities
about the value of making data publicly available. So
there are some scientific communities that are very,
you know, way ahead in terms of ensuring that datasets
are made publicly available. Sequencing data is
routinely made publicly available right now.

I think that that trend will continue to
expand, and other scientific communities will be more
standardly making datasets publicly available. And I
think we want to be deferential to those trends in the
scientific community.

Having said that, we will be -- we and others
in HHS, I expect, and across the Government will be
learning a lot in receiving these data management plans
from the scientific community about what's valuable and how these trends are emerging. And I think, as we start to see more, we can be a bit more prescriptive about where we think there is value in making datasets publicly available.

That's a longer-term vision for how this might work. I think the journals and their involvement in this, you know, may be an intervening factor here because, one, more journals will be requiring datasets to be made publicly available. But these are longer-term issues.

I will just add one last comment, which is, yes, we will be, I think, thoughtful in considering the data management plans that are considered, but we will be reviewing the merits of those data management plans. And the agency will actually sign off on data management plans as part of our requests for funding. So there may be -- there could conceivably be differences of opinions about that cost-benefit analysis and conversations about whether data needs to be made available.

CHAIRMAN FREIRE: Thank you.
I'm going to allow the questions to continue because it's an important topic. But I want to let the board know that you're carving into our coffee time. So keep your -- keep your questions pithy and to the point.

I have Dr. Sarwal, Dr. Psaty, Dr. Russell, Dr. Afshari, Kowalcyk, and Xie. So there we are.

MR. DOTY: Just go around the room.

CHAIRMAN FREIRE: Dr. Sarwal?

DR. SARWAL: Yes, thank you so much for this. I actually had two questions. The first actually --

CHAIRMAN FREIRE: These will be combined into one real quickly, right?

DR. SARWAL: Yes. They will be combined into A and B. So the first was actually about the publication access and the fact that in summer of 2015, you are actually going to compile the policy with regards to that. And my question was rather simplistic, is so if you actually have research funded through the FDA, and would you mandate that you have a restriction for the kind of journal access that you
Because as we all know, not all journals subscribe to the open access policy, and some of them will make their articles available after 6 months or a year in the open access space. But again, not all of them do that. So that was my first question is would you mandate the choice of journal to ensure that you actually had your research in an open access space?

And my second question was really about the data, is NIAID has done a very elegant job of creating a data portal called ImmPort, which allows for all data to be placed in a public access in a central server. And the reason I bring that up is making data available within local universities and local journal servers and making them accessible carries the risk, as we were talking about, 20, 30, 100 years from now, as some of those servers actually going down.

And so, what may be available today may not be available 20 years from now. And so, would the FDA be looking at a centralized server space, which allows for all the data to be managed primarily for the purposes of reanalysis later on?
CHAIRMAN FREIRE: So very briefly, access to journals and data.

MR. DOTY: I will very -- yes. Very briefly.

So I think the real -- one of the really shining parts of our plan regarding your question about whether there are specific journals that researchers would need to publish in is that our work around publication access is journal independent.

So if your journal does not collaborate with PubMed Central, we would have researchers deposit the final published version of their manuscript in PubMed Central within that 1 year after publication. And PubMed Central would, therefore, host the full text of that article in PubMed Central, you know, as part of their PubMed Central library.

So this is not dictating any particular journal. This is not requiring researchers to pay the money for an open access review of their journal article. This is entirely separate from that and independent of what journal is selected. So that is different from some of the private funding source public access plans that have come out recently.
Regarding whether FDA would have their own repository, that is not contemplated in our plan. We see a trend towards more and more discipline-specific, publicly accessible repositories coming online. We think that those would be excellent places for data to be stored.

I think you raise some important points about whether those specific repositories are up to snuff and whether they have the backing and the resources to maintain their viability going forward. Those are issues that we definitely do need to be thinking about, and but we would not be anticipating having our own FDA-specific repository.

CHAIRMAN FREIRE: Thank you very much.

Dr. Psaty has kindly ceded his time. Dr. Russell?

DR. RUSSELL: Just a quick question. It seems like with the data storage needs that all of us have been trained on using written lab notebooks to archive science. It's probably going to head toward electronic lab notebooks as the only realistic way to support what you're talking about.
Have you thought about accrediting, doing the hard work of accrediting different lab -- electronic lab notebook providers and sort of really being proactive in helping researchers identify which are the best electronic lab notebooks to use?

MR. DOTY: We definitely haven't been thinking about that. It's an interesting suggestion. I will say that we -- that really the electronic lab notebook issue is, I think, really separate from what we're thinking about here. It is not the case that our plan or our subsequent policy will be requiring any particular pieces of data to become digital. What we are focused on is that those pieces of data that have been made digital, particularly those that underlie publications, that those existing digital datasets be made publicly available.

So there would not be a need to be switching over from any written notebooks to digital notebooks. And so, that really hasn't been a component of what we've been thinking about. Obviously, I think the electronic lab notebook issue is -- has a long history
and is far more complicated than I can get into right now. But it is a little bit of a separate endeavor.

CHAIRMAN FREIRE: We have Dr. Afshari. Dr. McLellan, are you re-asking a question? Okay.

DR. AFSHARI: I'd like to follow on to Dr. Hait's comment about the Institute of Medicine report on the access to clinical trial data. It seems that that's a significant data with respect to FDA's mission.

And there's been a lot of discussion about the data that's published, but of course, there's a lot of ongoing clinical trial data or maybe for products that never reach the market that may or may not be published that there is a point in terms of access to that data, as it is federally funded in cases of where it's conducted within academic clinical centers.

So I was just -- I just wanted to comment in the sense that it didn't seem from your earlier response that FDA is really looking at that or has the plans to make some further comment in terms of recommendations or action from that report. It certainly lays out a number of really tough issues with
respect to data infrastructure and other components that would have to be overcome. But just I wanted to just understand whether that was going to be an ongoing work stream or a separate work stream from this current activity.

MR. DOTY: There are obviously overlapping issues. I would say for right now, I would think of them as separate work streams. I think we have a really challenging task here to be dealing with the data and public access issues that relate to the OSTP memo. I think, as you're pointing out, there may well be clinical trials and clinical trial data that is covered by our public access plan that would also be the kind of datasets that are contemplated by -- you know, under the IOM report.

And so, I think there is some, some overlap there. But I don't necessarily anticipate there being specific changes to our plan or policy that are clinical data specific. You know, there certainly are data issues around personal privacy information and things like that that are implicated when you're dealing with clinical trial data.
But I don't -- and I may not be just seeing far enough ahead, but I don't at this specific point see that there would necessarily be changes to our public access policy based upon the IOM report. I'm very much open to that and would be happy to be continuing that conversation. But I don't necessarily see that -- that being a direct impact on our policies right now.

CHAIRMAN FREIRE: Thank you very much.

We have not received, Dr. Hait, your question. Do you want to try and take the phone for a minute and see if the line is a little clearer?

DR. HAIT: I did submit it, but it's already been covered. I have a follow-up question about the IOM. So --

CHAIRMAN FREIRE: That was not clear at all.

DR. AFSHARI: I think he said that --

CHAIRMAN FREIRE: Yes, I think he said that you covered that already.

DR. AFSHARI: I did hear his original question, and I believe it was he was pointing out there is a potential conflict where, with release of
this data, it would allow reanalysis that may be in conflict to the original analysis that FDA does as part of its review, and was FDA prepared to deal with that potential conflict, should it arise through the data access policy?

MR. DOTY: Yeah, I mean, I would just say I think that's really separate and aside from what we're dealing with here, and I don't know that there's any need for me to comment on that. I mean, it's an interesting point, but I'm not -- I just think it's separate and aside from what we're working on here.

CHAIRMAN FREIRE: We have two more speakers, unless I've mistaken, Mark, you're giving up the time?

No, you're not. I'm sorry to tell you it's Dr. Kowalcyk, Dr. Xie, and then Dr. McLellan.

DR. KOWALCYK: So, first of all, I also want to thank you for undertaking this important topic, and I think increasing public access to data is very important.

One of my concerns, and I think it was related to an earlier comment, is more about the capacity to deal with these datasets and what the
agency is doing. I'm thinking in particular around big
data and as we move into that field, and also, you
know, there is increasing interest, at least in my
area, which is food safety, of bringing public and
private data sources together.
And certainly, that raises issues around
proprietary data, data from public-private
partnerships, and so forth and just the capacity of --
of handling this amount of data and this kind of data.
And just, I would just like you to comment on what the
agency is thinking about in that regard.
MR. DOTY: I don't know if I can comment
generally about the agency's thoughts or work regarding
big data or, you know, there's a lot of work going on
at NIH as well about big data. I don't know that I can
really comment on those issues more generally.
I do think -- I will just say that I think
that there are -- there are opportunities here in
terms of our public access policy contributing to the
work that's happening regarding big data, that the
focus would be, you know, ensuring that the datasets
that are made publicly available are made available in
ways that they can be ingested by researchers that are working to, you know, collect large amounts of data on various topics and analyze that data.

And that has been a big focus of the OSTP memo and, you know, a thought about how we go about this, that we make data machine readable and adjustable and usable and analyzable.

DR. KOWALCYK: I guess my question was really about the infrastructure and capacity of the agency to store long term big data sources.

MR. DOTY: Yeah, again, as I said in response to the previous comment, I don't -- or question. I really don't see and we have not contemplated in our plan that the agency would be making, as part of this policy -- I won't comment more generally about the agency. But as part of this policy, the agency would not be making significant investments regarding data storage, that we would be focused on making sure that datasets are made publicly available in the existing publicly accessible science discipline specific repositories and that, you know, we would be eager to be seeing those expand and become more robust and
provide more opportunities for sharing data in those ways.

CHAIRMAN FREIRE: Thank you.

I have, unless -- Dr. Russell, you're up again -- I have Dr. Xie and Dr. McLellan, and that will be the end of the discussion.

DR. XIE: That was a very good initiative, actually. A similar question, just a quick comment.

So this is an initiative, I don't know, have you interacted with NIH? Because NIH has a public database, PubChem, which is a big, millions records. And it'd be nice if we could integrate those together from the chemical to the gene to protein to the kinetic, and there would be one time, don't have to click or search again.

And also my lab is creating disease domain specific database. We would be happy to link to FDA to make more public accessible. So those are things that will make, as Barbara says, the big data initiative. So that would be a powerful giant.

MR. DOTY: Yeah, and as I said before, I think there are real opportunities here with this
policy to -- to have datasets combined, you know, from FDA combined with other datasets in the scientific community, whether it's PubChem or GenBank or others. And that I think there is a lot of work and thinking to be done, Government wide, HHS wide, on these topics.

DR. XIE: Even Europe, there can be millions of chemical records, too.

MR. DOTY: Right. So, you know, this is a big -- big topic and big issue. I don't think our policy will, you know, solve all of those issues, but I do think we want to be mindful about how we fit in with those larger -- those larger projects.

CHAIRMAN FREIRE: Thank you. Dr. McLellan?

DR. MCLELLAN: Yeah. I just want to be clear, Nathan, you are proposing that there would be no public data storage at FDA? That each of these agencies here would be required to push their data out some other place? Is that -- is that sort of what you're -- and are these guys all prepared? Is CFSAN and CBER and Center for Toxicology, are they prepared to do this sort of thing, to push their public data out and --
MR. DOTY: So, okay. So a couple of things. There is nothing precluding the agency from making investments to store data. I just wanted to be clear that our plan in particular was not committing ourselves or -- or in general stating that we would be developing an FDA-specific repository to hold all FDA-specific data in one place that can be, you know, searched and analyzed.

That's quite a significant, challenging investment. Perhaps that's something the agency would consider in the future, but that's not something that's specifically part of this plan.

I do think that where we're dealing with data management plans and dealing with issues around data access and data preservation more generally that clearly there are interests in the centers, regardless of this public access policy, for maintaining data, making it usable intramurally and extramurally that are going to continue. I think the big focus here is that we have specifically asked that researchers make their datasets that underlie publications available, make them publicly available to -- freely publicly available
upon publication.

And what I just wanted to be clear about is that as with the policies from journals that are developing and other funding sources, we would not be expecting that the agency develop a specific repository to house those datasets. But that it may be more logical to have to those datasets underlying publications made available in existing public repositories.

DR. MCLELLAN: I would just remind you that I actually believe the OSTP guidance was not specific only to data associated with publications, that it was to go far beyond that.

MR. DOTY: I agree. I don't -- I agree with you, and I don't -- I don't contest that. And as I said, the data management plans and how data is handled more generally, you know, may involve internal storage of datasets. It may involve agency repositories holding datasets.

You know, there are obviously ways in which the agency makes data publicly available right now through its own servers. I don't mean to diminish that...
or suggest that that's going away in some way or that every agency dataset is now going to be pushed onto publicly accessible discipline-specific repositories outside the agency.

Only that where we're now making a specific requirement around related to data underlying published articles, we want to be making that as consistent with the emerging practices in the -- from journals as possible and ensuring that there are other ways that you might make that -- those datasets publicly available.

You know, external datasets -- or external repositories might be the way. Publisher Web sites is an opportunity to make, you know, some limited datasets publicly available. There are opportunities, I think, even in PubMed Central to make supporting data or supporting materials publicly available.

So those would all be opportunities. I just don't want there to be a suggestion that we are committing ourselves to the FDA repository for data underlying published research.

CHAIRMAN FREIRE: Dr. Wilson has come on
bended knee with a request to have a very quick comment.

DR. WILSON: Very quick. I just -- I actually just want to clarify that, actually, the FDA requires that all data be -- all research data be retained indefinitely. We don't discard our research data. So all our laboratory notebooks are retained indefinitely.

So that's outside of the data access policy. So I just want to clarify that.

MR. DOTY: Right. And --

CHAIRMAN FREIRE: You mean internally? Yes.

MR. DOTY: Right. And related to, you know, Government records and FOIA and so on. So --

CHAIRMAN FREIRE: Well, Mr. Doty, you have done an amazing job at fending all of these doctors. So congratulations.

MR. DOTY: I don't mean to be defending. I really appreciate the contributions, the thoughts, the concerns because this really is a challenging issue for -- not just for FDA, for all Government agencies, and I really want to be hearing as much as possible.
So thanks very much.

CHAIRMAN FREIRE: Well, thank you very much. We now have a decision to make, and I ask the board what we want to do. We are 20 minutes off the mark. We're scheduled right now for a break. Should we take the break now, a 10-minute as opposed to 15-minute break, and ask Dr. Merkel's indulgence?

And then reconvene 5 minutes early than the 10:45 a.m. and then move on? Is that what -- I'm seeing heads shaking. So, Dr. Merkel, I will ask for your indulgence in moving this a little bit further back, if that's all right?

So, all right, and I will be ruthless. We will start at 10:40 a.m.

MS. MONSER: One quick announcement, too, for folks that wanted to have lunch preordered. We do have the menu now. I'm sorry we didn't have that earlier. I wasn't aware that we didn't. So if you want to see anybody, one of the ladies at the table out there and tell them your preference.

Thank you. See you in 10.

(Recessed at 10:33 a.m.)
(Reconvened at 10:42 a.m.)

CHAIRMAN FREIRE: Now we need to make sure Dr. Merkel is somewhere to be found.

(Laughter.)

CHAIRMAN FREIRE: There he is. Okay. So thank you for -- thank you to the board for that short break. We did manage to stretch our legs, I hope. And we are now at a very interesting point in our agenda.

I wanted to let the new board members know and remind the old board members that, in fact, the Scientific Achievement Awards recognize scientists at the FDA that have made outstanding contributions to regulatory science. The individuals are nominated by their respective centers. There is a two-tier process where the two top candidates for each award are sent to this board for review and for final ranking.

So having done these reviews in prior years, I want you to know that they are incredibly interesting, and you learn a great deal and you appreciate the work of the men and women at FDA even more by doing that.

So by tomorrow or the day after, we will be

Alderson Reporting
1-800-For-Depo
sending your way potential matches. We try our best to match your expertise to the actual work of the potential recipient to the final candidates. Sometimes we're not quite as successful because the board is not as broad as the actual expertise of these individuals. But you are going to be asked to review two or sometimes even three potential nominees and to give your scores.

This is something that we take very seriously. At the end of the process, there will be individuals selected for a number of categories. There will be individual and group awards given, and we expect to have those back by April 13th, Martha? I believe that's the case because it was originally April 12th, and we figured out it was a Sunday.

MS. MONSER: Yes. Yes.

CHAIRMAN FREIRE: And that wasn't such a cool idea. We didn't want to have our colleagues have to come in for that.

So today, and we do this at some of our board meetings, we ask the recipients of these awards to come and present their work. Today, we have the great
honor, albeit belatedly, to have Dr. Merkel, from the Laboratory of Respiratory and Special Pathogens at CBER, present his work.

Dr. Merkel, you know that I'm quite ruthless on the timing and the agenda. But we will certainly be very keen to hear what you have to say, and we will give you your full time.

Thank you.

DR. MERKEL: All right. Thank you.

Well, when you yell at me, I'll just stop talking.

Today, I'm going to talk about the work that we've been doing in my lab to try and understand the reasons underlying the resurgence --

CHAIRMAN FREIRE: Is the mike on?

DR. MERKEL: Yeah, okay. Sorry.

The work in our lab that is aimed at understanding the reasons underlying the resurgence of pertussis that we're seeing in the United States and throughout the world.

Pertussis is a highly contagious infection caused by a bacterium called Bordetella pertussis. I
think to really understand the severity of pertussis,
you have to look back to the pre-vaccine era. In the
pre-vaccine era, pertussis infection was nearly
universal by school entry, meaning that almost everyone
had pertussis by the time they were 5 years old. And
approximately 1 in 10 cases resulted in mortality.

In the pre-vaccine era, pertussis was
responsible for more deaths than measles and polio
combined, and it's still one of the 10 most common
causes of death from infectious diseases worldwide. I
think the fact that until recently pertussis was under
the public radar is a testimony to how effective our
vaccine program actually has been and continues to be.

If you look, this is a typical success story.
You can see that after the introduction of vaccines in
the 1940s, the number of cases of pertussis plummeted.
But unlike other childhood infectious diseases that
are vaccine preventable, pertussis was never completely
eradicated or completely eliminated in the United
States. At the lowest point, we had about 1,000 cases
a year, and you can see that starting in the late '80s
or early '90s, a very slow, but steady increase in the
number of cases of pertussis has been observed.
And if we look at more recent years, you can see that that increase has dramatically accelerated.
And the reality is we don't understand why.

If you look at our ability to vaccinate kids in the United States, you can see that we're actually very successful. About 95 percent of kids entering elementary school in the United States are up to date with their pertussis vaccines. We introduced an adolescent booster that's given at around 11 years of age in 2006, and you can see that in the last few years, we've reached a point where 80 percent of 11-year-olds in the United States have received their adolescent booster.

But in spite of this near universal vaccination in the United States, we're seeing this resurgence of pertussis, and I don't think we're going to solve this problem by vaccinating more kids. We can't possibly vaccinate more kids than we are today.

To try and understand what's going on here, we started work about 6 or 7 years ago to develop a primate model of pertussis. After a couple of false
starts, we identified the baboon as a good model of pertussis.

When we challenge infant baboons or toddler baboons, the equivalent of a toddler, with pertussis, you can see that we -- the animals are infected. This is by nasopharyngeal wash. We are able to recover bacteria from the animals at high levels out to about 3 weeks, and then the infection slowly resolves.

These baboons exhibit leukocytosis. This is a hallmark symptom of pertussis. In small children with pertussis, you can see levels of white blood cell counts that sometimes reach as high as 100,000 white blood cells per microliter, and we occasionally see that in the baboon. But as you can see, the average is about between 50,000 and 70,000 white blood cells per microliter. And again, this resolves over time.

But of course, pertussis is predominantly defined by its cough, and this was an important aspect of our model. Our model was the first animal model in which the animals coughed as a result of pertussis.

And this is just showing the average coughs per hour in a small group of baboons, and you can see they had a
significant cough illness that lasted about 2 weeks. So having established what we thought was a good model, we've decided to use this model to first look at the host response to pertussis infection. And this just summarizes a lot of work, one person's work for 2 or 3 years on this one slide.

But what we find when we look in an animal that's naturally infected with pertussis is we see a classic mucosal Th17 response in which antigen presenting cells produce cytokines that induce Th17 cells to produce IL-17, which induces the epithelial cells in the mucosa to produce chemokines and colony stimulating factors to recruit neutrophils and which enhances clearance of the bacterium from the airway.

And although we have a lot of work left to do to firmly establish this, we believe that this is the response that's required to prevent the colonization of the airway mucosa.

And in fact, we do see what we call a sterilizing immunity in that we do not recover bacteria from the nasopharyngeal washes of baboons that were previously infected and recovered. We call these
convalescent animals. So a natural infection results in a host immune response that prevents colonization into subsequent exposures.

So we now turned our attention to the acellular vaccines. These are the licensed vaccines in the United States, and we found that these vaccines prevented disease. Vaccinated animals showed no sign of illness. There was no white blood cell count. There was no loss in activity. There was no coughing. These were very happy animals.

But when we looked at their colonization, we found that these animals were pretty heavily colonized. The vaccine prevents the initial -- reduces the initial infection by about a log or two, but you can see that these animals are heavily colonized and, in fact, that colonization persists longer than is seen in unvaccinated animals.

So the vaccine is preventing disease symptoms. These animals aren't getting sick, but they are getting colonized, and that colonization is persisting for a very long time. And this, of course, raised the question as to whether or not these animals...
can transmit.

   But one of the things we wanted to look at
first was whether or not, you know, our challenge was
too artificial. So we took vaccinated animals and we
put them in a cage with an unvaccinated infected animal
to see if you could get natural transmission to
vaccinated animals. And you can see here that we did.

   Whether an animal was vaccinated or not
vaccinated, we saw no difference in the timing or the
duration or the magnitude of the colonization. But
again, these vaccinated animals did not get sick.

   So in this experiment, although it's a little
bit messy, what we did was in two individual
experiments, we took an infected vaccinated animal,
which was asymptomatic, and put it in a cage with a
naive animal and looked for transmission. And in both
cases, we saw transmission to the naive animal.

   So what this is telling us is that animals
vaccinated with the acellular vaccine can be colonized,
that colonization persists for a long time, and they
can transmit to other individuals around them, even
though they're asymptomatic.
Now we then moved on to evaluate the whole-cell pertussis vaccine, and what we found is that the whole-cell vaccine confers an intermediate protection against colonization. Again, these animals, whole-cell vaccinated animals don't get sick. They are initially colonized at the same level as acellular vaccinated animals, but they clear the infection more quickly.

And we determined that the exposure determines what we call the skewing of the adaptive response. So animals that are vaccinated, that convalescent animals have a very strong Th1 response and a very strong Th17 response and a very small, very low Th2 response.

The acellular vaccine is inducing almost the exact opposite response. It has a very strong Th2 response, a very nonexistent Th17 response, and a weak Th1 response. And the whole-cell vaccine looks more like convalescent animals in that it has a Th1 and Th17 response, but it's very low and doesn't have -- induce much of a Th2 response.

So our conclusions from this work so far is that we believe that antibodies against pertussis, in
other words, a good Th2 response will prevent disease. But it doesn't prevent colonization. If you want to prevent colonization, in addition to that Th1 response, you want to induce -- I mean, Th2 response, you want a Th1 and Th17 response against the appropriate antigens.

So, and I'm just going to change gears a little bit and talk about protecting newborns. This is a significant problem, concern in the United States because the most severe disease is seen in children under 2 months of age, and this is easily understandable because we don't start vaccinating kids until they're 2 months of age.

So kids under 2 months of age have no immunity, plus they're very small. Their airways are very small, and they tend to get more severe disease. This is where we see our hospitalizations, and this is where we see our deaths.

There have been a number of strategies over the years proposed to protect newborns. It was thought by many that boosting of adolescent immunity would prevent transmission to newborns. That turned out not to be the case. And it's probably not the case because
teenagers don't hang out a lot with newborns. So there's not a lot of opportunity for transmission there.

It is thought by many that cocooning would be effective, and that idea is to vaccinate, you know, the mother and father and siblings and grandparents, those people who come into contact with a newborn. This is difficult to implement. And I think our data suggests that it's also less likely -- it's likely to be not as effective as one would hope, given the fact that the acellular vaccine doesn't prevent colonization or transmission.

The neonatal vaccination strategy is the idea to vaccinate a child at birth, you know, by day one or two. The problem with this approach is even if it's effective, it still leaves a window of vulnerability in the first few weeks of life.

And finally, the strategy that has received a lot of attention is maternal vaccination. When we started this work, a lot of work had been done looking at immunogenicity in mothers and transfer of antibodies to infants in clinical studies. But we thought that
what we could add was an actual demonstration of effectiveness.

So this is just showing our neonatal study. In this study, we vaccinated newborn baboons on day two and also on day two and week four, and then challenged them on week five. And you see even a single dose given on day two protected these newborn baboons from challenge at week five.

Again, they were colonized for a long time, but they didn't get sick. And in the case of protecting newborns, preventing disease is the primary goal.

In the maternal vaccination study, we took female baboons in their third trimester of pregnancy and boosted them and waited for them to deliver and then challenged their infants at 5 weeks of age, and you can see that this was very effective. The infants born to mothers that were boosted in their third trimester, although they were colonized, they showed absolutely no sign of disease.

So we're actually moving forward with this to study -- actually, we are asking the question of
whether or not pertussis toxin alone would be
sufficient to confer protection by maternal
vaccination. We think that it will be, and the
rationale for testing that is that we believe this is a
vaccine, probably the most inexpensive, easy to produce
acellular vaccine one could produce, and we're
interested in promoting this idea for use in the
developing world.

So our thinking about next-generation
pertussis vaccines is we need vaccines to prevent
colonization. There are a number of approaches being
taken by other groups, including detoxifying the whole-
cell vaccine, generating attenuated live pertussis
vaccines. Our approach is to try to redesign the
acellular vaccine so that it induces the type of
response that we need directed against the appropriate
target antigens.

For both our work and for other people's
work, we think that the baboon model is providing,
already is providing as a powerful tool for
understanding pertussis pathogenesis and disease. It
provides us a really excellent model for testing our
assumptions regarding new strategies utilizing existing vaccines and driving development of new vaccines. And we think it will provide important preclinical data to support the effectiveness of new vaccines.

So this is my excellent crew here at the FDA, the CBER NHP staff, and also at Oklahoma, Gary, James, and Roman contribute a lot of expertise.

Thank you.

(Applause.)

CHAIRMAN FREIRE: Thank you very much.

Excellent work. Very exciting work.

DR. MERKEL: Thank you.

CHAIRMAN FREIRE: In the interest of full disclosure, I sit on the board of Kavi, and so these kinds of innovative ways of vaccinating are important not only here, but globally, as you mentioned.

Have I any questions? Yes?

DR. SARWAL: Fascinating work.

Congratulations.

I had a question that your inference is that in addition to the Th2 response, if you were to cause increase in Th1 and Th17, you would actually clearance
of virus. Did you actually test that in the -- it
looked like that was an inference, but did you actually
show that you could get clearance, and to what levels
you would need to induce Th1 and Th17?

DR. MERKEL: So the data that we have is only
correlative, right? So the whole-cell vaccine induces
a moderate Th1 and Th17 response, and it does a pretty
good job of clearing bacteria from the airway.
Whereas, convalescent natural infection induces very
strong Th17 and Th1 responses and results in prevention
of colonization of the airway.

So an experiment we have not yet started yet,
but that we're planning is to take a defined set of
antigens and combine it with different adjuvants that
induce different types of responses, Th1 versus Th17
versus Th2, and vaccinate animals and see what the
outcome is in the hopes of giving a much stronger
correlation.

CHAIRMAN FREIRE: Good. Thank you, Dr.
Sarwal.

Have we any other questions? Perhaps
somebody on the phone? Dr. Nolan? Dr. Hait?
DR. HAIT:  I'm good. Thank you.

CHAIRMAN FREIRE:  Well, thank you again very much.

DR. MERKEL:  Thank you.

CHAIRMAN FREIRE:  And apologies for the delay, but very exciting work, and we're very pleased that you came to us today to present it.

Thank you.

DR. MERKEL:  All right. Thank you.

CHAIRMAN FREIRE:  Very well. So also as part of the tradition of this board, we like to look into different programs at the agency, and today we have a presentation from Dr. Ashley, David Ashley, from the Office of Science, Center for Tobacco Products.

So, Dr. Ashley, the floor is yours.

DR. ASHLEY:  Right. Just one thing for clarification, it is Ph.D. and not M.D. But that's okay. On my card.

What I'm going to try to do today is give everybody an overview. I understand I'm going to hit some things, I'm going to hit them at a pretty high level. We're more than happy, if you are interested...
and you want us to come back and get some more, get
into a little bit more depth, more than happy to do
that. But I'm going to try to hit some things and hit
them at a pretty high level today.

CTP has the authority to regulate tobacco
products intended for human consumption to reduce harm
across the population. And the way it's described in
the statute that is provided is we regulate the
manufacture, marketing, and distribution of cigarettes,
cigarette tobacco, roll your own, and smokeless.

But we have recently put out a draft rule,
proposed rule to assert jurisdiction over other tobacco
products that meet the definition, which include e-
cigarettes, cigars, and hookah. And we are in the
process right now of going through the comments on that
proposed rule, and according to the Unified Agenda, we
are supposed to go out with a final rule in this
summer. And so, we are headed that direction.

The standard we have, as described in the
Tobacco Control Act, is really different than the
traditional standard that most of FDA follows in that
throughout, we don't have a safety and efficacy
standard. That standard was kind of -- there was an attempt made by FDA back in the '90s to exert our authority using that safety and efficacy standard over tobacco products, and the Supreme Court made the decision that that couldn't be done.

And so, Congress came back and provided new legislation that provided a public health standard. So everything we look at when we're looking at tobacco products is not safety and efficacy. It's all focused on what would benefit the public health, or are things appropriate for the public health? So everything is around a public health standard.

And when we look at that, what it really means to us is we take into account the benefits and the risks to both users and nonusers. So when we consider a product and we consider an action, we're looking at users of the product, but we also have to take into account nonusers of the product because we're looking at net population-level health. We're not looking at what's going to happen -- alone what's going to happen to people using that product. But we've got to look at what would happen to the population as a
whole.
So it's a different standard, and it's raised very interesting questions that we've had to deal with over the last 5 years.

Because of the standard we're looking at, there are multiple things we have to look at. So one of the things we have to look at and the science we have to get a handle on is the product. So we look at chemistry. We look at engineering. We look at microbiology around tobacco products.

Secondly, we look at the tobacco product user, and so we're concerned about toxicology, pharmacology. We look at clinical medicine, and then we also look very heavily at addiction and product use behavior because we're interested and concerned about the user of the product.

And then, finally, we look at the population as a whole. And so, we're trying to get a grasp on not just the user population, but what goes beyond that. So we look at environmental assessment and epidemiology. Consumer perception is a very big part of making assessments on tobacco products, and then we
have statistical analysis and evaluation to try to understand whether we're making a difference and how we're making a difference.

So it's a very broad set of science that we're looking at when we're evaluating tobacco products. I'm going to talk today about four of our authorities. There are a lot of authorities going on, but there are four things that I'm going to talk about specifically where science has a big impact.

And that includes restricting product changes to protect public health, prohibiting modified risk claims, decreasing the harms of tobacco products, and then educating the public about the dangers of tobacco use.

We know historically, from everything we do, that the tobacco companies historically have made major changes in their products, and this is actually some data from CDC that I had when I was there. And these are products called Skoal Bandits. They're small sachets with tobacco in it.

And sometime between August 2004 and December 2006, the tobacco -- this particular company decided to
dramatically change the levels of unprotonated free nicotine. I'm going to talk a little bit later about what that unprotonated free nicotine is, and I'll go into that. So I'm not going to go into it right now. But they made this change. This is before the act. If they decided to do this right now, they have to come to FDA and request FDA to authorize them to be able to make this kind of a change. Before this, they were changing those products constantly, but now they have to come to us for authorization before they make those kind of changes.

And there are a number of pathways that they can use to get new products on the market. The statute says that no regulated tobacco product can be changed or first introduced to market after March 21, 2011, without FDA evaluating the science and then issuing a marketing order.

I can tell you right now, just from experience, issuing marketing orders for products that you know will kill half the people that use it is a challenge. It's a challenge we face every day. And so, we're trying to develop that science and understand
better how to make those decisions, and we have made a lot of decisions based on the statutory standards. But there are three major pathways to get new tobacco products to the market. The first is a new tobacco product application, and this is the primary statutory pathway to get a product onto the market, involves premarket review. And the standard is that permitting the product to be marketed would be appropriate for the protection of public health, and that is the standard. So far, we have not filed any applications to go through this pathway. The industry has decided to avoid that to the point because more than likely because the phrase "appropriate for the protection of public health" when dealing with tobacco products.

A second pathway is called substantial equivalence, and this is very similar to what CDRH does in their 510(k) program. And actually, a lot of the language is very similar. And it's an alternative to new product applications where in two cases either the characteristics are the same as a predicate or the characteristics are different, but the product does not
raise different questions of public health, and we have to interpret that term "raising different questions of public health."

We have started scientific review on all of the SE reports, the regular SE reports that have been submitted today. We have resolved -- actually, now that 51 percent number is different since I sent the slides in. It's actually now about 56 percent. So we have gone up with that.

And we have resolved them either through making a decision about SE/NSE or because the report has been withdrawn. Most of those reports have been withdrawn after we have sent out a deficiency letter.

The products have changed, but products that are changed are introduced between February 15, 2007, and March 20, 2011, are allowed to remain on the market in a provisional status, awaiting our review. In FDA, we're actively beginning the review of a lot of these provisional reports, which were prioritized according to their -- how likely it was that they would raise different questions of public health.

So when we've gone through, we got about
3,000 of those provisional reports in-house, and as we've gone through them, we go in order of what we believe are the major public health concerns around those products.

Third pathway is called substantial equivalence exemption. It's an alternative to substantial equivalence and very limited area when there's -- the change is to an additive alone, the change is minor, and that the determination can be made that a full substantial equivalence report is not necessary to ensure that permitting the tobacco products to be marketed again would be appropriate for the protection of public health.

And so, one of the things we do in the Office of Science is we look at each of these applications to determine whether they should be authorized for marketing.

When I first got into tobacco about 15 years ago, I thought that tobacco products were actually pretty simple things. You think of them, you got some tobacco, you got a roll of paper, and that's pretty much it. Come to find out the companies really have
been engineering these things dramatically for many years, and so there's a lot of engineering aspects. There is a lot of tobacco blending, filter development that goes into.

So there's a lot of things in the products that can alter constituent delivery or product use. And so, when we look at these products, we look at them from the product standpoint very widely. We look at a lot of the engineering features and a lot of the chemistry and the makeup of the tobacco blend.

And the reason we do that is because changes in the tobacco blend can have dramatic effects on the levels of particular constituents in the products. For example, tobacco in a cigarette is not -- in the United States is not just a single type of tobacco. It's actually a mix of different types of tobacco.

So you can have Burley tobacco. You can have Bright tobacco. And the difference between those can be dramatic. So the levels of NNN, which is a known tobacco product -- known tobacco carcinogen, can change dramatically if you switch from Burley to Bright
tobacco. The NNK, which is another tobacco-specific nitrosamine, can change also.

So the blend itself is a critical feature in us understanding what will be the impact of public health of allowing these blend changes. The companies for years have made major changes in their product blending. Now we have to look at that and make the determination about whether that product should be authorized for marketing.

Switch gears a little bit. We also have the responsibility for looking at modified risk claims. Traditionally, the companies have made claims about their products. Back in the '50s particularly, there were lots of claims about doctors choosing their products, and their products are safer. There are lots and lots of claims about their product being much safer than other products as a means of getting people to buy and use their products.

They are now prohibited from making those kind of claims unless FDA makes the decision that those claims are appropriate and we allow them to do that. And they have to make a claim to base it on whether the

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use of that product will reduce the harm or the risk of tobacco-related disease, which is associated with commercially marketed tobacco products.

So no longer can they make those kind of claims. We go in and look to determine whether that specific product actually will reduce harm and whether -- what's going to be the impact on the population as a whole. And when we talk about modified risk, it's actually a very broad -- it covers a broad ground also because it includes labeling and advertising as well as any other means of communicating with the public directed to consumers through the media or otherwise. And so, it's a very broad authority.

When we look at modified risk, there are a number of things we have to weigh as we're looking at it. So we're looking at increased harm. We're looking at reduced harm.

Increased harm can come from a product being more toxic. Instead of quitting, smokers becoming dual users. Products that used in a way that makes them more harmful. Adults or youth initiate more. Or former smokers relapse more. Those are all increased
Reduced harm would be a product that's less toxic to the users. Smokers switching completely from a more toxic to a less toxic product. Products that were used in a way that makes them less harmful. Reducing initiation to tobacco products as a whole, or former smokers actually relapsing less.

And so, we weigh those increased harm versus reduced harm to try to determine what's going to be the population-level impact of allowing a modified risk claim on a product.

Third area is decreasing the harms for tobacco products. We know the process that goes forward to have a person that ends up dying from tobacco.

First, you start out with nonuse. There is some experimentation that takes place, usually in teenage years, long before kids can legally acquire the product. They are attracted to the product through a number of product characteristics and also advertising and marketing methodologies.

That experimentation leads to addiction,
which half of those people that experiment end up being lifetime addicted to those products, and that addiction then exposes people to toxic chemicals for their lifetime, resulting in disease and death.

And so, when we're talking about decreasing the harm of the products, we're looking at trying to break this process, the process going from nonuse to disease and death. And this provides us a number of different ways to try to address this.

Fortunately, the statute gives us very broad authority on -- in an area called tobacco product standards, and this is actual text from the statute itself. So we can deal with nicotine yields. We can deal with reducing or eliminating constituents, including smoke constituents. How the product is made. We can have product standards around testing. We can have restrictions on sales and distribution or the form and content of labeling. And those product standards give us incredible tools that we can use, if we've got the science to support them, to move forward and actually have a big impact on tobacco product disease and death.
We know that if you can get people to stop smoking, there is life expectancy that returns. So if you can get someone to quit at age between 25 and 34, they will get back 10 years of lost life. Even someone that quits between 45 and 54 will recover 6 years of lost life. So any way we can get people to stop smoking has a huge impact.

This is a study by Neal Benowitz, University of California at San Francisco, a very interesting study. He took a group of people who were not interested in quitting. He had them smoke cigarettes that had very low levels of nicotine in the filler and found that at the end of the study, a quarter of those people, again who were not interested in quitting at the beginning, decided to quit at the end.

So actually using these products in a way allowed those people to make the decision to stop using products when they got to the end. Basically, what can happen in this case where the people are using reduced nicotine products, they will break the connection between smoking cues and the addiction. And once that connection is broken, people have a much stronger
ability to make a decision to quit. While that nicotine addiction and those cues are connected, it's very hard to break that cycle.

We also know that there are certain products that have widely different levels of carcinogens, and this is data that I published when I was at CDC looking at different cigarettes from around the world and their levels dramatically different. And actually, the level, where it says "U.S. brand," are when I first started this study, I assumed the U.S. brands would be much lower levels of carcinogens than brands bought in other countries.

The reality is that U.S. brands have much higher levels, and that's because of the type of tobacco blend we have in the United States. So, in reality, the way that tobacco products are made in the United States actually increase the level of tobacco-specific nitrosamines to which people are exposed to, and when you look at biomarkers of exposure, you see the same thing.

So if you live in New York or Minnesota, you're going to have much higher levels of biomarkers.
of exposure to nitrosamines than if you live in Australia or Canada, where they use a different type of tobacco in those cigarettes.

In addition, we know what -- another thing that's been proposed that's actually very interesting is moving from cancer into noncancer hazard. It's been estimated that nearly 90 percent of the noncancer hazard from tobacco products is due to acrolein. It's a single chemical that's formed in the burning of tobacco.

And there are also already known ways to reduce acrolein. Philip Morris put out a product called Marlboro UltraSmooth back a number of years ago, and they put charcoal in the filter, and that charcoal will actually reduce the levels of acrolein. Unfortunately, that product was not a market success, and so they have pulled that product off the market.

Yeah, it's amazing, isn't it? But we know how to reduce the levels of some of these chemicals. And FDA has the authority, once we get the science together, to be able to move forward with some of these product standards.
Let me get back a little bit to what I was talking about earlier about free nicotine, and there are three different forms of nicotine you can find in tobacco products. There is -- well, there's actually two. There is a diprotonated form, which you don't find in tobacco. Then there is a protonated form and an unprotonated form.

The unprotonated form is also called free-base nicotine, and that's the same as free-base cocaine. It's the same principle, where you add a base. It changes it. It takes all the charge off, and this moves through the membrane much faster.

So it gets in the bloodstream, gets to the brain much quicker. And depending on the pH of the product, either the smoke or a smokeless product, you can get nicotine to the brain faster and make the products more addictive.

This is some data on variation in unprotonated, which is free nicotine levels in 40 different U.S. smokeless brands, and you can see they vary dramatically. What's down in the lower left-hand corner is what a lot of people refer to as "starter
brands." Those are intended for kids to get started into it because if you give them a full nicotine brand, it's very, very hard to just take those in. It's so harsh.

But after a while, those low nicotine levels don't satisfy, and so people generally graduate up the scale. Most brands end up in the 4 to 5 milligrams per gram level of unprotonated nicotine, and that's where most of this stands. If you're a real man, you go on up the scale and really take in some free nicotine.

But I want you to just look at the values on there. I'm going to particularly point out where Copenhagen Regular is and Skoal Bandits. They are at different dramatic levels of unprotonated nicotine.

And when you look at the delivery of nicotine into the bloodstream, you get very different levels. So the speed and the amount of nicotine that gets in the bloodstream and, therefore, gets to the brain is very different, depending on those free nicotine levels. And they have traditionally for years manipulated that free nicotine in order to get the kind of product to appeal to particular users.
Now last thing I want to talk about is educating the public about the dangers of tobacco. We need the science to identify the most effective means, and we have authority to move forward with that, including education campaigns, health warnings, and harmful and potentially harmful constituents.

We have a really superb education campaign that is out. It's been out for just about a year. Has anybody seen the education campaign? If anybody has seen it, it does worry me a little bit because it's aimed at at-risk teens. And so, the TV shows they're showing it at, showing -- I've seen one. I saw one.

Yeah, you'll catch one every once in a while. But if you're not seeing them, that's probably actually good because the TV shows we're putting it on are not aimed at you guys. It's actually aimed at at-risk teens. They have been very effective.

Love to come back sometime and bring Kathy Crosby, who heads our communications folks, and have her present these to you. They are excellent. The great thing is they're scientifically based.

One of the things we've done before moving
forward with this is we got our scientists involved and made sure that whatever they were saying was scientifically based. And it's pretty tough to do a public education campaign and attract attention and have an impact on something that's scientifically based.

Generally, science is kind of boring, and so you have to work the real science and combine it with some terrific minds to make that appeal to kids. If you start talking about kids -- to kids about lung cancer, they blow you off and say we really don't care about lung cancer. If you start talking to kids about getting wrinkles on their face, that's a big deal.

And so, having to learn how to do that well was really a challenge, but we've got those. And they will continue to come out.

Graphic health warnings. Court of Appeals for the D.C. Circuit held that the graphic health warnings that we put forward were in violation of the First Amendment. So we're undertaking research to go back and relook at that so that we can continue to pursue putting graphic health warnings on tobacco
And then, finally, there is a part of the statute that talks about public display of HPHC data. It says the Secretary shall publish in a format that's understandable and not misleading the levels of chemicals in these products. And one of the things that's challenging is making it in a way that's understandable and not misleading to a layperson because these levels have been used for years by the tobacco industry as a means of attracting more users.

And so, we are looking to this very carefully and making sure that before we proceed forward, this data is understandable. Trying to make scientific data understandable to the layperson, and sure you guys understand that, is also very challenging.

We have a lot of research work we're going forward. We have put forward our research -- our scientific priorities, which include the diversity of tobacco products, reducing addiction, reducing toxicity and carcinogenicity, adverse health consequences of tobacco use, communications, the marketing of tobacco products, and economics and policy. We're working very
closely with the Centers for Disease Control and Prevention on surveys and on laboratory analysis. We're partnering with NCTR on some things that they are very good at that we can rely on and we can really get very good data from them, including microbiological agents. Alternative biomarkers to assess product harm. Smokeless tobacco carcinogen pharmacokinetics and genetic toxicology of the smokeless products. And there are a bunch of other products also. But we're working very closely with NCTR in a very good partnership, as you mentioned earlier.

We're working with the National Institutes of Health. We have -- NIH has actually set up a separate program, called TRSP, Tobacco Regulatory Science Program. Before I go on, I will say every year, we're putting out about $200 million in new research dollars around tobacco regulatory science. We have completely altered the landscape of tobacco research by putting this funding out.

I just got back recently from the -- last week from the Society for Research on Nicotine and
Tobacco, and it's amazing the number of studies that are being done now to support FDA needs and the number of studies we're funding. So it's actually exciting.

We also have 14 Tobacco Centers of Regulatory Science. We have the Population Assessment of Tobacco and Health, which is a longitudinal study of about 50,000 users and nonusers that we're following over time to understand transitions, how people switch between products, what motivates them to use products, and then, eventually, what leads to the death and disease from tobacco products. Never been done before around tobacco, and we're putting that forward.

And that is in the process. At SRNT last week was we had the first presentation to the public of data from the first wave of that study. We're putting out competitive revisions, administrative supplements, and research training grants through NIH. We're also working with some nongovernment research institutes, including RTI and Westat, which is serving as the contractor who is running the Population Assessment or tobacco -- of Tobacco or Health study.

We've made a lot of progress since the first
Surgeon General's report 50 years ago, but there is still a long way to go. We still have about 480,000 people in the United States dying from cigarette-related deaths. Ninety percent of all adult smokers start before age 18. Half of those become addicted before they're old enough to legally buy tobacco.

Each day, about 3,300 kids smoke a cigarette for the first time, 2,800 smoke a cigar for the first time, and 1,300 use smokeless tobacco for the first time. For us, the strength of the science base is critical if we're going to institute lasting change and have a far-reaching impact.

Thank you.

CHAIRMAN FREIRE: Thank you, Dr. Ashley. I am just blown away. What an amazing presentation.

Thank you very, very much.

Dr. Weaver?

DR. WEAVER: Yes. Thank you.

This week, I saw a study where teens are flocking to e-cigarettes. What do we know about the relative risk of those, and how do we communicate to this group?
DR. ASHLEY: Right now, as of today, we do not have regulatory authority over e-cigarettes. They are included in our deeming regulations. So if that -- when that deeming regulation goes out, we will then have regulatory authority over e-cigarettes.

And I make that clear. E-cigarettes not for therapeutic use. E-cigarettes for therapeutic use are already under CDER's authority, and so CDER has that.

E-cigarettes are an interesting thing. They can be either a salvation to the tobacco issue, or they can be an absolute disaster, depending on how they're regulated. The job we do to properly make sure that those products, they maximize the population health benefit and we minimize the population health harm.

If e-cigarettes serve as a wonderful pathway for kids to start using and to graduate from cigarette -- to cigarettes, it's a disaster. It is an absolute disaster. If they serve primarily as a gateway for smokers who have been wanting to quit for years and have not been able to completely -- to switch to those products and, hopefully, eventually quit completely, they are a boon to help save 480,000 lives.
It all depends on how well those are regulated, and rest assured, we feel that burden every day.

CHAIRMAN FREIRE: Thank you for asking that question. I think it was on many of our minds. I have Dr. Jenkins, Dr. Xie, Dr. Russell.

Yes, thank you.

DR. JENKINS: Thank you. My question has already been addressed.

CHAIRMAN FREIRE: Very good. Dr. Xie?

DR. XIE: I have a very similar question. I was curious. All the data you presented is not under study for the e-cigarette. It's the traditional cigarette, right?

DR. ASHLEY: The studies I presented are data that are publicly available, yes.

DR. XIE: I mean the study is not on the e-cigarette because you said that tobacco -- in the second slide, it says all of tobacco, including all e-cigarette and cigar and the hookah. So the data is not on those?

DR. ASHLEY: That is correct. We have got
the number I think is 50 research projects going on right now that we're funding on e-cigarettes. That research is ongoing. We're beginning to see some of that data coming in. I didn't present any of that today, partially because it's not been published yet by the researchers and also because we have to be careful about the interpretation of that.

But we've got about 50 studies that we're funding on e-cigarettes right now, which range all the way from the chemistry of the liquids to engineering of the products, all the way to people's perceptions, and so the full range.

DR. XIE: NBC News talks about billions market, and also last week movie "Focus" also showed the e-cigarette. So the FDA will have some act on implementation on those, right, eventually you think?

DR. ASHLEY: We have stated in the Unified Agenda that we plan to have a final rule summer of this year.

DR. XIE: Thank you.

CHAIRMAN FREIRE: Thank you. Dr. Russell?

DR. RUSSELL: I hope this isn't
controversial. Is your center going to attempt to regulate marijuana that's being sold in those States that have legalized recreational use?

DR. ASHLEY: That's not controversial whatsoever because our statute is very clear that we regulate things that are made or derived from tobacco. If marijuana is made or derived from tobacco, yes, we will regulate it. If it's not, we won't regulate it. So it's not hard to answer, actually.

CHAIRMAN FREIRE: Thank you. Dr. Reiss?

DR. REISS: Thank you. Excellent presentation.

There are some professional societies that really don't want to have anything to do with tobacco-related research. I was wondering if you've run into that, and has it caused a problem for you all in terms of the research that you're doing and any other random thoughts you have about that.

DR. ASHLEY: That's interesting. I have not heard that whatsoever. I know that there are a lot of societies who've refused to take tobacco money, and I can understand that very clearly.
I've not heard anyone that has been afraid to take our money. One of the things people have actually asked, and it's an interesting thing, yes, because we're totally funded by user fees, my salary is paid by the tobacco industry, I mean, in a way. It comes through. It goes to Congress. It's appropriated.

What we try to explain to people is that the money goes to Congress. Congress then appropriates that money to us. And so, because of user fees, that money all comes from Congress.

So the big advantage there is it's no tax money. There is no tax burden on the U.S. public for the work that we're doing. The tobacco companies are required to pay for it. But I've heard no one have a problem with taking our money.

CHAIRMAN FREIRE: Thank you very much.

I have Dr. Sarwal, and I wanted to give an opportunity to the members who are on the phone in case they want to speak.

Dr. Sarwal?

DR. SARWAL: Yes, thank you very much.

I actually learned a lot today. As a
pediatrician, I actually interface a lot with adolescents, and the perception seems to be largely in the adolescent's mind that this is the safer new way to start smoking. And so, we have children with chronic disease who still are under the peer pressure to undertake and go into this.

So one thing that I would like to perhaps get a better understanding is the three things that I took away are the nitrosamines, the acrolein, and then your free nicotine base. These are all the bad players in this whole scenario. So I'm sure e-cigarettes decreases some of that, and I'm not totally sure what.

But I think it continues to have the harmful effects of some of these combinations, and is this something that the FDA, who has so much now knowledge about really the toxicity profile and what it does, could you release some more information really stressing that this is not the harmless way to start smoking?

DR. ASHLEY: What we're trying to focus on, because of our statutory requirement, is population health. And so, we are looking at users like you're
concerned about. We're also looking at nonusers, and so we have to include that entire calculus in what we're doing.

And so, as we get the science we need, we will be moving forward and educating when we have the science we need. There is still a lot of science that needs to be understood about these, and the problem -- one of the problems you run into with any kind of -- and I'm sure everybody sitting on this side of the table would agree with me, products can't be lumped necessarily into one group.

You can't say everything falls into one category. E-cigarettes are that, very clearly. E-cigarettes range -- and again, I can come back if you want me to give you a more in-depth discussion of e-cigarettes.

E-cigarettes range from what we call the cigalikes, which looks like a cigarette. If you didn't look carefully, you'd think maybe it was a cigarette. It delivers very little nicotine. It ranges from those kind of products to what they call tank systems, which is a system that may be that big, that big around, full
of nicotine and people suck on, that delivers a ton of nicotine. And so, trying to categorize all e-cigarettes into one group is very -- it's fruitless because you can't do that.

One of the things that we're trying to push researchers particularly is properly characterizing the product they are talking about so that we can understand. There have been studies that have come out that say e-cigarettes are great for cessation, and there are other studies that come out that say e-cigarettes don't help cessation whatsoever.

Part of that issue is the fact that they lump all these e-cigarettes into one group, and both of those studies may actually be true, depending on exactly what the product is and the different products. And so, we're trying to wade through a bit of the confusion to try to make sure that there are very clear messages and the answers are clear before we go out and start making very broad generalities.

CHAIRMAN FREIRE: Thank you.

Dr. Gibbons, do you have your flag up? Yes.

Okay. Thank you.
DR. GIBBONS: So your last comment just struck something I wasn't going to ask about, but I'm going to start here. I understand you're trying to make the point that e-cigarettes are different, at least in part because of differing levels of nicotine delivery. But you showed slides saying that's the same thing for cigarettes, too, and you showed -- and you talked about how the tobacco companies have been manipulating nicotine levels over the years, but yet we group them all as one thing.

So I don't really understand why you can't do that. I understand what you're saying about the differences, but why is it a salient point for e-cigarettes and not for regular cigarettes?

DR. ASHLEY: Actually, one of my biggest points was that cigarettes are not the same. When we regulate cigarettes, we look at individual characteristics. When I put up, for example, I put up that chart that had the little cigarettes on there that showed all the different properties, all of those things can change, and all of those things can make the cigarettes different.
And so, when we do our evaluation, we're looking at each cigarette and the differences from one to another. And so, actually, I guess I didn't get my point across very well because one of the things that we do regulating tobacco products is consider the fact that they are very different, and that we have to regulate them as individual products and make decisions between one and the other.

DR. GIBBONS: So that's helpful, but when you talk -- that does not come, at least to me, it doesn't come clear when we talk about regulating and we talk about problems with cigarettes. You know, we very rarely sort of say problems with this type of cigarette versus this type of cigarette. So you might think about that going forward.

Taking me back a little bit to medical school days, but I always found it interesting when we're talking about sort of carcinogenic and health-harming constituents in cigarettes. When I first looked at this in medical school, I was blown away by the fact that I was told at that time that there were over 3,000 constituents in every puff of smoke.
And every time I've looked at it since then, it's gone up. The last time I looked, I think it's between 6,000 and 7,000. It may be higher than that. But we focus on NNK and NNNs, the three or four that we know of, which are bad. But the point is most of the constituents that are in the tobacco smoke, we don't really have any information or not enough information on. So even if we know about those two or three, there could be a whole lot of other things you get in each puff that -- that are really quite harmful. Just wondering what you thought.

And my last comment is on the very low nicotine cigarettes, and you made the comment that it may help people actually quit. Just wondering, was that a controlled study that you showed up there? It wasn't clear to me that it was.

DR. ASHLEY: Let me see if I can get to the first one first. We have identified a list of 93 harmful, potentially harmful constituents. There are probably more than that, but we've identified a list of 93 that national/international organizations have also
identified as of concern.

You have a number of constituents now is 7,000 and above that, and so there's probably more than 93. So we are focusing on those 93, and to actually deal with that, you probably actually have to reduce the list down a little bit more.

Again, I didn't -- I could give you a whole day worth. Here, I just had half an hour. Because we're concerned about metals. We're concerned about a lot of other things.

The study was a controlled study. It was a study, I'm trying to remember now because I can't remember off the top of my head, whether it was a -- it was a study that was -- it was a study in a natural environment. So they didn't have them come into a clinical research facility and stay there for 6 weeks. They did try to control for the possibility that they would go out and actually cheat, and there's a lot of research that's been going on trying to figure out how to stop and how to incentivize people in those kind of studies from cheating and buying other cigarettes and supplementing. So there are definitely
challenges to those kind of studies.

CHAIRMAN FREIRE: Thank you. Dr. Bahinski?

DR. BAHINSKI: I'll be brief. So a quick
question regarding, you know, since you are funded
entirely by user fees, are there any restrictions on
the research that you can fund or what the publications
can come out of that research?

DR. ASHLEY: The research is restricted to
things that are in our regulatory authority. So there
are certain things that we don't do. I didn't have
that slide up there. For example, taxes. We can't --
we can't fund research on what are the impact of taxes.

We can't fund research on therapeutic
therapies for cessation. There are certain things that
don't fall within our authority. We cannot fund those.
Other than that, no. So we're funding very broadly,
except for those things that fall outside our
regulatory authority.

CHAIRMAN FREIRE: Thank you very much, Dr.
Ashley.

I will end the discussion here. I would be
interested in knowing at some point how this maps onto
global efforts for tobacco control -- but not now -- as well as the metrics. Have these advertisements been successful? And it may be too soon to tell, but it would be interesting.

DR. ASHLEY: Actually, it's not. But it's actually not too early to tell, but I'm not the expert on that. What you need to do is bring Kathy Crosby in, and she could give you the lowdown on all of that.

CHAIRMAN FREIRE: Thank you. Thank you very much.

This board has four subcommittees -- the Subcommittee on Science Moving Forward, the Commissioner's Fellowship Program Evaluation, the CERSI Program Evaluation, and the newly formed Office of Regulatory Affairs Food Emergency Response Network. This morning, we will be a bit ambitious, and we're going to change the program slightly to allow Dr. Russell to scoot under the wire.

So we will have two reports from -- the first report, as is noted in the program, will be by Dr. Yaszemski and then very quickly followed by Dr. Russell, if Dr. Russell will agree to that change?
Mike, thank you.

DR. YASZEMSKI: Would you like us to speak from the podium or from here? Here is okay. Can our IT person, can you advance them for me when I ask, please? Thank you.

This is a progress report of the Commissioner's Fellowship Program Evaluation Subcommittee. I'll review the things we went over last time and then talk about our update. The outline will be to talk about the CFP.

Which one is it? This one here. Thank you.

The outline will be to talk first about the CFP organization, our committee, our draft recommendations to FDA, and the remaining agenda items and timeline.

The CFP began in 2008. Its goals are to attract top-tier scientists to FDA for a 2-year program that includes classroom coursework, mentored projects, and participation in the regulatory review work, and to serve as a recruiting tool for the FDA.

The requirements are 11 regulatory science courses, a project on the topic of interest to FDA.
under the guidance of a scientist mentor, and to participate in regulatory review work.

Here is our committee: Dr. Hait, Dr. McLellan, Dr. Meyer, Dr. Ognibene, and myself. We started in August of '14, and our service will complete on 31 July this year.

Now the draft recommendations that we have so far, we were given nine questions. We don't have recommendations on all of them, and I'll go over those recommendations that we've already agreed on to propose to the FDA so that we can get feedback from everybody as we go forward with this as to whether these recommendations make sense, if somebody wants to add to them, suggest something different on that topic.

So on the first one, what improvements, if any, should FDA consider to meet the goals of the Commissioner's Fellowship Program? The funding has steadily decreased from $12 million in 2010 to $3 million in 2014.

Now the subcommittee recommends that the CFP budget become and remain a stable line item in the FDA budget, with cost of living increases included in the
budget planning process. Because as we get to what's an ideal number of fellows, what's an ideal length of time, it's a hard target to plan ahead if the budget keeps changing every year.

Next, what options should be considered regarding recruitment strategies and eligibility criteria?

We feel that training people who do not stay at FDA and who enter industry and academia upon graduation from the CFP is just as important as recruiting future FDA employees and should be elevated to a goal of the CFP. Secondly, the entry requirements for engineers -- that is either bachelor's, master's, or doctoral degrees -- should be extended to all applicants because for all other applicants, a doctoral degree is needed, and thus, all three degrees should become the uniform entry criteria requirements for the CFP.

Next, from question four, there are three program requirements: coursework, regulatory science project, and regulatory review work. Of those three, we feel that the regulatory review work is very
important and valuable and should remain as is.

With respect to the coursework requirement, the committee feels that adding the option for a master's degree, for example, an M.P.H. in collaboration with a local university, would be a good idea.

Now this mixes also with one of the questions that states are there other programs within the FDA or are there programs outside that could fulfill these requirements? And as we've heard earlier today, there are several universities that have degrees program -- degree programs, degree-granting programs in regulatory science. And it may be that rather than starting a new one, using one or more of those universities' programs would be good.

We also feel that developing the current regulatory science curriculum into offerings of Web-based electronic online courses, in addition to the traditional classroom courses, would be better. Flexibility will be good because different users, which may range from people who have just graduated college to professors on sabbatical, will have different needs,
different requirements for them to participate, and we feel flexibility would be good, and online coursework would be a plus.

Now the regulatory science project program requirement. We feel this is a good requirement, and we feel that the FDA should shift the focus of the regulatory science project to the needs of the fellow.

The current project selection is largely based on both FDA-identified needs and the preceptor's recommendation. We recommend that these selections include the fellow's input into the project selection process and attempt to honor that input as much as is possible.

The other questions, number five, what changes, if any, should the FDA consider regarding the current 2-year program length? We recommend that we query past fellows, whether they be at the FDA or in academia or industry, regarding their thoughts on the program length.

Among the questions to ask, ask if the length was optimal with regards to the CFP's value in their current job. Again, the issue of flexibility.
Consider flexibility in the program length. Fellows' needs will differ. The move to Web-based coursework might allow fellows the flexibility to complete some coursework at home, spend a lesser time at the FDA, during which they would complete the regulatory work on the project.

We lumped six and seven together because progress accomplished and outcome measures seemed to us to have a little bit of overlap. With respect to progress, we recommend that the FDA prepare and execute a questionnaire for graduates of the CFP whether they are at the FDA, in industry, or in academia.

And among the questions, ask do you have a plan to share your knowledge of regulatory science at the FDA, at your company, or at your university? We talked a lot about training the trainer and the effects of this program, which we think are very good, will multiply if the trainers are asked how are you spreading the word based upon what you learned?

Our timeline. After this meeting, we're going to have a conference call to set -- to develop focus group questions for the April 10th subcommittee
site visit to the FDA. The reason April 10th was chosen is that's an already-scheduled meeting of all 12 members of the advisory panel, and otherwise trying to get 12 of them together with 5 of us would have been very difficult.

So we're going to show up on their meeting day. That's on April 10th. We'll meet, go over the questions that we develop in our conference call. If we feel we need any additional data, we'll request that from the FDA after that meeting. We'll prepare from those data and the data we've already gotten a final subcommittee report and brief the Science Board at the July 29th to 30th meeting.

Happy to answer any questions. Thank you.

CHAIRMAN FREIRE: My goodness. That was surgical precision.

DR. YASZEMSKI: You asked me to make it short.

(Laughter.)

CHAIRMAN FREIRE: Thank you. That was amazing.

Any questions or -- or issues? I actually
We are considering later on the science training coordination proposal, and I don't know if you're going to be here for the discussion. But I think it would be interesting to see how the two jive.

DR. YASZEMSKI: I'll stay.

CHAIRMAN FREIRE: Thank you.

Dr. Russell?

DR. RUSSELL: So I've been asked to update the board on the Science Looking Forward Subcommittee activities. I think I was asked to do this mostly because my accent most closely matches that of Martin Philbert's.

The committee started its work almost a year ago in terms of its discussions, and you can see here a list of the committee members. Really, I think the purpose of this report is to build on the very important work that was done at the Science and Mission at Risk report that was done almost a decade ago, and the realization from the agency that it was time to take another look at all of the activities of the agency in science and come back with a set of
recommendations really drove this agenda. I think the agency is looking for us to do essentially three things. One is to comment on what the agency should be doing. Two is to comment on who they should be doing it with. And three is to comment on how to make sure they do it at a superb level.

So there are, therefore, three areas in which our committee is active. One of those areas is looking at the priorities, activities, and emerging needs. And I'll come in a moment to what's been happening in terms of the activities to get ready for this.

The second area is to look carefully at extramural programs and collaborations and to evaluate what's happening, what isn't happening, and what should be happening in that area.

And then, lastly, as I mentioned, the underpinning of all of this is that everything that the agency does, it obviously desires to do at the highest level, and so the subcommittee aims to take a very careful look at scientific excellence and ensuring that that environment at the agency supports that.

We have been incredibly impressed as a
subcommittee by the work done in preparing for our work at the agency. They produced the FDA Science Moving Forward report for us that really provides an incredibly valuable foundation for the work that we will do. And to be honest, I think everyone on the committee thanks the agency for the work that went into this voluminous document that's full of important information.

That document, once it was in place, sort of opened the door then for a lot of work. I can tell you, I think I speak on behalf of everybody on the subcommittee, that we're probably spending more time on this FDA subcommittee over the last few months than on any other activity in our day jobs, with multi-hour long conference calls seemingly every day, but I think it's actually just every week.

But it's a lot of work because the agency does so much rooted in science, and one of the most important things for our subcommittee was to become ingrained in what those activities are in order to be able to formulate important questions.

So we've had multiple telephone conferences.
We've split up into three subgroups and are preparing for a site visit. Those subgroup areas are listed here. And with their chairs, each of the subgroups has three or four people in it, and we're really driving towards a March 31st site visit.

There may be another opportunity for the subcommittee to get together in person to make sure that we stay on an incredibly aggressive timeline and deliver a draft report to the board by July 2015. Perhaps the board would not be too disappointed if that timeline wasn't met, but we're working really hard to make sure it is.

Our goal is not to replicate the depth and time taken to do the Mission at Risk report, which was a huge report, and really our goal is, in Martin's words, to produce a pithy report focused mostly on recommendations and to use the FDA's work that they did in preparing the foundation for us heavily in generating that.

So I'm sure at our next meeting, we will be able to talk much more about what -- what we discovered in the March 31st site visit. We're all very much
looking forward to that rapidly approaching day. 

Happy to answer any questions.

CHAIRMAN FREIRE: Thank you.

There are members, of course, of the

subcommittee present. Anybody who would like to make a

comment to either of the two presentations, I welcome

the floor.

(No response.)

CHAIRMAN FREIRE: Well, I can tell you that

it does seem like we have calls every day. But they

are every week, as was just said.

This is part of the performance plan for the

Commissioner, in fact, for the year. That's the reason

why we are taking this very seriously and why we would

like to meet that deadline.

We understand and are overwhelmed, frankly,
as committee -- subcommittee members of the amount of
work that has been done and is being done by the FDA,
particularly in response to the 2007 report. So we are

doing our best to work hard to make sure that we do a

fair and good job and that we recognize the amazing

work that has already been done.
So thank you all very much. Thank you to the members of both committees, the subcommittees. And unbelievably, we're actually ahead of time, having dispensed with another item on the agenda before the 12:00 p.m. timeline.

So, Martha, any logistical issues for lunch?

MS. MONSER: Yeah, for the lunches, for folks who have actually preordered lunch, they're going to be available for us in the -- there's two meeting rooms right behind us. It's in the further -- further meeting room, and we can have lunch there. And I think that's the biggest announcement, where your lunches are.

For folks who haven't preordered lunch, the kiosk is open, and it's basically the same fare at the kiosk versus what you'll be getting in your lunch boxes.

We'll resume promptly at 1:00 p.m. Please make sure to be back here maybe a minute or two early. The Commissioner will be joining us promptly at 1:00 p.m. to give some remarks. She is downtown for hearings today.
Dr. Ostroff will also be joining us at 1:00 p.m. He is with the Commissioner today, as you can well imagine.

So, and if there are -- as I said, at 1:30 p.m., I don't expect we'll have anyone here for the open public hearing. So we'll move the agenda forward with the regulatory science training coordination at approximately 1:30 p.m. And I've already emailed the staff who will be presenting that to, hopefully, get them here.

So I think we will break for lunch now, and we will see you promptly at about -- about an hour from now.

Thank you.

CHAIRMAN FREIRE: Thank you.

(Recessed at 11:58 a.m.)

(Reconvened at 1:03 p.m.)

CHAIRMAN FREIRE: Ladies and gentlemen, we're starting. Thank you.

(Pause.)

CHAIRMAN FREIRE: So I'm going to -- I'm going to get started. Thank you all for coming back
promptly.

I am delighted that Dr. Hamburg is able to join us for a few minutes. I believe you know that she's on Capitol Hill today, accompanied by Dr. Ostroff, performing her duties as FDA Commissioner and, hopefully, having a successful meeting with her colleagues on Capitol Hill.

Before I hand the microphone over to Dr. Hamburg, the board would be remiss if we did not take a moment to express our gratitude to her for her leadership and trust of this Science Board during her tenure as Commissioner of the Food and Drug Administration. She has, in our estimation, been -- certainly in mine as well -- been an extraordinary Commissioner, and this agency and the Nation have benefited from her leadership and from her wisdom.

She has, in fact, set a very high standard for all Commissioners to follow. So we are very sorry to see her leave. But we're delighted that she can join us, and I believe she is on the phone at the moment.

Dr. Hamburg?
COMMISSIONER HAMBURG:  (on telephone) Yes.  1  
Hello.  I am on the phone.  I am really pleased to join 2  
you at least by phone.  Do you hear me okay?  There's 3  
an echo on my end.  
CHAIRMAN FREIRE:  We hear you with a little 4  
bit of echo.  But --  
COMMISSIONER HAMBURG:  All right.  
CHAIRMAN FREIRE:  Are you on speakerphone, by 5  
any chance?  
COMMISSIONER HAMBURG:  I just changed to 6  
holding the hand whatever it's called.  
CHAIRMAN FREIRE:  Much better.  Thank you.  
COMMISSIONER HAMBURG:  Okay.  Yeah, so I just 7  
actually completed budget hearings on the House side, 8  
and so forgive me if my mind is a little bit addled.  
But one of the interesting things about budget hearings 9  
is that it's kind of a mental gymnastics where you go 10  
from tanning beds to sexual dysfunction drugs to 11  
substantial equivalence criteria for tobacco products 12  
to new drug approval.  
So, you know, it can be any -- they can ask 13  
you about anything.  So it's quite an experience and 14  

one that I'm sure my successor will enjoy.

But, you know, let me begin by thanking all
of you for your continued support and commitment to the
work of the FDA, and the roles that you've taken on on
the Science Board, you know, really do matter and, you
know, enables us to get access to some of the best
minds out there in various areas of our activity, and
also helps to underscore how, you know, science really
has to be at the center of everything that we do at the
FDA.

And we need to continue to support our
scientists at the FDA. We need to be challenged in our
scientific rigor to make sure that we're addressing all
of the issues, asking the right questions, aware of
important advances in science and technology that can
make a difference in our work, and importantly, that
we're engaging with the broader scientific community.
Increasingly important as we try to both
leverage the expertise that's out there in new ways and
really work in truly new partnerships in order to more
effectively oversee the products that we're responsible
for. So thank you so much, and you know, I have always
taken great pride in the work of the Science Board.

And frankly, the work of the Science Board at various points has been, you know, truly pivotal to our work, either focusing attention internally on problems or needs or opportunities for FDA or through the work of the Science at Risk study, you know, really focusing attention on the importance of science at the FDA and how dramatically and critically underfunded it had been. So I leave with sadness that I will no longer have a role working with all of you, but knowing that you will continue to contribute to the things that are most fundamental to the FDA and its mission.

I think I also can feel very good as I leave about what has been accomplished in the last couple of years and, most importantly, very good about the leadership team that I'm leaving behind. I have, I will admit, thought at various points about stepping down from this job. It's definitely one that requires 24/7 commitment and little time for balancing other important aspects of life.

But I did not feel I could leave until I had the right constellation of people in a set of critical
roles. So I want to just walk you through some of that because it certainly matters to the FDA, and I think it matters to your work on the Science Board.

You know, first and foremost, I think you all know that Dr. Stephen Ostroff has been named as Acting Commissioner. He came to the FDA to be Chief Medical Officer and Senior Public Health Adviser for Food Safety within the Foods Program. Quickly got moved into the Acting Chief Scientist job a little more than a year ago, and then now he finds himself or in a few weeks will find himself as Acting Commissioner.

But I think that reflects the quality of his work and, you know, his seriousness of purpose in terms of how he takes on these tasks and, you know, really delivers. And I have been watching him in the last couple of weeks, as he is becoming more familiar with the responsibilities of the Commissioner, including sort of shadowing me on the budget hearing prep process.

And I'm just so impressed by his ability to grasp the information, identify the critical questions, and the, you know, breadth and depth of experience that
he brings to this role. So I know he will do it
differently, but I think he will really be just
excellent in this new role. And I certainly wish him
the best of luck, and I encourage all of you to support
him as best you can as he takes on these new
responsibilities.

You also probably know that I recruited Dr.
Robert Califf to the FDA as Deputy Commissioner for
Medical Products and Tobacco. And he actually
officially came onboard at the end of last month and
physically has been here this week and is settling in
and I think is very excited and energized by this role,
and he obviously brings just an extraordinary
background and set of experiences to his role as a
global leader in cardiology and clinical research and
healthcare quality.

And having most recently been in the position
of Vice Chancellor of Clinical and Translational
Research at Duke University, you know, he knows a lot
about science and research that's relevant to FDA, and
he knows a thing or two about management as well. And
you probably, many of you are familiar with him from

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other aspects of your professional life. Maybe from his prior experience with the FDA, including when he was on the Science Board Subcommittee on Science and Technology.

And he's had a lot of interactions with the FDA over time, whether from serving on advisory committees or helping to develop and lead some important public-private partnerships in the biomedical product innovation and clinical trial innovation area.

So I think that is just a huge addition to our FDA team, and he will make an immediate important contribution to our mission on a very wide range of issues.

I also want to welcome Dr. Susan Mayne, who joined FDA earlier this year as the Director of the Center for Food Safety and Applied Nutrition, CFSAN. And I'm just really excited about her recruitment as well.

She's an internationally recognized public health leader and scientist who comes to the FDA from Yale University, where she was -- had an endowed chair in epidemiology at the School of Public Health and also
was chair of the Department of Chronic Disease Epidemiology and Associate Director of the Yale Cancer Center.

So she's, you know, really very broadly knowledgeable. She's conducted extensive research into the complex role of food, nutrition, and other health behaviors as determinants of chronic disease risk and, of course, has deep expertise on cancer.

She hasn't worked as directly with FDA as Dr. Cahill, but she's not unfamiliar with FDA and their world of policy from her service on the Food and Nutrition Board at the National Academy of Sciences. And she also served on a Nutrition Advisory Committee for the FDA, and she's worked with other Government agencies, including she was on the Board of Scientific Counselors for NCI and worked closely with the U.S. Department of Agriculture on developing practical applications of research.

So she's going to bring, I think, a new strength and focus on science to CFSAN at a critical time and, you know, will provide I think a very important contribution to the leadership team of FDA.
So the last person I want to mention is Dr. Lu Borio, who no doubt some of you know from her work on medical countermeasures and -- and most recently really coordinating and galvanizing the FDA response to the Ebola crisis. But she has agreed to serve as Acting Chief Scientist, as Dr. Ostroff moves over into the position of Acting Commissioner. And I think she's very skilled and has demonstrated her leadership in terms of working across FDA's scientific and public health efforts in the different product centers. She has worked hard on advancing our regulatory science initiative, our FDA scientific professional development and scientific integrity efforts, and you know, most importantly, really building up a medical countermeasures product that has enabled us to really make huge contributions in terms of new product development, innovative regulatory science approaches to approving or assessing products in context where there is no natural population to study and really figuring out strategies like the animal rule. And thinking about where there are limited populations to study, how to apply the most
rigorous science in terms of building the evidentiary base.

And the work she's done on Ebola has been really lauded from the Secretary of HHS and the head of the National Security Council at the White House and others because she's been so instrumental in coordinating our response, really reminding people that FDA has a critical role in helping to make new diagnostics available even while they're being accessed through our emergency use authorization, not our traditional approval process.

But also working with the research community, NIH in particular, but many others, and WHO and international organizations, to help design the clinical studies that need to be done to understand the safety and effectiveness of a range of emerging vaccine products and therapeutics for Ebola as well as the diagnostics.

So we are in good hands. You are in good hands, I think, with the leadership team that will be aligning at this time.

And as I said, I do feel very proud of what's
been accomplished and thank the Science Board for your contributions. We've really done remarkable work in a number of key areas, and it's been a critical time in terms of expansion of FDA authorities and responsibilities with several major laws that have been passed and that we're now implementing, starting with the Family Tobacco Prevention and Control Act in June of 2009.

The FDA Safety and Innovation Act, FDASIA, which gave us a set of new authorities and responsibilities in terms of new user fee programs for generics and developing our biosimilar pathway and also highlighted some critical areas of regulatory science and research from biomarker development to innovative clinical trial design, to strengthening the science of meta-analysis, to really trying to find new ways to integrate patient perspectives and patient-reported outcome and risk-benefit frameworks that reflect the real-world experience of people living with the disease into our research and development framework for new medical products.

So, in addition to that, we had FSMA, the
Food Safety Modernization Act, which the historic transformation of food safety from a reactive system to preventive and also recognizing really for the first time in a formal way our responsibilities around the world in terms of the globalized food supply and what it requires for us to be able to assure the same set of standards are being followed for safety and quality, whether the product is coming from China, India, or Chile, as if it's being manufactured in the United States.

And it's a huge set of tasks, but -- but very important. And of course, FSMA noted that and gave us new authorities and responsibilities for food. FDASIA also recognized that on the medical products side.

And then another piece of legislation, the Drug Quality and Safety Act, addressed compounding pharmacies following the tragedy of the contaminated steroid and the meningitis outbreak that occurred a few years ago because of the now identified as criminal activities of a particular compounding facility. But that same act also gave us additional authorities around track and trace to assure the supply chain.
globally and domestically.

So all of that has been a huge amount of work but has helped us to better position for many of the challenges of the 21st century. We worked hard, and this is where the Science Board has been key to really strengthen science within the walls of FDA and beyond and to really bring new focus on the importance of regulatory science as an underfunded and under addressed arena of our overall research enterprise.

And we have, you know, really been engaged in a number of activities that I think speak to the importance of our work and the way it's making a difference for people in the real world. You probably are aware that we, in the last year, approved more novel drugs and biologics than in almost 20 years. Approvals that, you know, really reflected important areas for new treatment from cancer to hepatitis C and Type 2 diabetes, as well as the most new drugs for orphan diseases since the Orphan Drug Act was enacted over 30 years ago.

And impressive proportion of the new approvals were first-in-class therapies, which
obviously represent new approaches in the treatment of disease. And you know, some of the new drugs truly transformative, including a cure for hepatitis C. And we also approved many important biological products, including a number of groundbreaking vaccines for meningitis B, flu, and certain types of human papillomavirus.

So we are really, I think, entering this new year from a very strong position in terms of how our medical product review programs are working, how we're delivering on the promise of science for people, but also recognizing that we are learning a lot about what still needs to be done and entering a critical new period in terms of the advances in science and technology that are going to drive new, better products and more targeted therapies and the need for us to keep pace with the regulatory requirements.

And that's one of the reasons I'm so excited that Rob Califf is with us. I can't think of anyone better to help FDA think through some of those important issues, and you know, we are, you know, really thinking in some new rather out of the box ways.
You may have seen some of the coverage or actually seen the document that we put forward around next-generation sequencing, but really moving away from the historic paradigm of one diagnostic, one disease to how do you cope with a diagnostic tool that gives you, you know, thousands, hundreds of thousands different pieces of information potentially and information that you weren't looking for necessarily when you did the test and where the level of certainty about how a finding will relate to the presence of disease or the risk for disease is very variable.

So we're really trying to develop a whole new framework that involves engaging much more with our partners in the scientific community and really using curated databases to help us with our regulatory decision-making. But that's just one example of many areas where we really have to rethink our old models and put in place new ones.

So it's an exciting time. And again, where the Science Board, I think, is well positioned to really help us figure out the best approaches and how best to utilize the resources we have internally, but
also how to engage because it's clear that in so many
domains of our activity, the only way we're going to be
able to get the job done, both scientifically and just
from a human and dollar resource point of view, is to
find new, better ways to partner.

You may be aware of a couple of other things
that I should just mention in passing. I talked about
compounding. We're implementing that important new
law, the Drug Quality and Security Act, and that is a
major focus for components of FDA as we develop and
implement policies that will address both compounding
by State-licensed pharmacies in terms of the law
clarifying where FDA had a role to play and when we
didn't, but also creating a new category of registered
outsourcing facilities that will choose to be under FDA
oversight, including good manufacturing practices and
reporting of adverse events. And this is for
facilities that are making sterile injectables.

So we also recently, in late 2014, finalized
two new rules around menu labeling for restaurants that
represent chains of 20 or more and for vending machines
where the company owns 20 or more. We'll require
calorie counts on labels and availability to other nutritional information, and I spent a lot of time at my budget hearing this morning explaining why this had value and how it would actually work.

But I think, you know, it is a step forward in terms of responding to consumer interest and, hopefully, will help consumers make more informed choices about food that they eat outside of their homes. And in fact, it's about a third of calories consumed are food outside of the home. And I think about half of the money spent on food is on food consumed outside of the home. So it's not unimportant in our modern lives.

We also proposed changed to the nutrition facts label, which is the listing of nutritional ingredients and components of the nutritional composition that's on the back of processed foods and certain other foods. And this is the first time that the nutrition facts label has been updated in 20 years since it was first put in place, and this reflects advances in nutrition science and understandings about health and nutrition, as well as understanding how
people actually eat.

If you really look at some of the labels, you see that the serving sizes used really don't reflect what people eat today. Unfortunately, people tend to eat larger volumes than were reflected in the behavior patterns 20 years ago. So we're updating that as well.

That's a proposed rule that will be finalized at some point after we go through all the various comments we've gotten in, and also we're doing some consumer testing to look at different ways of presenting the data. Probably the most notable thing in that proposal has to do with the recommendation to include added sugar as a category unto itself.

I mentioned already the Ebola outbreak response, but I would just that it was really -- of course, it's ongoing, but very exciting to see how the different components of FDA came together to use our authorities to the fullest extent possible to really promote and protect the public health, both domestically and abroad. And really, our contributions to the national and global policy development were quite notable, as I said, whether helping to expedite
the development and availability of investigational medical products for Ebola, including providing the regulatory advice and guidance to commercial developers that was really necessary, but also working with counterpart U.S. agencies to support medical product development and really accelerating development programs.

Also, collaborating with WHO and in some instances I think to bring a stronger regulatory perspective and some rigor to the work that they were trying to coordinate and also, of course, to facilitate access to investigational medical products for patients with the Ebola, as well as making available some of the investigational diagnostic tests that really especially early on were important in helping to, you know, target resources and care for patients with the Ebola.

And also we were monitoring for fraudulent products that were claiming to prevent or treat Ebola and, sadly, had to take action on a number of occasions to prevent people from spending money on products that wouldn't work and, sad to say, prevent governments from spending very limited dollars on products that were
truly frauds.

So we, finally, with respect to Ebola, also did send some of our Commissioned Corps officers over to the Ebola treatment units that were set up. I think we sent them to the -- only to the first Ebola treatment unit that was set up in Monrovia, Liberia.

But anyway, those are just some highlights of things that have happened I think since the last time I talked to you. I also would be remiss if I didn't mention that there is a very significant activity unfolding on Capitol Hill called 21st Century Cures, which is an effort spearheaded by Chairman Upton of the House Energy and Commerce Committee, in partnership with Congresswoman DeGette, a Democrat from Colorado, who's been very involved in science issues, but of course with broader engagement of House membership as well, to look at ways that they can help to advance biomedical product innovation in this country.

And on the Senate side, Lamar Alexander, the new chair of the Health, Education, Labor, Pensions Committee, HELP Committee, is taking up a similar agenda in order to really look at what Congress can do
to help this important arena of activity for biomedical
science and to improve healthcare and to improve
economic productivity and global economic
competitiveness.

So we've been participating in these efforts.
I would say that we clearly are strongly behind the
concept and want to do everything that we can to make
this a successful effort. We also are very mindful of
the fact that some of the things that have been
proposed are worrisome because they will give us
unfunded mandates asking us to do things that we don't
have the resources to do, sometimes things that we
don't think will really have value added and some
things that we think may be downright dangerous, such
as timelines for mandatory approval.

If we don't review something in a given
timeframe, it's automatically approved, even when we
don't have the resources to necessarily apply to all of
the things that could emerge, and one could really
create some very problematic circumstances. We also
are concerned about not lowering standards for safety
and efficacy.
But we have been able to engage in very good discussions with Members of Congress and their staff. There's a hearing next week with the Senate Health, Education, Labor, and Pensions Committee that's just beginning to look at some of these issues, and I'll be testifying there.

We clearly share the goal of streamlining processes and achieving efficiencies where possible, and we just want to make sure that we continue to hold the standards for good science and meaningful review and approval of products that come before us.

And recognize that in many key areas, the regulatory approval process and especially our timelines for approval are not the barrier to progress. It's actually making sure that the right science is getting done and advancing our understanding of human biology and the underlying mechanisms of disease that allow us to develop the new, better products, the products that are really targeted to addressing the mechanisms of disease that are applying advances in understanding, genomics, et cetera, and that also give us the new tools that we need to make more effective
and efficient regulatory decisions.

So it's a very exciting time, as you all know. We just want to work with Members of Congress to make sure that we build on the momentum that already exists in terms of the very significant advances that we've made in terms of our regulatory processes, in terms of our ability to help advance regulatory science to better support the most efficient and streamlined approaches to product development and review.

And that we don't burden the agency, which is already stretched thin, with unfunded mandates that will make it harder to do our jobs. And again, obviously, Rob Califf will make a huge difference as we move forward on these efforts.

And we will very shortly be resuming user fee discussions. It seems hard for me to believe that another cycle of that is coming up, but probably sometime towards the end of the summer, we'll be starting those discussions now in four areas -- drugs, devices, generic drugs, and biosimilars.

And that's an important opportunity for some of the legislative activities as well because, in that
context, we can more effectively link new activities
and requirements with sources of funding.

So I have been talking a long time. Forgive me for rambling on. But let me just close by talking a little bit about the Science Board's report that will be the follow-on to the 2007 report, FDA Science and Mission at Risk. I know that you very shortly will be hearing from Dr. Alan Russell about the status of the forthcoming report on FDA Science Moving Forward.

But I really want to underscore how important this is and to thank the board's Science Looking Forward Subcommittee and those within the FDA who have been working to help support this effort. But I think it comes at a very critical time. The 2007 report had a huge and positive impact getting people to sort of sit up and pay attention to the fact that, number one, FDA was a science-based agency; number two, that the quality of our science really mattered and had many, many sort of concentric circles of impact on medical product development, on healthcare, on the medical product industries, et cetera; and that we had to be positioned to address the complexities of a rapidly
changing scientific landscape.

And I think that we're now at another critical juncture where we need to reinforce those messages and extend them in terms of more than ever before, I think the importance of FDA being viewed as a partner in the whole product development and regulatory review process is absolutely essential.

We know that the more researchers, whether in academia or industry, understand the broader regulatory context, the quicker a promising idea in science can actually start to move into a more targeted development context and the greater the likelihood of it actually making it over the finish line into a real-world product that will matter for people.

And as there's more pressures also on really delivering on science, you know, we need to be thinking very carefully and have the knowledge and the tools necessary to really be able to create a scientifically rigorous, but highly productive environment for medical product development and review and, in my mind, to really continue to strengthen and extend regulatory science at FDA, in academia, and in industry. And you
know, with partnerships cutting across disciplines and sectors and also across borders as well, I would say. So I think that this is really a critical time. A lot of work has been going on behind the scenes, I know. I won't be Commissioner 100 percent for sure when this board report is issued later this year, but I look forward to reading every single word. I hope I'll be in a position to make constructive comments about the report and how helpful it will be. But I cannot underscore, you know, really the importance of this work, the timeliness of the work, and encourage you all to continue to make it a priority.

So let me conclude and just, you know, again say what a pleasure it's been to work with so many of you. I'm not actually breaking up crying, but I am choking on my water.

But my decision to leave -- if you hear a quaver in my voice, that's what I was responding to. But the decision to leave was a very hard one, and I must say there were more than a few tears shed at various points as I thought about what it would mean to
leave the relationships developed inside and outside of FDA and the extraordinary commitment of so many people inside and outside of FDA to really advancing the work of this extraordinary, unique, and essential agency.

And the membership of the Science Board clearly fits into that set of extraordinary people and organizations that support our work and have supported me as Commissioner. So I really look forward to being able to hear about and watch your continuing input to the FDA.

Certainly the works that you will do, as reflected in the Science Moving Forward report and other more public activities, but also on a personal note, thank you for the opportunity to have worked with you, and I look forward, in one way or another, to continuing these relationships.

And with that, I will stop talking.

CHAIRMAN FREIRE: Thank you, Peggy.

(Applause.)

CHAIRMAN FREIRE: I hope you can hear the round of applause even through the -- through the microphones here. We really are honored, as I said

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earlier, to be part of this board. And I'm, frankly, breathless. I don't know how you can possibly keep all of this in your mind.

We've gone from medical products to food safety. We've gone to added sugar to, you know, the science-based and the importance of the science to 21st Century Cures. And my head is reeling, but I have to tell you that we are in awe of not only what you've accomplished during your tenure, but of the staff that is here at FDA, the new staff that you've brought onboard and the staff that has served this agency so well for so many years and that we're proud to have with us.

So I don't know if there's anybody on the board that would like to say a few words? Dr. McLellan?

DR. MCLELLAN: Peggy, Mark McLellan calling here. And just to say I echo this, anyone who could come off a Capitol Hill hearing and be as succinct and clear as you are with us now, that's just amazing. Having been there, done that, it's a formidable task.

I just want to lay a comment out here that
you have been particularly empowering of this board, and I think many of us, both at the board and hallway conversations, have remarked on that. Your legacy has been reflected, of course, in the leadership as you've gone through. But really, from our perspective, it's been amazing to see the engagement in real-world issues and conversations that you have empowered us to be a part of, and I certainly appreciate that.

COMMISSIONER HAMBURG: Thank you.

CHAIRMAN FREIRE: Dr. Yaszemski?

DR. YASZEMSKI: Hi, Dr. Hamburg. Michael Yaszemski here.

I'll start with the end. Thank you for your service and best wishes for whatever is next in your life.

I wonder if you could leave us with what we'll call "Commissioner's intent" and let us know perhaps the two or three top things that you would like to see the board address after you go out of this role.

COMMISSIONER HAMBURG: Well, that's a big opening. You know, I think a couple of things. One is the need to continue to underscore the importance of
science at the FDA. I mean, it seems almost ridiculous, but there still really is the lack of appreciation of the expertise that we have and that we need and the fact that there are opportunities in science that are being under realized because the scientific regulatory perspective of FDA is not being brought to bear.

So this notion of FDA, you know, really working in partnership, as I said, across sectors and disciplines to bring this, you know, sort of regulatory science awareness into the way that research is being thought about and undertaken at a much earlier time I think is critically important.

It means, you know, really supporting different kinds of partnerships that include FDA. It means I think really reshaping some of our -- our staffing within FDA, and this will be a big lift.

But we know that the early engagement of FDA and the continuing engagement with FDA as a product is being developed really matters in terms of doing the right studies, asking the right questions, and really streamlining the development process. And we've seen
that with the breakthrough designation and, you know, a lot of our recent approvals over the past few years. And so, you know, it's a different paradigm, you know? It really shifts from the earlier model of people at the FDA waiting for the application to sort of cross our threshold to a much more active engagement.

And I think, you know, thinking that through, what does it mean and how do we get all of the partners in science to support the vision and then how do we get the vision actually supported in terms of dollar resources and our ability to hire and retain the right people internally is going to be really, really key.

I also feel very strongly that the changed environment in terms of the global marketplace and complex supply chains and products that we regulate increasingly being manufactured in whole or in part in countries all around the world, you know, has just shifted the nature of our responsibility and the demands on FDA. And we need to continue to keep a strong focus on that.

We need to think about ways we can apply
technology, whether it's information technology for risk-based approaches, for screening or new, more rapid diagnostic technologies that can give us quicker answers and literally move the freight more quickly. Or new ways to really partner with counterpart regulatory authorities and industry to create more of a global safety net.

But we need to be both strengthening and extending the programs that are already in place that I think are really working and making a difference, but we have to keep thinking creatively about how we're going to address this problem because the vulnerabilities are huge. And I think that it's one of the areas that people recognize in sort of isolated cases and when there's a problem, but the magnitude of the problem and how it bears down on us every single day with this set of associated risks and vulnerabilities, I think, you know, remains underappreciated and under addressed as well.

I've just gotten a yellow slip that I have to go up actually back to Capitol Hill for a meeting on the Senate side to prepare for the budget hearings
there next week. So I'm going to have to sign off.

There are many more things probably that I could have raised, but you know, those two areas certainly are top on my mind and reflect priorities that I developed while here. And so, of course, I have to confess I have a slight vested interest in having them continue to be priorities as new leadership takes over.

But again, I'm sorry I can only be available by phone. I'm sorry that I have to now leave rather abruptly. But I do really appreciate the work we've done together and take great pleasure in knowing that more good work is going to emerge.

CHAIRMAN FREIRE: Thank you, Dr. Hamburg.

And go get 'em.

COMMISSIONER HAMBURG: All right. Bye-bye.

CHAIRMAN FREIRE: All right. Quite -- quite a tour de force there, and I certainly don't envy anybody that has to talk about bedpans and erectile dysfunction, I think she said. So that's quite a -- quite a big gamut.

Martha, do you we have anybody for the open
session?

MS. MONSER: Is there anyone in the audience who wishes to make any comments during this now open public hearing session of the Science Board?

(No response.)

MS. MONSER: Seeing no movement, we will carry on forward with the next item on our agenda.

CHAIRMAN FREIRE: Thank you very much. We are ahead of the agenda, which was the whole point of the day. So I'm delighted that we could achieve that goal.

We have an interesting proposal on the table on regulatory science and creating a consortium around regulatory science. And for this, we have three speakers, I believe. So we will start the conversation with Leslie Wheelock. No?

MS. MONSER: Bob Meyer.

CHAIRMAN FREIRE: Bob? Oh, I have -- sorry, I apologize. I have a different agenda in front of me. But I can read just good.

DR. MEYER: So I get to start it off. First of all, I want to thank you for this opportunity to
talk to you in support of this proposal. And also it's
good to be here for much of the meeting as well and
hearing Dr. Yaszemski's excellent summary of our
progress on the Commissioner Fellow subgroup to date as
a part of my being here.

So what I want to do just very quickly is
provide an academician's perspective on the need for
coordination of regulatory science training. I am the
Director of the Virginia Center for Translational and
Regulatory Sciences at the University of Virginia, and
although I'm using their logo, these are my opinions
and not necessarily those of the school's.

So it's very clear that regulatory science as
a training or educational opportunity is of increasing
interest at many universities, including my own. Some
of these are new programs. Some are retooling or
extensions of regulatory affairs programs that have
been going on for quite some time.

And they differ very much in terms of what is
actually offered as the end product. Some are
certificate programs. Others are building towards
full-fledged master's programs, and some are coming
with or without -- or going to the extent of with or
without Ph.D. programs as well.

To date, there are some informal networks
that exist to bring together interested academic
facilities and people. A good example of that is the
University of Rochester convenes monthly discussions on
various topics related to regulatory science, and
that's got fairly broad participation, but it is an
informal network.

Back in August of last year, the PhRMA board,
in conjunction with the University of Rochester and I
believe it was Georgetown, organized a gathering of
interested parties from academics from industry, and
actually, FDA attended that as well. The intent of
that was really to go through some discussions about
the proposal for common curriculum standards and
standards of learning, if you will, with regard to
regulatory science.

I think a few things struck me out of that
meeting. First of all is there's a very rich and
diverse capabilities across the programs. For example,
some programs are very strong in device expertise.
Others perhaps more oriented towards drugs.

I will stop here and say I'm not going to touch on tobacco because that's actually got a fairly rigorous regulatory science enterprise going on. But I'm really focusing more on therapeutics here, as that's what I know, and it's really the group in which we're involved at this point.

In any case, some are more slanted towards drugs, devices, some more towards translational science and clinical trials, others more towards pharmaceutics and pharmacology.

By the end of the day, a little bit discouraging, we actually devolved into a discussion as to what regulatory science even was. So it was -- it was kind of a sobering way to end a meeting where you were trying to get to a common curriculum standards. I think the discussion, however, made it clear that the focus was really in the eye of the beholder, and some groups are seeing it more as regulatory science means drug development and clinical research. Others saw it more as almost an extension of regulatory affairs with a new word appended.
Now there were, I would say, fair agreement - there was fair agreement coming out of that meeting on high-level pillars of curriculum and core competencies, but the definitive output of agreement and adoption of those, I would say, is still a work in progress. FDA was at that meeting and participated, but in terms of actually driving the conversation, I think for various reasons, that's not been the case. And I would pose that they perhaps should be.

For one thing, as we heard earlier, FDA is in need of a robust, interested talent pipeline. I put "interested" in there because I think many people in academics certainly don't think of the FDA as a viable career pathway, but people who engage with FDA and spend time here I think ultimately do. And I think more importantly from the perspective of FDA actively participating and driving this conversation is that FDA alone knows what areas of regulatory science would benefit them most.

Also, from the academic side, as much as there is good will and intent, academics is not well set up to coordinate and collaborate sometimes even
within schools, but certainly between schools. You know, these programs have divergent internal resources and expertise in terms of particular areas of pedagogy that they can play in or their area of science, and I think it makes sense from my perspective to look to leverage those capabilities and expertise across universities rather than to lead to redundancies and siloed effects that could end up being inferior.

Right now, I would say anywhere -- in academics, in industry, in FDA -- there is no one who really has the day job of leading to collaborative mechanisms and coordinating scientific projects and curriculum across institutions.

So from my perspective, taking into account the fact that I've spent time in FDA and in industry, as well as now in academics, I think just allowing for an undirected organic growth of regulatory science training leads to a few risks. One is that the training programs don't end up meeting the expectation of future employers, and I would include industry and FDA in this.

You know, the fact that Dr. Hamburg just
cited that one of the keys to success in development programs is early and active engagement with FDA suggests to me that one of the legions within industry— and it's, I believe, true -- is a deep understanding of what the regulatory expectations are and how that can help shape the science.

It also, if we have an organic growth, rather than a directed growth, it makes it difficult to really effectively have interchanges between -- I apologize for the typo there -- interchanges between academics and FDA and amongst academics. And then it misses leveraging this whole than could be greater than the -- than the individual institutions and really address the full gamut of regulatory science training in a coordinated fashion.

So I'm going to end there, and I guess we'll perhaps take questions as a group later. But thank you.

CHAIRMAN FREIRE: Thank you very much, Dr. Meyer. Appreciate it.

And yes, we will take questions at the end.

This seems to be your day, Ms. Wheelock.
We've had you there now, what, third time today?

MS. WHEELock: Thank you.

So I'm going to follow up Bob's presentation in talking about our FDA's initiatives to closing this regulatory science gap.

So just a quick overview. I'll just go over some background on regulatory science from the FDA perspective and then go into the various initiatives that we are doing here at the agency. So educational resources, speakers, curriculum, some regulatory science discussions across the Nation, and then our training programs. And then conclude with what we see as the benefits for having -- for doing these regulatory science initiatives.

First, some background on regulatory science.

As you probably remember in 2010, it was FDA had an initiative to fast-track innovations to the public. And part of that initiative included translational science, but also it introduced regulatory science, which FDA defines as the development and use of new tools, standards, and approaches to more efficiently develop products and to more effectively evaluate
product safety, efficacy, and quality.

So some of the things that we've been doing in the last several years -- and we've been doing these all along, we're just putting a lot more emphasis on them -- is educational resources on our Internet site. So we've consolidated all the centers' training, and there is one site to go to. You can access this site from the home page. It's a learning portal for students, fellows, and senior scientists.

We also have a site where we're -- CDRH, for example, has developed course materials for educators to use. So some examples of the opportunities that are on our Web site, FDA 101, the CBER, CDER, and CDRH Learn actually a compilation of a lot of the training that is actually used to train FDA staff. It's how to -- you know, the product development and product review.

CFSAN has courses, CTP, CVM, and CTR, and ORA. So it is representative of all the centers here at the agency, and it's, I think, a resource that students and fellows can use and learn about the regulatory process.
We also have always participated in conferences, whether they're conferences by external organizations, but also our own FDA-sponsored conferences. And so, upcoming on May 27th and 28th, for example, of 2015, the FDA is sponsoring an FDA Science Forum, where we'll be highlighting regulatory science here at the agency, and it will highlight the eight priority areas that was presented in our strategic plan.

So that's just an example, and there is a Web site that captures all the conferences that we at the FDA sponsor and also collaborate under co-sponsorship agreements.

We also, as mentioned earlier when Carol was speaking, really try to now work with academia. And so, the CERSIs are one of the programs that we have. The four CERSIs -- University of Maryland, Georgetown, University of California, San Francisco-Stanford, as well as Johns Hopkins University -- as you saw earlier do have master's programs in regulatory science.

And these, there are others that centers are collaborating with academia to develop as well. And we
have a Web site for those programs.

One of the things we do or we are -- you know, we go out and talk, and when academia is thinking about curriculum is not to forget industry in this piece because industry has a piece of this, quite a large one. So think of them as also instructors who can teach a lot of what is what they know.

Think about your instructional strategy. Try to get a higher level learning so that you're not just talking about, you know, knowledge acquisition or comprehension, that you're getting to higher levels of application analysis, and this is evaluation of content. So teaching through K studies or collaborative learning.

Also thinking about training programs at industry, where there would be that inclusion of interactions with the FDA. As Bob said earlier, understanding the regulatory process is important. So if these training programs do exist with industry, individuals could actually participate in all the industry meetings and learn quite a bit from those interactions.
Next, the FDA has -- staff across the agency have been participating in a lot of regulatory science discussions. These are just a few. The Institute of Medicine back in 2011 had a workshop addressing Strengthening a Workforce for Innovative Regulatory Science in Therapeutics.

One of the CERSIs, University of Maryland, had a workshop on Degree Programs in Regulatory Science, and Bob earlier mentioned the PhRMA Foundation. Another example is TERMIS, which is the Tissue Engineering and Regenerative Medicine, had an entire session on regulatory science this past December.

The FDA also has training programs where we will bring in students and fellows. And on this page are examples of our student programs. So we have an ORISE Research Participation Program, which all the centers have, students -- regulatory science student internship at the agency level. You can see at the center level, Center for Devices and Radiologic Health, Center for Drugs, Center for Veterinary Medicine.

JIFSAN has a program with the Center for Food
Safety and Applied Nutrition, as well as NCTR has a program. And these are all listed on our Web site so you can see them.

And then also we have programs for postgraduates. The ORISE Research Program. Again, all the centers participate. We have the FDA Service Fellowship Plan, which are the staff fellows, which all the centers participate in. The FDA's Commissioner's Fellowship Program, and the FDA-NCI/NIH Interagency Oncology Fellowship Program. And then the CDRH Medical Device and the CTP Regulatory Science.

These are just a few examples. Again, all of our programs are listed on our Web site. And our intent through these is to bring people in to raise -- to train them, hope some of them may stay, but also that they will go back out and they have an understanding of the regulatory processes.

So, in conclusion, the benefit that the agency sees for having -- doing these regulatory science initiatives is that we will be preparing a workforce that are prepared to work in areas of product development and approval, that hopefully will be less
time to orient and be trained at the agency. It takes about 2 years, on average, to train someone who comes in with no background in regulatory science. And then also it's an opportunity for the regulatory science space to develop new tools, standards, and approaches.

And with that, I will conclude. Thank you.

CHAIRMAN FREIRE: Thank you very much.

Another very good overview. Thank you again.

Let's continue the discussion. And for this, we ask Dr. Clingman to come to the podium.

I direct you to the back page of the proposal that we were submitted. We are asked to address four questions -- strengths and weaknesses, what are the priority areas, how do we envision the CERSIs playing a role here, and what would be a quick win?

So, Dr. Clingman?

DR. CLINGMAN: Thank you.

First, I would like to thank the board for this opportunity to present to you this proposal for building on the range of activities that Leslie just mentioned and also addressing gaps in traditional
academic programs that Bob so eloquently discussed as well.

And I would also like to note that it was refreshing to hear about the number of accomplishments that the agency has made during Dr. Hamburg's tenure. And I'll also note that she used the term "partnerships" about 20 or so times. So, and I think that really speaks to the importance of partnerships in advancing FDA's mission and especially for advancing a coordinated approach to regulatory science training.

The agency often receives requests from academic institutions to collaborate on curriculum development as well as other training activities. While the agency, as Leslie mentioned, is engaged in a number of these collaborative activities to advance regulatory science training, these activities are limited to only the few institutions that we have formal partnerships with, and so only those institutions are able to benefit from the exposure to the agency's expertise.

So we propose here a coordinated approach to regulatory science training under a consortium that
would enable FDA to reach a wider audience with respect to shaping regulatory science as a discipline.

The overarching goal of the Regulatory Science Training Consortium is to foster the development of a robust education and training environment in regulatory science by addressing gaps in traditional academic programs, through providing continuous learning opportunities for academic, industry, and regulatory scientists, and ultimately, by preparing the future regulatory science workforce of FDA, as well as our stakeholder organizations that we collaborate and communicate with.

The concept of the consortium is aligned with the FDA's 2010 report on Advancing Regulatory Science for Public Health. In this report, the agency pledges to promote scientific excellence, provide professional development and continuous learning opportunities to our staff, as well as the external communities. And we also speak to the importance, again, of partnering with academic organizations, our regulatory counterparts, and other stakeholders to foster scientific exchange programs.
Since the issuance of the 2010 report, and as Bob also mentioned earlier, there have been a number of new regulatory science training and degree programs created. We recently counted about 30 or so such programs in the United States, but most of these programs are based on regulatory affairs rather than the science of product evaluation. And unfortunately, there is little coordination of these programs with the agency.

Given the increasing number of academic programs, there is tremendous opportunity for FDA to expand our collaboration with NIH and our other stakeholders to impart regulatory science knowledge and training to the external community and also have the opportunity to stay abreast of the best and most current scientific information available.

To coordinate efforts, we propose a public-private partnership approach, which would provide a framework for bringing together FDA and the various stakeholders to leverage resources and bridge gaps in regulatory science education and training. We envision NIH and our internal counterparts as key partners in
this effort.

The consortium would be coordinated through a neutral ground or third-party convener that would provide administrative oversight of the consortium. We also propose a coordinating committee comprised of representatives from each of the stakeholder organizations who would help identify the needs and priorities of the activities of the consortium. And we envision four product streams or program areas, which build on FDA's existing training activities.

Curriculum development, and this is to include blended learning opportunities, as well as online modules and case studies, which could be made available to all stakeholders.

Academic exchange programs, where regulatory science professionals would spend time training in multiple settings, including industry, academia, and regulatory agencies.

A sabbatical program to provide opportunities for senior and mid-level faculty to train within the review divisions and other offices throughout the agency.
And building on FDA's current fellowship portfolio, we propose the development of fellowships geared towards specific therapeutic areas, as well as specific regulatory science disciplines, and these would be opportunities for postgraduates and early career professionals. The idea would be that these programs would be focused on identifying challenges and innovative tools to advance development in the particular areas.

In addition to the training activities that Leslie spoke of earlier, and I believe she also mentioned this one, but I just wanted to give you an idea of some of the existing activities that we're engaged in that could be leveraged under this approach. And this is a case study developed by CDRH on device development and the clearance process. It's modeled after the Harvard Business Review case study, and currently, several universities are starting to incorporate this and other case studies into their training efforts. CDRH is also working on similar case studies on drug development and the approval process.

This is the first partnership between FDA and
the Reagan-Udall Foundation to support regulatory science training. The Alzheimer's Association is a key partner in this effort as well, and it's a 2-year fellowship which is focused on identifying opportunities to advance development of treatments for Alzheimer's disease.

We are currently building on this partnership model with the Reagan-Udall Foundation to create fellowships and training opportunities in other areas, such as tuberculosis.

This is a course developed by Dr. Bob O'Neill, CDER's senior adviser on biostatistics, in collaboration with Boston and Harvard Universities. It's a course on statistical and quantitative methods, and again, this and the previous examples are all opportunities that could be leveraged under a PPP model to reach a larger audience.

And here are some potential areas of focus to expand our education and training programs. These areas were identified in the 2010 report on Advancing Regulatory Science as priority areas. This is not an exhaustive list, and I won't go over every activity or
discipline here, but just to highlight some.

CMC, clinical pharmacology, clinical trial design, patient-reported outcomes, as Dr. Hamburg mentioned, and also endpoint development, assessment and identification of therapies and treatments for rare diseases, and also looking at new analytical methods to support food safety.

So we recognize that bringing together multiple stakeholders to develop a coordinated approach to regulatory science training is an ambitious goal. Therefore, we envision a staged or tiered approach to implementation, and perhaps starting with a pilot project of some sort.

One phase, one initial step, rather, would be to establish a coordinating committee, again comprised of multiple stakeholders, that would be tasked with the goals of assessing gaps in existing programs, identifying and prioritizing opportunities, training needs, and surveying the landscape of regulatory science content that is available as not to duplicate efforts, but to offer content to support existing academic programs.
Also, I believe it would be important to start thinking about developing metrics to assess the utility of a PPP approach to training.

And this concludes my presentation, and thank you.

CHAIRMAN FREIRE: Thank you very much, indeed.

Any comments from the board? Yes?

DR. JENKINS: So thank you very much. A very comprehensive overview and clearly a huge need in the system.

So a couple of questions, clarifying questions really. As I was reading the proposal, I had two key sets of questions. One was related to your vision of the final product, whether that's going to be more around facilitating and curating and enabling all of the resources out there to date so that the students can go and more easily find their way through and navigate what's out there versus an organization or an entity that is looking to create new materials and to, therefore, act as really a center for the provision of new learning and professional development opportunity?
So that was my first question. I think you have to get that really clear as you set out on this journey.

The second set of questions was -- was really more related to the way that the final state is envisioned. It seemed to be, you know, there's a coordinating committee, a consortium, and then this nonprofit entity that sits above it.

And I do think that whilst I agree that the initial step would be to bring together a forum of stakeholders, I would urge you to look to other examples of multilayer efforts because you're going to have to start to think about, you know, who's employed in which one, how they're measured, how they're funded, where they sit, who they report to. And so, I would encourage you from the outset to have a view on that and to keep it simple.

CHAIRMAN FREIRE: Thank you very much, Dr. Jenkins.

Any comments?

DR. CLINGMAN: Thank you for -- yes, thank you for those comments and questions.
So I'll start with your first question around the really -- I guess the focus of the consortium concept. So I would say it's all of the above to your question. Certainly, I think, as low-hanging fruit, it would be an opportune time to really look at what FDA, for example, currently has, what we -- what we have internally.

FDA, we sit on a just -- just a vast amount of training content that we use mainly for internal purposes, but I think it would be very important to see if we could look at ways that we could modify that content and make it easily available to be shared across multiple stakeholders, including within universities. So I think that curating, the curating piece would certainly be sort of a low-hanging fruit, if you will, opportunity.

But I also think that there is value in developing new content. I believe, Bob, you spoke of this before, maybe in our own conversations. But that a lot of universities, while universities are starting to work in this space, each university has their strengths, right? And so, I think it would be
important if we could come together and really identify areas that would benefit or disciplines and knowledge and content in specific areas that would benefit multiple academic organizations and start thinking about what that content would look like and form a collaborative effort around getting that done. And I would look to Bob and Leslie, if you have additional thoughts?

DR. MEYER: You said it well.

DR. CLINGMAN: And also, to your second question about the coordinating committee and looking at other examples of public-private partnerships, I absolutely agree with you. There's no need to reinvent the wheel here. We can look to the various models. For example, the IMI in Europe, they have the PharmaTrain Consortium, which is sort of a program under IMI, and they're doing similar things here. I believe they are offering a master's program, and they're really looking across and enabling students to really tap into training, components of training programs throughout Europe.

So that's an idea to look to, and it's a
public-private partnership. They have a sort of a
public and private funding mechanism and things of that
sort. So that's one example that we could look to.
And also we can look to current public-private
partnerships that FDA is involved in that are not
necessarily -- do not necessarily have the goal of
education, but still I think from an infrastructure
perspective would be great to look at and see how
they're modeled.

DR. JENKINS: Can I just -- I forgot to make
one point. It's just a very small one. I'd strongly
courage you to think about the word "training."
In the initial request, there was this use of
the word "learning." And you know, I think as you're
putting together this approach for the next generation
of talent, I think learning and professional
development as a concept should really figure very
strongly rather this notion of training, which I have
to tell you I think today is more of a historical term.

DR. CLINGMAN: Absolutely. Thank you for
that.

CHAIRMAN FREIRE: Interesting distinction,
but an important one.

I have Dr. Psaty next.

DR. PSATY: Bruce Psaty. I strongly support the regulatory science training or learning. I was struck here that you seemed to be trying to do two very different things that work in very different dimensions.

So the academic exchanges, sabbaticals, and fellowships look to me to be kind of a brokering activity and a coordinating activity across institutions and groups. Curricular development or curriculum development brings in a whole more complex set of activities.

I think I'm really just following up with Dr. Jenkins' point -- a whole set of much more complex activities. Is the FDA going to, you know, offer an M.P.H. or a Ph.D.? Is it going to be the CERSI groups? Now the CERSI groups are split between research activities and some, you know, regulatory training activities. Is it other groups?

And so, the whole idea of developing a curriculum is just orders of magnitude more difficult,
complex. You're coordinating with academic institutions, which can be byzantine.

I like the idea of making the FDA kind of publicly available to participate in these and to help lead these so that the training programs, as they might turn out to be, would be most useful for FDA and industry. But it just seems like a whole, much very difficult activity. And this thing just listed them, all four, as if they were equal, qualitatively equal, and they're not.

CHAIRMAN FREIRE: Any reactions or comments?

DR. CLINGMAN: Absolutely. Thank you for your comment and your recognition that this is a tremendous sort of effort that we're proposing here. To speak to the earlier part of your comment about FDA sort of more or less getting into the business of developing degree programs and things of that sort, and I'll also ask my FDA colleagues to chime in as well. When we started thinking about this consortium idea, it was not the intent to really duplicate what's going on in academia. We realize that academia is in the business of developing courses and
training opportunities.

But we also recognize that FDA has -- we can lend a tremendous value to the discussion of what regulatory science is, what are the priorities, things of that sort. And I think we're looking to supplement or add to and enhance with, for example, with respect to curriculum, developing online modules, for example, in pharmacovigilance or pharmacogenomics, things of that sort, that could then be utilized by academic programs.

So that's what we mean by curriculum development. I think that's examples of what -- we're looking to supplement what are the gaps. And so, then can we develop -- help -- help universities, help others develop content that could be widely shared across the stakeholder community?

DR. PSATY: Are they asking for that content?

DR. CLINGMAN: They definitely are.

DR. PSATY: Okay. I mean, then that's useful.

DR. MEYER: I also -- I wanted to just add a comment there. I think the other thing is, while those
are four separate concepts that fall down or, you know, come out at the bottom of that slide, I actually think, particularly with if you're not just seeing this as training in regulatory affairs, but really fundamentally understanding how the scientific challenges play out in a regulatory environment, experiential learning is going to be critical.

So I think having a program where there is relatively well-coordinated and an ease of movement between academics and FDA, and to my mind, those arrows should be both ways. So that I think part of this is the opportunity for FDA people to do sabbaticals and academia as well.

But in any case, I think being able to not only learn about things in the classroom or online, but then to experience how they play out and what the ramifications are over, you know, not just an individual decision or science in an individual area, but how that plays out in a broader context of the regulatory environment is critical.

CHAIRMAN FREIRE: We have some comments from our colleagues from the FDA. I think you were first.
DR. POLLACK: A couple of points. Training for regulatory science, if we talk about training a regulatory scientist, if at the end of the day I then need to have someone who has experience in cardiovascular disease, I will choose the person who's had the training in cardiovascular disease.

So I am concerned that if we start to train the generic regulatory science, we'll create a cadre of unemployable people. We need to be mindful that there is -- there are specialties involved in the different centers. And so, there is a baseline of what people might need to know in terms of the thinking process, the logical process, the engineering process. But that has to then be built on further.

So creating master's and Ph.D. programs I think is very early in the notion of what regulatory science is. And the other question comes out of some of the discussions that were had by the CERSIs the other day, which you alluded to, is that we're making the assumptions that the universities are all happy to share their information and their academic resources of developing curriculum. Well, that may not be the case.
CHAIRMAN FREIRE: Thank you.
I'm going to give the floor to Dr. Dunham, but I want you to know that I have Dr. Bahinski, Dr. Reiss, Dr. McLellan, Dr. Afshari. And I'd like to say a couple of things as well.

DR. DUNHAM: Thank you very much. I won't be long.

I just want to reiterate that, in fact, we do have the rapport that I think we value with academia because they get to help us, and we can help them. The curriculum is usually full. But there's areas that we can assist them in.

But at the same time, I think we learn so much, and they're also a conduit for looking at and understanding what we need on regulatory science and policy. And they do ask us for assistance, and we've had many of them come in and give lectures and vice versa. We have been asked to go to the schools and give lectures.

And I couldn't agree more with online. There is so much more flexibility that way. You can reach a lot more students and schools. But this is the
partnership that we've been embracing and that we all value, and I hope we can continue to do more and more of this.

Thank you.

CHAIRMAN FREIRE: Thank you very much. Dr. Bahinski?

DR. BAHINSKI: So I think one of the points in the first presentation rang true is not knowing what regulatory science is, especially from an academic perspective. I think, you know, one of the things that the FDA can help is actually focus those ideas and what does regulatory science entail?

And that can help guide developing the curricula because I think right now it's kind of the "wild west." Everybody has their own ideas and are kind of bringing those ideas to bear. And you can have within universities these big discussions on what it is, and things aren't moving forward because they're just going round and round and round.

I think dovetailing on one of the other comments was this is really kind of on the job training currently. And I think the idea of a two-way
internships or collaborations is very, very good. For one, it brings the FDA folks into touch with academics that are, you know, developing new tools that could be -- potentially move into the arena of regulatory science and ways to evaluate regulatory science.

It also gives the academic people a perspective on what is the qualification process. They often come in and think, oh, I've got the best biomarker or animal model and really have no idea what it takes to actually validate that or, in the FDA parlance, qualify that tool. So I think that would be a very useful thing to have, you know, kind of a two-way collaboration.

And also, lastly, you know, kind of the longer-range goal, you know, the idea is to develop people that have the training, but often groups like for toxicology, they have accreditation programs and a DABT that kind of standardizes the skills of the people. Is there a thought -- you know, again, that's a more longer-range goal -- of having that type of thing, and who would oversee that kind of accreditation process?
CHAIRMAN FREIRE: Thank you. Comments?

DR. CLINGMAN: I don't have the answer for that. So I'll offer up the floor to my FDA colleagues. So, but that is something to consider in the future. Thank you.

CHAIRMAN FREIRE: Okay. Seeing blank -- oh, Dr. Meyer?

DR. MEYER: I was just going to say I guess my perspective is whoever does do that, I would think it important that FDA be integrally in that discussion and not more on the periphery of it.

CHAIRMAN FREIRE: Dr. Reiss?

DR. REISS: Okay. I would like to follow on on some of the comments about curriculum and some of the comments that Bob also made during his presentation. I think one of the critical things that we need to do, actually, in the short run is to decide exactly what we mean by these definitions and terms because of all the stakeholders.

So we've been talking about FDA, academics, but also industry is really a stakeholder. Pharma is a real stakeholder in this. Because each of those

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different stakeholders sort of sees the world in a slightly different manner, in a slightly different way of thinking.

So from the industry perspective, for example, it's about integration, strategic thinking, innovation. You know, whereas, from the agency perspective, it's slightly different. And of course, from the academic perspective, it's a different perspective as well.

So I would like to see -- I would like to see a lot of work sort of focusing around definitions and how we integrate all of these perspectives. There is certain scientific knowledge that can be gained, but it from my perspective is the integration of all of these different scientific perspectives and thinking that we need to really teach and train people on moving forward.

So, so I would like to see a little bit more of that, a little bit more discussion around that.

CHAIRMAN FREIRE: Thank you. I think that speaks to the consortium that you tried to put together, at least a committee that would look at these
things, if I'm looking through your slides. But that's something, in the back of my mind, they could tackle. I think definitions and what we mean is extremely important.

I have Dr. McLellan, Dr. Afshari, and Dr. Kowalcyk. Oops, one more.

DR. MCLELLAN: Thank you.

Let me first congratulate you. I think this is great, really brilliant. The focus on the consortium approach I think is really square on. It's one of the ways you are going to build partnerships with external universities. They're going to be there partly because FDA is there and adding their imprimatur, if you would.

I love the concept of the case studies. I just think that's a rich, rich environment, and the sooner you could move to true real-life case studies, even more richer because that's reality. That's what companies are really going through and see that absolutely in the Harvard Business School model of things. It's an incredible learning process and highly, highly successful. So I'd urge you to keep
that up.

The question as to whether FDA should be connected, I don't think this would succeed without that direct personal connection. That is what adds validity to building this whole area. And schools, as byzantine as we sometimes are, are hungry looking for new opportunities to build these kind of training partnerships, educational partnerships, and move forward.

So congratulations.

CHAIRMAN FREIRE: Thank you.

Thoughts or comments on that?

(No response.)

CHAIRMAN FREIRE: Yay!

(Laughter.)

CHAIRMAN FREIRE: I do want to interject here and put myself in the queue. I have some experience in the formation of these public-private partnerships, and I think we have to remember they're tools. They are not goals, in and of themselves. They're mechanisms for you to get something done and something accomplished.
And key to the partnership is not only who are members of the partnership, but who's going to fund it? And there's a big hole in this proposal because I don't see anywhere who would fund it. So that's issue number one.

Issue number two is don't create a bureaucracy when you don't need one. So I think that creating a nimble mechanism through this partnership is definitely the way to go.

I am concerned about fellowships because they're evergreen. So in creating this partnership, you have to be very clear as to where the sources are for funds are going to come. If this is something the agency is going to be able to put forward, is this something that you're going to have the Reagan-Udall Foundation, for example, attract monies from industry? You already have ready-made partner there that could actually help you implement this.

So, for me, the question is not should you? The question is how will you, and how do you do this so that it has sustaining power, so that it has legs, and so that you don't start something that then is going to
fall apart?

Curriculum development is, indeed, the hardest part, but it's fundamental. Without curriculum development and without the academic underpinning to understand what it is you want your people to know when they come in the door and when they go to populate these different parts that FDA needs to interact with, it's absolutely critical.

And with all due respect to all Federal agencies, while we are respectful of your mission, not necessarily do you have time to do training the way an academic institution does it. And so, the participation of an academic institution there is critical.

There are examples of this. You have pilot projects. I would definitely start by putting a pilot project here and prioritizing. I don't think you can cover the waterfront, but don't forget the funding. Who are your logical funding sources? What is the agency prepared to put on the table? What are the universities prepared to put on the table? What are the users, the pharmas, and the rest of the
constituency willing to put?

This is not a trivial question, but it's a critical question.

All right. Apologies to Dr. Afshari.

DR. AFSHARI: Yes, thank you.

I keep having in my head that analogy of the blind man and the elephant, where everybody is seeing a different aspect of this, and I do think that's one of the major challenges when you talk about the world of regulatory science. I think everybody has a different definition of what that means and what they'd like to get out of that and how they'd like to contribute.

So I, again, would just like to applaud your effort to put a consortium together and to have that multi-dimension dialogue and to bring that perspective together, but to realize that you do have to have an end goal. And that's going to be challenging when you have so many different stakeholders and perspectives.

I had a similar idea to Tony down at the end of the table, which is thinking about borrowing from cases that have worked really well for other types of disciplines and areas of science where you have many
different ways to bring education, learning, and development forward, but that in the end, you actually focus on standardizing the product of what you'd like to achieve through some sort of certification. And so, you know, he brought up the toxicology boards. You know, there is other types of certifications and licensing that happens.

And actually, some of the funding to sustain that is actually driven by the learners who are very motivated to do that. And so, where there's a desire that there may be a certification that will be something that may be highly desirable by future employers, be it in the Government and private industry or in academia, that's going to be a strong motivational element for those who do want to have professional learning and development to say they'd be willing to put some of their own personal dollars on the table to help fund some of those activities and those, those curricula, so to speak, to hear from the experts and to learn.

And so, again, you could bring forward ideas that that learning and that ultimate certification is
going to be a combination of knowledge, but also case
studies and real-life experience may be coupled with
continuing education that allows it to be nimble as the
science advances. Again, not that different from other
types of boarding or certification where you have to
have a continuing ed component in order to maintain
that certification.

So it may provide you a mechanism to allow
you to corral the diversity that you'll get from
different universities and others who'll be interested
to engage, but maybe not so interested to engage in a
very proscriptive or very bureaucratic fashion. It's
just an alternate thinking, and in your model, kind of
where you have your neutral third-party convener could
be just a very small effort that is kind of the
ownership of that type of a certification activity.

CHAIRMAN FREIRE: Thank you.

Comments on Dr. Afshari, or I realize I
didn't give you a chance to react to what I said
either. So that was a smart move on my part, but not
intentional.

(Laughter.)
DR. CLINGMAN: No, I just want to, you know, thank the board for all of your very informative advice and constructive comments. So these are things that we can take back internally and really start thinking about. I totally agree with you that the elephant in the room is the funding, and you know, we have some ideas of how this can be funded based on other public-private partnership models.

But you're right. It's all about identifying a common need, that people are willing to put their money where the mouth is, so to speak, and fund this. So those are things that we need to think about.

DR. MEYER: So I know that FDA can't do this, but not everyone here is with FDA. I would suggest if anybody has pathways to provide input on the 21st Century Cures draft, one of the things that I thought was horribly deficient in there was money for this kind of regulatory science, the science itself, as well as training.

There were a lot of assumptions about FDA being able to move quickly forward in defining certain things around, you know, biomarkers and alternate
So it's not going to be a short-term answer, but I would just encourage anybody who does have the kind of input with the staffers or congressmen to think about whether that should be a part of what Congress does in terms of this important legislation.

CHAIRMAN FREIRE: Thank you.

Yes, some of us have, in fact, read the bill. But there's no money anywhere in the bill, which is very interesting.

Doctor -- let's see, Dr. Kowalcyk?

DR. KOWALCYK: So I would like to also congratulate you on putting together this proposal, and I think that, you know, there is a lot of need around regulatory science. And as somebody who's spent part of my career working in industry, part of my career working in academia, and part of my career working in NGOs in the policy arena, I know that the importance of having that varied experience and kind of the impact it's had on my thinking as my career has evolved.

So there are a couple of things that I want
to focus on. One is I think the experiential learning is a critical part of this, and personally, I can't overstate that. The second point that I have is that, you know, when we've been talking about stakeholders, we tend to think about stakeholders as, you know, Government, industry, and academia. But there are NGOs, which play a critical role in the regulatory process.

And they need to be brought into the fold because the nonprofit sector is a significant stakeholder in the development of policy and implementation. And so, I would suggest that you expand your perspective on stakeholders, as well as who you would engage in potential fellowships or experiential learning opportunities.

My final comment is more general, and it's something that I have been watching. I've been watching the regulatory science field with interest for the past couple of years, and one thing that has struck me is that it's very oriented toward the drug side of FDA. And food safety often seems to be -- which is, of course, my area of expertise -- often seems to be an
afterthought.

But there are significant -- first of all, food, the regulatory paradigm for food is much different than the paradigm for drugs. And therefore, you're going to have different learning needs, I would envision.

But I think that there are very significant regulatory science needs in the food arena, and of course, it also begs the issue as we have food oversight split between two agencies, as well as lots of actually thousands of State and local agencies. And so, when we think about regulatory science in the food arena, I think you also need to start thinking about how you would engage the other regulatory agencies that are involved in that.

It's not just under FDA's oversight, and so as you put together this consortium, I would encourage you to include those other partners, like U.S. -- like Food Safety Inspection Service at USDA. But also, for example, FDA delegates most of its food retail inspection activities to the State and local health departments or agricultural departments across the
country, and they have significant regulatory science needs as well.

I mean, they are looking at workforce crisis issues. You know, they're facing a workforce crisis as well. And certainly, this situation is not going to get any better as the world continues to have an increasingly global food supply and with the implementation of FSMA.

So it's more of a comment. I mean, I think most of what I've seen has been strengths, and I just think that that's one area that needs a bit more attention in this proposal.

Thank you.

CHAIRMAN FREIRE: Thank you.

Any comments or follow-on?

(No response.)

CHAIRMAN FREIRE: All right. Dr. Sarwal, you had no brilliant thoughts to give us anymore? Come on.

(Laughter.)

CHAIRMAN FREIRE: Very well. Thank you.

Question number three, what do you envision the roles of the CERSIs in this effort? My bias is

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that once you define what the "it" is, the CERSIs and
the different stakeholders will identify how they can
become part of the consortia or the partnership. My
sense is not to prescribe at this point what they ought
to be doing up front. But I'm happy to take other
thoughts from the board.

Dr. Jenkins?

DR. JENKINS: I was reflecting on the
discussion around the access between Government and
academia, and clearly, that is extremely important.
And there was some mention of industry, and I was
trying to really reflect on how industry might best
interact and engage with this effort, and that's where
I think this comes in.

It's certainly a huge area of concern, I
think, for a number of us in the industry, been in the
industry for many years, that we have now a huge gap in
a pipeline of regulatory talent to meet the needs of
our sector, particularly in the small industry sector,
so in the biotech sector. And I think that that's
where the industry engagement might come, which is
building these collaborations between industry and the
CERSIs to allow for industry to perhaps evolve their own internal learning and development programs in collaboration with the CERSIs.

It's been very difficult for those of us running large regulatory functions to work out how to accelerate and enable the training of our people, certainly the next generation. So I would -- I would -- I would give some focus to that when you interact with industry.

CHAIRMAN FREIRE: Thank you. Dr. Reiss?

DR. REISS: Yeah, I was just going to follow up on that comment, too, because it was part and parcel of the comments that we're making and a follow-up to Bob's point, I think. And that along with the definitions is a potential opportunity here for reframing where you're coming from and where you're going to be going with this.

Because from my perspective anyway, if you look at this from the bigger perspective or the wider perspective, what we're really talking about is development science or innovation science, if you may, of which regulatory science is a part of but is not
necessarily the main driver.  

But if you broaden the concept and think about it that way, it will include a lot of the stakeholders. It will help to focus on sort of what the goal, what the experiential opportunities, the case studies and so on and so forth might lead and provide sort of a broader context for training and education.  

So, so that's where I think the encouragement should be, as well as which stakeholder should be at the table.

CHAIRMAN FREIRE: Thank you.  

Reactions or thoughts from any of our FDA colleagues before we bring this to a close?  

(No response.)  

CHAIRMAN FREIRE: Thank you very much.  

I think you've heard from this board that we think this is a very important issue. Don't get in your own way when you're trying to do this. Streamline and get the wind behind your sails so that you can coalesce this into something that will be successful.  

And yes, the funding is an issue.  

Yes?
MS. MONSER: Bill Hait had a comment from email.

CHAIRMAN FREIRE: Oh, okay.

MS. MONSER: And his comment was that a key part of his regulatory science group, and he's at the Janssen Group with Johnson & Johnson, is biostatistics and quantitative sciences.

He said that, "We have moved our group to China, where we find tremendous talent pool and enormous interest in this aspect of regulatory science." So the question is, "Could FDA set up programs in China to attract new individuals into the field?"

CHAIRMAN FREIRE: Oh, my.

DR. CLINGMAN: And I'm looking at Jan. He may have more information on this. But I know that we are working through our international -- Office of International Programs on activities in China, and perhaps this is one that we could leverage those existing relationships to do. And I know we do a lot of recruitment within Office of Translational Sciences and Office of Biostatistics, you know, abroad.
So we're -- we're mindful of that.

CHAIRMAN FREIRE: Why don't we reserve the
answer to that question for when you come back to us
with a more refined, you know, tighter proposal and
maybe put that as part of the issue?

Dr. Meyer, do you want to say something?

DR. MEYER: Well, I was just going to add
that I think certainly speaking for our own
biostatistics program, we actually have a fair movement
of folks from China into our program. And I think if
some of the university programs interdigitate and work
with FDA, the connection to a talent pool coming from
Asia will be made partly through academics.

CHAIRMAN FREIRE: Well, thank you very much.
I will bring this part of the discussion to the end,
which then puts us at my closing statements, which are
going to be very brief.

They're going to be thank you very much.

It's going to be a -- it's been a very good day. We
look forward to our next meeting. A lot of work ahead
of us, and a special thank you to all of the FDA staff
for their support and their guidance.
I would like to do a final round of comments or questions from anybody in the board who would like to do that. So I am going to open the floor. Yes, please, go ahead.

DR. WEAVER: Since we have new leadership with CFSAN in the Office of Food and Veterinary Medicine, I would propose that we bring Susan Mayne and Mike Taylor, to invite them to share their vision for the future for their programs and have a prolonged discussion so we can find out if there's ways we could help them.

CHAIRMAN FREIRE: Thank you very much. We will ask Martha to coordinate that.

Yes, Dr. Kowalcyk?

DR. KOWALCYK: So I will second that. I think, given the implementation of FSMA, it would be nice to hear from the Office of Foods and CFSAN about their vision and potentially regulatory science needs that they have in implementing this new law.

Thanks.

CHAIRMAN FREIRE: Thank you very much.

Any other final comments?
MS. MONSER: I wish that Dave White, Dave White is the Chief Science Officer at the Office of Foods and Vet Medicine, he was here earlier with us today. He had to -- he had to run off to go back to CFSAN today to deal with pre-hearing briefings. So if he had been here, he might have been able to address something very -- very -- just very quickly for us. But you know, we've got a lot of stuff going on, but I'll take that back to the team.

CHAIRMAN FREIRE: Thank you.

I just received an email from Dr. McLellan saying that he supports this as well.

So Dr. Sarwal?

DR. SARWAL: Yes, thank you.

I'd just like to say that in the future, I'd like to make a suggestion that if we can get more input about the kind of regulatory processes that should surround e-cigarettes, as well as marijuana use, which is becoming increasingly legal in States, to be considered for perhaps future discussion, it would be great.

CHAIRMAN FREIRE: Wow, we're queuing up quite
a list of things to do. Remember, this is you're going
to be working on this.

MS. MONSER: This may be a 3-day meeting in
July.

CHAIRMAN FREIRE: Well, thank you all very
much.

Please go home safely and get ahead of this
storm. Thank you.

(Whereupon, at 2:54 p.m., the meeting was
concluded.)