THE BROOKINGS INSTITUTION

THIRD ANNUAL SENTINEL INITIATIVE PUBLIC WORKSHOP

Wednesday, January 12, 2011

PARTICIPANTS:

Welcome:

MARK McCLELLAN
Director, Engelberg Center for Health Care Reform
The Brookings Institution

Keynote Address:

MARK McCLELLAN
Director, Engelberg Center for Health Care Reform
The Brookings Institution

Sentinel Today: FDA Perspective:

RACHEL BEHRMAN
Director, Office of Medical Policy
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

JUDY RACOOSIN
Sentinel Initiative Scientific Lead, Office of
Medical Policy
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Session I: Mini-Sentinel Accomplishments and Plans for Year Two:

MARK McCLELLAN, Moderator
Director, Engelberg Center for Health Care Reform
The Brookings Institution

RICHARD PLATT
Professor and Chair, Department of Population Medicine
Harvard Medical School and Harvard Pilgrim
Health Care Institute

LESLEY H. CURTIS
Associate Professor
Duke University School of Medicine

KRISTEN ROSATI
Partner
Coppersmith Schermer & Brockelman, PLC

BRUCE FIREMAN
Biostatistician and Research Scientist
Kaiser Permanente, Northern California

* * * * *

P R O C E E D I N G S

DR. McCLELLAN: Good morning, everyone. We're going to get started in just a minute. I'd like to ask you to take your seats. We'll get started right now.

I'm Mark McClellan and I'm the director of the Engelberg Center for Health Care Reform at the Brookings Institution. I am very pleased to be welcoming you in out of the snow to today's Third Annual Sentinel Initiative Public Meeting. It is really good to see so many not only familiar faces, but faces who are leaders in many different aspects of issues related to drug safety, on getting better evidence on medical products, and it's nice to see this program which is now in its third establish something like an annual tradition with so many new things to talk about every year.

This is an extremely important topic and an extremely one, improving our ability to conduct effective and efficient surveillance of medical products, and products that people are actually using is a very important aspect of improving public health, improving decision making, improving the quality of health care and even avoiding unnecessary health care costs. I hope you will agree that after the discussion today thanks to the collaborative spirit, the collaborative public and private spirit around this set of initiatives we're seeing a lot of progress. It's a big and challenging topic but it's one that thanks to all of your efforts we're really taking on together.

As in years past, we're going to try and take stock and look forward at this meeting today. The purpose is to conduct an interactive dialogue between the FDA; the many collaborators with the FDA in implementing this new post-market active surveillance system and of course all of the stakeholder communities who care so deeply about these efforts. The specific objectives that we have today include discussing the

status now and the future plans for the Sentinel Initiative and engaging in a thoughtful and constructive discussion with all of you about that progress to date and about how to set and achieve some meaningful expectations for moving forward. This is a pretty large conference. Even despite the weather we filled up this room and we have an overflow room next door to welcome you and we'll be transmitting everything from in here to next door, it may be a little bit quieter, and we're going to I think need that space. But even in a conference this size, we're looking forward to the participation from everyone here. You all may have seen an earlier version of this agenda for our plan for today and there is one change here from that earlier version. That one featured a keynote presentation by then FDA Principal Deputy Commissioner Josh Sharfstein. As it works out, today is Josh's first day as the Secretary of Health and Mental Hygiene for the State of Maryland so that he cannot be with us this morning but certainly sends his regards.

After I'm done with these opening announcements and logistical issues, I'm going to make a few brief remarks that are going to fill in some of that slot by providing a little bit more substance framing the discussion that we're going to have during the course of the day and is also going to give us plenty of time for all of these very important topics.

After this initial opening, the FDA Sentinel Team is going to provide their perspectives on where we are now, where is the initiative today and where it's going next. That's the FDA's perspective on Sentinel today. Then we have a series of panel discussions with hopefully active participation from many of you. In Session 1, investigators from the FDA's Pilot Project, the Mini-Sentinel Project, will provide an update on their progress, including year-one achievements and the developments of the policies and tools and infrastructure that have taken place during the first year of Mini-

Sentinel, and then their plans for the year looking ahead. Again we're going to have plenty of time for questions and comments on these presentations.

Then we'll move on to Session 2 in which panelists from a number of stakeholder groups are going to share their perspectives and their thoughts on Sentinel's progress to date, future directions, key issues to watch for and suggestions for how to address coming challenges and, again, a lot of time for discussion of these perspectives with all of you who are here today.

Then in Session 3 we're going to hear from a panel of senior leaders at HHS and two large health plans about other federal initiatives that also utilize electronic health information for evidence development that are facing some of the same technical challenges and have some not unrelated goals in terms of helping to support better decision making by doctors and patients. This include initiatives for measuring quality of care, initiatives related to comparative effectiveness research, and because of the similar kinds of challenges they face both from an infrastructure standpoint and method standpoint and all the other policy issues involved, there may be some potential applicability of the lessons from Sentinel, the infrastructure from Sentinel, to support these kinds of purposes or reinforce all of these public health and quality improvement goals. That's the outline for the sessions for today. Again this is a large meeting but we're going to run this with a significant role for active participation from all of you and I'd like you to keep that in mind.

That brings me to a few housekeeping comments for today. One is that this is an open and public meeting as part of FDA's commitment to an extensive and transparent process for implementing the Sentinel Initiative. Press have been invited here today, the workshop is being recorded so that everything said here is going to be on

the record. The presentation materials from this meeting will be posted on the Brookings website and on the Sentinel Initiative website within the next few days and will be available to everyone, even those who couldn't make it.

For those of you who are panelists today, I'd like to make sure you know Michelle Wong. There's Michelle right there in the front row. She's very nice. But it's also her job to make sure that we have plenty of time for discussion during these sessions so that she will have a signal for you when you're approaching the end of your allotted time and we'd like to try to keep to that as best we can remembering that with all this time for discussion that will be a lot of time for more details to come out in the discussion part of these sessions. The opening comments that you're going to hear from all of our panelists are just meant to set the process going and get some key ideas on the table and we want to focus on that discussion and back and forth part of the meeting.

Panelists also be mindful of turning on your microphone before speaking. I think there are some switches on these and hopefully those will work smoothly during the day. Also throughout the day there are going to be many opportunities to ask questions as hopefully I've made clear from this overview. If you have a question or comment, please wait until we get to that part of each session and then we'd like to move through these as efficiently and constructively as we can. When you get the microphone, please identify who you are and please try to keep the question and comment as concise as you can. I know a lot of you have important, significant and meaningful views about how some of these Sentinel issues should be addressed and we certainly want to air those as well, but we are going to try to do this in a way that respects the limited amount of time and large number of people that we have here today and the large number of issues that we want to discuss as effectively as possible.

Also if you are in the overflow room and you want to participate in the Q&A part, there is a dedicated microphone or there will be in the back of this room for everyone to use so that just because you're in the other room doesn't mean you should not plan on participating if you have a comment or question to include.

So that's where we are in terms of the meeting for today. Let me pause there and make sure I didn't miss anything about logistics. Again thanks to everyone for coming. This is not ideal Washington weather and it's probably not ideal weather from where you were coming from as well and we have people who made it out of Atlanta which is very impressive to get to this meeting. We really appreciate all the participation. This has been a tough week in a lot of ways for many people in the country and this is the kind of public-private collaboration that I think gives me a strong sense that we can accomplish a lot together so that I appreciate everyone being here and contributing to try to move forward on these critical issues.

Now instead of a keynote address you're going to get a little bit of a brief overview from me of some of the topics that are going to come up during the course of the day, some of the progress that's been made and some of the issues that we're dealing with. With a group as diverse as this, with some people who have been devoting their lives to active post-market surveillance issues over the last few years, people who have lots of interest in health care policy but haven't been as focused or haven't had time to be as focused on Sentinel and this particular set of projects, I'm going to try and provide a bit of an overview and update that hopefully provides a little bit of something for everyone. I think my staff overstated this a little bit by calling it a keynote address, but it is going to provide some context for the course of the day and hopefully get us off on all of the key issues that we're going to try to address that, and that is toward this goal of

better post-market evidence for medical product safety and the key role of this set of initiatives in our nation's broader public health and health care improvement objectives.

This is a little bit of a complicated chart but I think it highlights just how much as been going on since the legislation creating FDA's new initiative related to Sentinel and FDA's new post-market activities which began as part of the 2007 Food and Drug Administration Amendments Act. That act mandated that FDA develop a system to enhance their ability to monitor the safety of medical products once they're on the market and it was envisioned to be something that would complement FDA's existing system, spontaneous adverse event reporting, Phase IV studies of the more traditional type, not to replace it but to provide a more comprehensive set of tools and hopefully work synergistically with some of these other resources that were available.

As you can see from the slide, there have been a series of steps to lay the groundwork for the Sentinel system over the three years since that law was passed and what you're going to hear about in more detail today is how these components of Sentinel implementation have moved forward, and I think very importantly how much they represent a real collaboration between the public and private sectors. In fact, one of the first things that was launched after the FDA Amendments Act was passed was a privately led effort, the Observational Medical Outcomes Partnership, which had participation by FDA and a range of independent experts and has focused on a number of the technical challenges, statistical challenges, data challenges, data aggregation challenges and the like, that underlie the implementation of a program like Sentinel.

This is not straightforward work. The data systems involved are diverse. While large numbers of patients and large numbers of users of medical products and large potential control populations can be included, they are typically in observational

settings and sometimes without consistent or as complete information on clinical details as one would like. They raise a number of technical issues from a data standpoint, the aggregation standpoint and the statistical methods standpoint and OMOP has taken a number of steps to identify and then take on those technical challenges to provide some technical insights about how these efforts can be most forward. Many of you here today may have participated in OMOP's annual meeting over the last couple of days where a lot of these issues were discussed and again a lot of progress has clearly had an impact on some of the other steps on this timeline that OMOP has continued its efforts throughout this three-year period.

Also in the course of implementing the Sentinel system, FDA contracted to develop Mini-Sentinel. That's a pilot program that will inform the development of the Sentinel system. That contract was developed over 2008-2009, there were some pilot contracts awarded as a prelude to that and then the Mini-Sentinel contract was awarded in 2009. It's a partnership between the FDA, Harvard Pilgrim Health Care and a range of other institutions, including HealthCorps, the Kaiser Foundation Research Institute, Humana, Rutgers, Vanderbilt, the University of Pennsylvania, the University of Iowa, Harvard Medical School and many others. I could go on. So it's a very broad-based effort to help with implementing some initial pilot versions of Sentinel activities. Along the way obviously there have been a lot of other activities and opportunities for input for trying to develop the key ideas underlying the Sentinel program.

These opportunities include some of the forums that we've been involved with and I'll say more about those in a minute, a series of other public workshops and FDA-led stakeholder meetings, a lot of efforts to try to bring forward ideas because again there is really no way to implement this program without public-private collaboration.

Those stakeholder meetings and these early workshops and these early pilot steps identified a whole host of issues and challenges that would need to be addressed to developing more effective and confident capacity for meaningful active post-market surveillance. As I said, they also highlighted the value of a transparent, collaborative process involving a broad range of stakeholders to help bring this effort together providing not only comments and ideas but for many of these stakeholders, active involvement in leadership. This isn't a project that is or can be conducted by the FDA. It's required real technical input, hands-on sweat equity from many of the stakeholders and many private-sector participants in this effort to solve the challenges.

We at the Engelberg Center are trying to help support this kind of participation and reinforce this process. As I showed you on a previous slide, we convened a number of meetings and workshops to discuss particular issues, to look for practical solutions and discuss and debate those kinds of solutions for developing better post-market evidence. I think these ongoing efforts, ours and those sponsored by others, are important mechanisms for developing the ideas on post-market surveillance and it's also included a lot of opportunities for experts from outside of Mini-Sentinel as well as patient and consumer advocates, representatives from industry, health care professionals and others to participate in this process.

Among these different activities have involved our roundtable webinars. These are still ongoing and I would encourage those of you who haven't participated that it's a good way to hear about some of the many activities taking place around the country again many of which are outside of Mini-Sentinel and outside of directly FDA-sponsored efforts but that are still relevant to this whole set of issues related to post-market safety and better evidence on medical products. These webinars are open to the public, we

have more coming up soon and we'd delighted to have additional participants.

In addition, there have been a number of expert workshops. These are typically very technical discussions of particular near-term challenges for active surveillance implementation. Some of these have included things like technical methods for implementing a network infrastructure. This workshop explored the feasibility and requirements for using a distributed data network for active surveillance and I'll talk about more about that in a minute, the tools that are required and the issues that may influence data and analytic partner participation.

Remember that this being a partnership, one with active work required by the participants, the data holders in the effort, need a process to make sure that works for everyone and is sustainable so that those network infrastructure issues are very important early on. There are legal issues and these are extremely important, issues like protecting patient privacy and confidentiality, issues like addressing potential liability issues that may arise in the course of evidence development which is at least in process and not always complete and not always definitive but can still raise liability issues so that those are very important to address. Clearly methods themselves for working out potential signals and identifying them and strengthening them for reaching more definitive conclusions, an area where OMOP has also been very active.

Finally, another critical topic is how, when and to whom to communicate findings from active surveillance again since the answer aren't always completely clean and arriving on one specific data with major insights that never were there before is much more of an ongoing and incremental process in many cases. So there are lots of activities related to expert workshops.

Implementation meetings. These involve convening groups of senior

leaders from both the public and private sectors to explore upcoming issues related to implementation looking a year or two ahead at what needs to be addressed and trying to discuss it, plan for it and make sure that all of the key implementation challenges and ways to address them get on the table. Some of the previous meetings here have included discussions of different organization models for the Sentinel systems as well as ways to ensure meaningful participation from data and analytic partners.

Then finally and very importantly for today, our annual public workshop. So that while there is a lot going on obviously with FDA, Mini-Sentinel, other Brookings activities, other organizations, there are a lot of websites that provide regular information about Sentinel's status, this annual meeting is intended to try to bring all of that together for people who may not have time to focus on this all the time or who are maybe focusing on specific issues but want to take a step back and think about the big picture of where things are and where they're headed. This annual meeting is intended to provide an opportunity not only to step back and think of where Sentinel is and where it's going overall, but to provide an opportunity for a broad base of direct feedback on Sentinel's direction to the FDA, to the Mini-Sentinel investigators, to everyone who is involved in this very important and very challenging effort. We have more information available on all of these issues on our website and again I would encourage those of you who want to do more or get involved more with Sentinel activities or at least be up to date on what's going on with them to think about ongoing participation in some of these other activities.

Thanks for the contribution of a lot of people in this room, as we'll hear about today there has been a good deal of progress toward achieving the goals of the Sentinel Initiative. In fact, in conjunction with this meeting this morning, and this kind of timing never works out, we've very pleased that the *New England Journal of Medicine*

has published a perspective from FDA, Brookings and the Mini-Sentinel team outlining the structure and function of Mini-Sentinel. It's been a good complement to the updates that you're going to be getting at this meeting today. The article is available on the *New England Journal* website starting this morning and we're going to try to make copies available to all of you who are interested in getting one before lunch. In this perspective we talk about the process that was used to create Mini-Sentinel's distributed system which is now operational and capable of querying potential safety signals on over 60 million patient lives. It describes Mini-Sentinel's ongoing and future priorities. It emphasizes the importance of stakeholder engagement as we've talked about already for providing not only the ideas and the pathway to effectiveness but the momentum for this kind of public-private initiative to continue and succeed. Then it also highlights Sentinel's potential as a key foundation in a much more effective learning health care system. It's a distributed system. There's not one database somewhere. But it's quite a remarkable resource for gathering evidence and for learning more from the practice of medicine and from the practice of health care in this country.

Mini-Sentinel is definitely a work in progress, but as the article highlights all the work that you have contributed over the last several years, it makes clear that there has been a lot of progress and some key features are now clear and that's what I want to talk about now and again we're going to discuss a lot of that in more detail during the course of the day. But in terms of some of these key features, first the framework for Sentinel is clearly a distributed database network. That means there is not some central warehouse or data repository somewhere where everyone's information, increasingly complex information, gets dumped and held. Instead, the underlying data used in the project stay with the data owners, the people who are actually using these data for the

delivery of health care, the payment of health care, for actual health care activities in some way.

The basic idea here is if there is an interest in a safety-related question and it's an oversimplified version, the basic idea is to try to find among all these data partners a common way of defining say a numerator and denominator, a denominator of all of the individuals who might have been exposed to the medical product and a numerator out of those who had some kind of significant adverse event. The basic idea of this network is if everybody does that the same on each of their own data, then the summary information coming out of that, the numerator and denominator, can be combined. It's more complicated than that in practice, but that's the idea, distributed data that stays out in the cloud or in its own homes wherever the data are and it's only brought together in a summary fashion to answer the relevant questions for safety and effectiveness.

Of course going along with that, to confirm the cases, to take further steps, there's going to be the capacity to trace back to the original data holders and the original data itself to confirm cases and things like that. So you can think about this as bringing the policy question or the safety question to each data source rather than taking each of the data sources and bringing it to the question.

There are some clear advantages of a distributed network and these are the reasons why things are evolving the way they are. Each of the partners in this analysis maintains control of their own data because they're close to it and they help make sure that their own data aren't being misinterpreted. This also helps with important privacy protection since the individual data are staying where it's being used for patient care already. This does create some challenges, too. There is real work needed by

analysts at each of these data sources, real involvement on an ongoing basis and that's why I've been emphasizing partnership and the need to create momentum and a sustainable infrastructure for all of these participants to continue to participate actively. It does require some real work on their part. And there needs to be a process to get agreement on consistent methods that can be applied across all these sites to get to meaningful results with this system and also the limitations of those methods needs to be commonly understood by the whole environment by the whole set of participants.

In this approach it is critical to collaborate effectively with a wide range of stakeholders, health plans, integrated data systems, health care providers with electronic records or supplemental information that's needed for investigating a safety question. They are all analytic partners. They're not just data providers into some warehouse. It's an analytic partnership, a distributed analytic partnership.

This has led to a number of issues and a number of challenges and real hard technical problems for implementation which are being addressed but which are certainly not fully resolved and are still part of the ongoing Sentinel implementation effort. Some of the issues that the FDA and its collaborators on active surveillance are still working on include developing a generalizable framework for refining safety signals. What does the science of active surveillance really look like? Developing established protocols for answering common safety questions. With this distributed network, the more there can be common, well understood, validated accepted procedures, the smoother this whole process will go in terms of addressing each application, each safety question, in an efficient and timely way.

Also important is having a mechanism for continuing to solicit input from experts in the public to continue to improve the rigor and the credibility of the methods

and results. OMOP has been doing a lot of work here in supporting the technical side of things as well as many of the investigators inside and outside of the Mini-Sentinel project, but without question there are many technical and statistical issues that still need further work and we'll talk about some of those today too.

Then very importantly, developing strategies to educate health care professionals on how to interpret and to apply the information from active surveillance along with all the other sources of evidence that they need to keep track of and keep up to date on so they can in turn help patients make informed decisions about their care, and similarly I should say education for patients and consumers about what all this evidence means for them and how they should interpret steps and reports that come out of the active surveillance system again are not always going to be completely definitive that all of a sudden we didn't know anything and now we know everything about a safety question and that's not the way this ongoing active surveillance system is likely to work. A lot of those issues are things that we're going to cover today because there are ongoing challenges and ongoing areas that active surveillance needs to address.

It's obvious in all of this that continued engagement with the wide range of stakeholders who care deeply about these efforts is going to be essential to the overall program's success. Stakeholders like the people who you're going to be hearing from today have an important role to play in providing guidance and insight and helping to help realistic expectations for patients, the public and for lawmakers about what Sentinel can and cannot do. There are also significant implications for medical product developers who have a major interest in better evidence related to the safety and effectiveness of their products. Health care professionals have a huge role in interpreting this evidence as I just described. And finally, patients and consumers need to be involved throughout

the process to help set priorities, to help ensure that health information is used effectively and appropriately and to ensure that the activities and the results of active surveillance are communicated effectively.

The Sentinel Initiative is developing at the same time as many other steps are taking place that are intended to provide better evidence for decision making. Recent legislation and many private-sector initiatives are exploring and expanding the development and use of electronic health information to answer a broader range of important health care questions to provide a stronger evidence base and strong decision-making support for doctors, patients, health professionals and others in our health care system. There are a number of issues that arise when health information is used for purposes like this, purposes other than direct patient care. These secondary uses of health information are potentially important but they raise a number of also important policy issues and those are still very much being explored and are going to be over the next couple of years. What gets all the press these days is the health care reform legislation in terms of expansions of coverage and new subsidies and so forth, but this is also a critical time for evidence as we're moving to a system that really has potentially much richer data but with data that presents a lot of questions about privacy, about appropriate use and appropriate methods for using it and about bringing that information to bear more effectively for better decision making. It's a critical period for evidence in our health care system as well, and the Sentinel system is really a unique part of that because it is so extensively developed already thanks to the efforts of here.

Again, there are 60 million participating in Mini-Sentinel, large efforts using public-sector data as well so that potentially an important foundation for how these kinds of policy issues can be resolved in other settings related to better evidence in our

health care setting as well. All the work on data infrastructure, privacy and security concerns, development of appropriate analytic methods, participation of data partners and analytic partners on a sustainable basis, all these issues that Sentinel is dealing with I think have important implications for these broader challenges facing our health care system. Of course, the big issues that still need to be solved go to those other areas as well for things like effectiveness research, quality measurement and reporting, creating a sustainable mechanism for participation by data and analytic partners, developing active public-private partnerships that are governed effectively, extending our capacity to appropriately link and analyze different data sources while protecting patient privacy, ensuring all stakeholders have meaningful roles in these activities, they're challenges for Sentinel and they're challenges for the rest of these other key activities in our health care systems.

So that's why today is so important, not that we're going to solve all these problems, but you have an opportunity here today to participate in right now what I think is one of the most important set of initiatives related to these core issues for the future and wellbeing of our health care system and for the future health of Americans. So today is a very important part of this process of moving toward better evidence, more personalized evidence on safety as part of moving toward a much more effective, efficient evidence-based health care system and I want to thank you all for joining us to participate in that effort.

That brings me to end of my opening and framing remarks. We're not going to have questions and discussions of this because what we really want to focus on is the panel presentations where all of these issues and I'm sure many more are going to be discussed I think much more extensively and eloquently than I've been able to do in

these short opening remarks. I'd like to move right on to that right now with our first set of remarks on Sentinel Today from the FDA perspective so that we're going to hear a few words from some of the leaders at FDA on this effort. That includes Rachel Behrman, director, Office of Medical Policy at the Center for Drug Evaluation and Research, and Judy Racoosin, the Sentinel Initiative scientific lead in the Office of Medical Policy, the Center for Drug Evaluation and Research.

Rachel and Judy, come on up and let's get started with your perspectives. Thank you.

DR. BEHRMAN: Good morning, welcome. Actually, Mark's covered pretty much everything, so I can just say ditto or choose to emphasize a few points. I will choose to emphasize a few points.

First of all, on behalf of the Agency I would like to add our welcoming thanks to everyone who has for the past three years been marching a long beside us, so, certainly, patients and consumers and their leadership representatives here today, and our data partners without whom there would be no initiative; our colleagues from OMOP; our colleagues from regulated industry; our colleagues from Boston, from Harvard.

And just as an aside, I'd like to say that when we think about causal relationships, ever since we started working on them there has been a substantial increase in the amount of snow in Washington. So is that right? Is that a signal we should pursue or not? And if so, how? What are the methods that would help us determine whether or not it's correct?

And, obviously, our colleagues from Brookings without whom we really would not be where we are today. I mean Mark put up that time, sort of a timeline, and what was not shown for the right before the official relationship with Brookings was the

invaluable assistance Mark and his colleagues provided to us right from the beginning. I guess it helps to be an ex-FDA commissioner as well as health broad perspective on health care.

So we stand here three years later at our annual meeting much farther along than I would have expected, and I'm delighted to say that. I think that thinking back in, at least in my years of federal service which at this point are amazingly 20, the only other time I saw this kind of really rapid progress which was accomplished only through collaboration was something Mark has emphasized repeatedly, and appropriately so, was the early, early days of HIV drug development.

Now, there, there was an obvious or what people perceived as an obvious tangible threat by a virus, a deadly virus, and everyone could coalesce or collaborate around that threat. Here the threat, and I think it's quite real and in a way much more impactful, is much harder to articulate it. It's the I don't want to say crumbling of -- or would it be fair to say crumbling of our health care infrastructure and our ability to deliver care, our ability to afford to deliver care in the way we as a country want to and should? That's a real threat, but it's much less dramatic than a virus, and yet, from the beginning we have had aptly the Agency, the Food and Drug Administration have had absolutely no trouble engaging the communities that need to be engaged and want to be engaged in helping us move this forward.

And, Mark, there are two points with which I want to quibble. One was you said no way to implement without a public-private partnership, but three years ago that was absolutely on the table as a question with a big question mark, and I think we have proven -- so the first thing and harkening back to Mark's comments about it's been a tough week, and when we see forward progress like this, it makes us very hopeful -- we

can't fix the entire world, we can fix a piece of it. I think we have proven in this, in this collaboration -- I'll talk a little bit about the specifics -- we've shown that the federal government has a better way to function; that had we gone it alone and done it in silo which -- and there were advocates for that -- we would not be where we are today. And instead, we are far ahead of where we could have imagined being and have a much richer, more productive and more effective program through collaboration.

So, Mark, I think the answer is, yes, we now know there's no way to implement it without public-private partnership. I think that was in question three years ago, and we've answered that question, and that, we hope -- we'll talk today -- can dramatically influence the way other parts of the government -- the Agency, but other parts of the government -- think about moving forward on related efforts.

The other piece I wanted to quibble about was the distributed model. That again is a serious question three years ago. Absolutely on the table, now it seems, as my children would say, like a no-brainer. So things that seemed insurmountable, problems that seemed insurmountable three years ago -- and I'm looking at Kristen and I'm looking about some of the privacy issues where we just were all holding our heads in our hands -- we've gotten way past the discussion about oh, my goodness, the data can never, ever, ever move, to how do we protect it? How do we protect the patient and the consumer, but how do we maximally protect them by making sure their information is being used optimally? And thinking creatively about what is involved in that.

So our discussion has become far more sophisticated and far more productive. So that talks about the partnership that we have, one thing we have accomplished, because this is, I think, the first meeting where we're actually talking about tangible deliverable accomplishments. The first meeting was if you will meet and greet.

The second meeting was a little bit more priority setting. I see (inaudible) nodding her head yes. This meeting is the first time we're actually presenting results. Now, that doesn't mean I'm going to tell you Drug A causes B, although I do think working with Rich does cause snow in Washington, but that's my opinion. And, therefore, I think the Harvard crew should come and shovel my driveway when we really get dumped on.

But so we -- I think we've answered the partnership collaboration question how to fully operationalize that is not -- is a work in progress, as was proven last night, as we -- past -- personally past my personal bedtime -- but we were still struggling with some slides because one thing we learned was that we're very used to working in a regulated industry, and we have a language and systems in place. Now we've gone to a different community, the academic community, in a different way.

In other words, we're not reviewing your INDs and your NDAs as we usually do. We're very, very different. We've learned how to learn to develop a language and methods and so forth. And what is obviously sensitive to us is not obviously sensitive to a different community and vice versa. And we're having to learn to be very sensitive to those issues because those become stumbling blocks and ultimately could become deal breakers if we don't fully understand the priorities of each sector and make sure that they're articulated and addressed. Not everyone gets everything they want.

We all have to lose some of our, if you will, autonomy, but at least we have to think it through, make conscious decision, make sure it's on the table, and then move forward. Otherwise, if we don't understand what brings people to the table and what drives them away, we no longer have a collaboration. And in that sense, Mini-Sentinel and Sentinel in general is a very good work example of the kinds of things that

we need to work through as we move forward.

And I'll talk in a minute about where we're headed, but I do want to spend a couple of minutes on communications. Mark touched on communications in one way, which is -- and we follow and talked a lot about this: How do we get this kind of data out there in such a way that makes sense, that's not misleading, and it's constructive? In other words, again saying that because we're working with Harvard we're getting snow, if it were on the more serious subject that could be very destructive. We'd say, okay, fine, we won't work with Harvard anymore and we'll solve the snow problem. But when you talk about a drug and misinformation or partial information or confusing information kind of filtering out, that's a serious problem for us.

Now, we -- FDA -- have maintained and are convinced we -- not that we're such experts at communication, but this is not a different problem for us than we have every single day, but working in this environment is very different. And that point was driven home by the press reports this week about the saxagliptin study. And you'll hear a lot more about that as a methodology in a little while, and I'm not talking -- I'm not going to be talking about methodology other than to emphasize that the methodology is in its infancy.

We really don't know how to do this, so we have to learn as we go. But we chose this Saxi study very, very carefully. Judy Racoosin, who's our scientific lead in collaboration with the Center, put together with the candidates, we went through them; but one crucial point that was missed is, what was absolutely critical is that -- as Judy likes to say -- what's the plan? Well, the plan was that there's an ongoing randomized control trial. So we have a plan. We have a safety net. If we don't understand the information we get, we will have other information such as if we wanted to go back to my

snow example, we look at the *Farmer's Almanac*, we could really figure out if indeed there is to be more snow.

So the press reports that, I don't know, just said we chose Saxi because it was diabetes, chose Saxi because MIs, chose Saxi because we thought it would make Congress happy, chose Saxi because we wanted to pick on those particular companies, whatever. They weren't quite right, and we have to figure out how to operate in this collaborative environment. Our thinking will not always be that clear, but at the end of the day, because Mini-Sentinel is a contract from the federal government and from the Food and Drug Administration, we will make certain decisions, and we will make those decisions as transparent as we possibly can. But there will be times when we won't be able to be completely transparent, and that is the truth.

The next point I want to make is similar, similar to that one. It talks about managing expectations, and Mark touched on this as well. Sentinel, it's not in its infancy anymore, I think we're all the way to toddlerhood, but we are learning how to do it. And we have to somehow make sure we always communicate that, that as we now do talk about results, and as we do talk about developing methodologies, we're very clear about what the limitations are, what we can and can't do, keeping our eye on the future, not only building toward the future, building towards this national resource, but we're going to have concrete deliverables along the way. And what they mean and how impactful they are, we have to frame very, very carefully, and that's clearly where we need the help of the community of people who really understand what's going on and with the strengths and the limitations.

I think the last point that is really tricky is how do we get from here to where we want to be, and that's the answer we don't have. Just as three years ago I

could not envision being where we are today, and I wouldn't be able to describe exactly what we already have, how we go from here to the national resource we want to have, that we need to have that has a sustainable business model, that has a shared infrastructure, that meets the needs not only of the Food and Drug Administration -- and that, obviously, is going to be our first priority -- but understanding that we do not in any way want to encourage duplicative activities. As we've said in the paper, there are -- health care information, it's a precious national resource, we don't want to waste it -- and we certainly don't want to waste the resources that are involved in understanding and analyzing and so forth.

We not only are short of financial resources, we operate on a very small budget, we are very short of experts to know how to do this, and as a nation we haven't quite yet figured how to rev up training those experts, so we cannot afford to be running parallel systems. So how we engage and make sure that the federal government is on the same page, that all the various activities are on the same page, that we're not querying data partners for the same information in six slightly different ways. How we get from here to there; how we influence the national dialogue is not entirely clear, but it is definitely through for such as these.

So Judy's going to spend substantially more time on this than I have on the specifics of what we've accomplished and where we're going, and Rich will follow with more detail. But I think we can sit back today and not rest on our laurels -- we have an enormous amount of work ahead of us -- but I think be very satisfied and, in fact, amazed that we have succeeded in developing an adverse, transparent, and accountable collaboration which I believe is precedent-setting. And I think others who've had (inaudible) can think about that. It took us a lot farther and invented a lot faster than

when we had thought.

As I said, we had an obvious, tangible threat such as a virus. And at meetings such as these and the various other activities that have been outlined by Mark in terms of having Brookings help march us along, we have to be vigilant to anything that can derail us. We have to be willing to course-correct whenever we need to and remembering that at the end of the day we are all here for the same reason, which is to better the health of this country, to the people in this country, and that we are inventing are we go a much more modern approach to doing that, although it will still be only one tool in our toolbox -- just like saying working with Harvard with snow proves snow -- Sentinel will never be alone, Sentinel finding, but it should help us very much modernize how we think about our therapies.

Thank you. (Applause)

DR. RACOOSIN: Good morning, everyone. I'm going to give you a little bit more detail about the activities that are comprising the Sentinel Initiative. Here we are two and a half years into the official program. I'll talk a little bit about the background and why we're here in the first place, talks in a little bit more detail about the pilot programs that you've already heard mentioned that have been underway for about a year and a half to help us actually pilot how we might conduct an active safety medical product safety surveillance. I'll revisit our convener activities on active medical product surveillance that you've heard described, but I'll put a little bit of FDA input into that and then wrap up by talking about the public-private partnership, OMOP, or Observational Medical Outcomes Partnership you've heard a little bit about today, also.

So just revisiting the FDA Amendments Act of 2007 for a moment, Section 905 is about -- talks about active postmark-at-risk identification and analysis.

And, specifically, it says that FDA should establish a postmark-at-risk identification and analysis system to link and analyze safety data from multiple sources, and it laid out specific goals for the number of patients that should be included in such a system. And that was 25 million people by last July and 100 million people by next July or a year from this July. And there's a little checkmark next to the 25 million because in July of last year we did meet and exceed that goal out through the Mini-Sentinel distributed database which you'll hear a little bit more about later.

Another component of Section 905 specifically said that FDA should be a utilizing data from a variety of sources including both federal health sources and private sector sources. And so two more checkmarks there as we have included out federal partners and our federal partner collaboration which I'll be speaking more about as well as the private sector in the Mini-Sentinel project.

Now in response to the FDA Amendments Act, a mandate to create this system for postmark-at-risk identification and analysis, FDA launched the Sentinel Initiative in May of 2008, and the goals of that program are listed on this slide. Specifically, one of the goals is to improve our capability to identify and evaluate safety issues in near real-time. So for those of you familiar with FDA, we have -- we have had for many years spontaneous reporting systems that capture reports that are either submitted to manufacturers who are then required to report them to FDA, or FDA can accept reports directly from health care providers and patients.

But these passive systems require FDA to await those reports coming in, and that can be a lengthy process as people experience potential problems, have to think about reporting them, report them to their practitioners, et cetera, and so we need a way of learning about safety issues more quickly, identifying them and evaluating them. So

that's one goal of this active surveillance system. The other is to enhance FDA's ability to evaluate safety issues that are not easily evaluated through the spontaneous reporting system.

So these are improving our access to special populations like children and the elderly expanding FDA's access to longer-term data which in some regard will likely require us to be able to link between databases in an anonymous way and, finally, expanding FDA's capability to look at adverse events that occur commonly in the population. The spontaneous reporting systems do quite well with rare, uncommon events that are often considered to be related to particular medical products. It's much harder to understand common adverse events like MI and fracture because generally they're not even reported to the database, and even if they are, we don't quite know what to do with them because they occur commonly in the background.

But by creating a system that has a defined denominator and has compared our groups, we can improve our capability of looking at these common events. And so I just want to reinforce that the active surveillance system that we're developing is intended to augment and not to replace the systems that we currently have in place.

So moving on to the pilot programs, I'm just going to briefly mention, highlight Mini-Sentinel because you're going to be hearing a lot more about it, but specifically this is the pilot that we have intended to develop the scientific operations needed for the Sentinel system and to create a coordinating system that has a capability of having access to relations with data partners to create a distributed system for us to pilot the evaluation of safety issues that are coming up from a variety of centers and from free market development things that are occurring in a post-market period. And this gives us an opportunity to evaluate how we might evaluate these safety issues in this

kind of distributed system, and we can come to understand what are the barriers, what are the challenges, and to really work on evolving the data infrastructures and the scientific methodologies that are needed to do this.

The federal partners' collaboration is our small distributed system with our federal partners, the centers for Medicare and Medicaid services, the VA health system and the Department of Defense. We are doing this project through interagency agreements, and the difference in this small distributed system is that we are not utilizing a common data model, and I don't -- I'm not sure that that phrase has been used today yet, but you'll be hearing more about it.

One of the approaches with a distributed system is that in order to run an analysis similarly across all of the data partners, each of the data partners transforms their data into a standardized format so that one analytic program can be run, and that's the model that's being used in Mini-Sentinel and that's the model that's being used in OMOP as well.

With our federal partners that is not part of the program; however, our approach has been to develop a common protocol, develop standard definitions for our exposures and outcomes as well as developing a common approach to the analytic methods and then for each of the data -- each of the federal partners to implement the protocol in their data setting, and this gives us an opportunity to understand how do we interpret data from the safety evaluations when we are not using a common data model, recognizing that we're trying, as part of the Sentinel Initiative and trying to understand a range of approaches to doing things, what are the challenges when you do one of these active surveillance evaluations without a common data model versus when you use a common data model which we're learning about from Mini-Sentinel and OMOP.

So that's the approach that we're using with our federal partners, and it's been a very productive collaboration, particularly because our federal partners, they have specific -- as they take care of their patient populations, they have specific safety questions that are important to them, that are important to FDA, and we can collaborate to better understand that and improve the care all around.

As you've heard today already, the Brookings Institution is leading our activities, our convener activities on active medical products surveillance, and this has really been an invaluable collaboration. It has allows FDA to access experts in the areas that are important to helping us develop an active surveillance system and the various topics of expert panels, the active -- the medical product surveillance roundtables. Some of them are listed on the slide, but it really has allowed us to access the expertise that we need as well as hearing about the latest projects that are going on in various -- the fine aspects of how do we do this.

So how do we think about linking data anonymously? What has been the experience of other projects that have tried to do active surveillance in their own settings in a state-based way and in other federal initiatives related to H1N1, what did that experience -- what were the lessons learned there that we can apply to Sentinel?

So this whole effort has been really tremendously helpful in gathering all of the expertise because, as you've heard today, we're getting, we've gotten where we're going or where we are today and where we're headed because of all of this collaboration and with all of the various smaller advances that groups are making. We can learn about them and in the active surveillance implementation meetings try to bring all of those bits of information together to think about how, ultimately, will we stand up the Sentinel system.

And finally, the public workshops like the one today. We really are appreciative to Brookings for helping us bring everyone together for these important discussions.

I'm going to finish by mentioning the Observational Medical Outcomes Partnership. Mark described this earlier. I just want to revisit it for a moment. It's a public-private partnership between the pharmaceutical industry, FDA, and the foundation for the NIH. And it's really been -- it's a research effort focused on developing methods for use in observational data for active surveillance. The goals have been to conduct this methodologic research as well as developing open-source tools and capabilities and really establishing a community around research in this area.

As Rachel mentioned, we are in need of more people moving into the area of development and conduct of active surveillance, and a project like OMOP is important in creating this research community to move this forward. If there are graduate students out there in the crowd, come work with us because we can use your help.

I'd encourage you to go to the website because a tremendous amount of materials that OMOP has developed in the area of methods development and data characterization tools are there as well as the description of the common data model and the other work that's been done. As was mentioned yesterday was the OMOP symposium where the results of the main OMOP methods experiment that were conducted through the first two years of the project were presented, and clearly tremendous progress has been made and beginning to understand the methods landscape. But there's a lot more work to be done, and, fortunately, OMOP will be continuing for another year.

So I think you've probably gotten the sense that this is a long-term,

complex initiative, and we're really -- we are implementing it in stages as the scientific methodologies and the data infrastructure evolves. We are
-- it's of utmost importance to us to maintain the privacy and security within the distributed system, and you'll hear more about the privacy panel that has been part of Mini-Sentinel that has helped develop the policies in that area. And we are here because we want to hear from all of our stakeholders so we can continue to address concerns that may come up as we move this program forward.

And, finally, we are really interested in trying to address how the eventual Sentinel system can function as a national resource, as has been mentioned, and really complement other federal initiatives that are using distributed systems. So we know within the HHS immediate office and within ARC there are projects going on to use distributed systems for comparative effectiveness research and product quality initiatives. And we want to make sure that we can move this effort forward in as collaborative a way as possible so that, as Rachel mentioned, we're not making duplicative efforts, and we can use our resources together to move all of our initiatives forward.

Thank you. (Applause)

DR. McCLELLAN: Thanks, Judy. Thanks, Rachel. Just again, warning you about the discussion from here, Rachel and Judy are going to participate in a discussion after the first panel where we're going to try to get into more depth about a range of issues around Sentinel implementation to date, and some of these issues going forward. So I want to hold any sort of big substantive questions until then. But I did want to check right now, does anybody have any clarifying questions about Mini-Sentinel, or about anything else you've heard so far?
We'll hold off on the substance, just any sort of clarifying technical questions?

Okay, that's going to be a pretty good discussion in a little while, so thank you all for coming up now. They will be back in a little bit after we hear from the remainder of this first panel. And I'd like to ask all of our first panelists to come up while I introduce them. This set of a group of Mini-Sentinel investigators who are going to provide an update on the pilot's development and future plans. And again, we're going to have an extensive discussion here so that we weren't going too long without a break. What we're going to do is hear from all four of them and then take a short break and reconvene for really an hour of discussion with Rachel and Judy as well about all of these issues related to Mini-Sentinel.

But right now I'm looking forward to hearing their opening comments, and let me introduce very briefly Rich Platt, the professor and chair of the Department of Population Medicine at Harvard Medical School and Harvard Pilgrim Health Care Institute. Rich is the PI on the contract with the FDA to develop Mini-Sentinel. As I mentioned earlier, this includes a very large and diverse set of organizations.

Next, Lesley Curtis is an associate professor of medicine at the Center for Clinical and Genetic Economics at Duke University School of Medicine.

Next is Kristen Rosati, a partner at Coopersmith Schermer & Brockelman, PLC. Thanks for making it here today, Kristen.

And also Bruce Fireman, who's a biostatistician and research scientist at the Division of Research at Kaiser Permanente in Northern California, who will talk about they have been involved in Mini-Sentinel to date and will give you some, I think, a good set of perspectives on where Mini-Sentinel is and what's coming up.

So, Rich, let me turn this over to you.

DR. PLATT: You know, being the principal investigator usually means

you're the guy who gets all the complaints, and I have to say this is an extraordinary activity because I'm probably the person who is having the most fun in this activity.

I tried to make a slide showing the names of the people who have been actively engaged among the 27 partner organizations involved, and it turns out that the fund size is really too small to do that. But I'll say that the things that the four of us are going to talk about involve the substantive involvement of about 150 people who are engaged in a meaningful way in creating the things that we're talking about. And that's only on the contractors' side. There is also a large number of people at FDA who have been very active participants in making this work.

So there isn't time to name names, but I will say that Rachel and Judy and Moe Serrob have been as good a set of federal partners as I've encountered in what's getting to be a long career of working with federal agencies. So this is really not only an activity that is successful as it goes, but it's also one that's quite a positive experience.

This is a slide that Janet Woodcock used just over a year ago in which she laid out the things that FDA was expecting of the Mini-Sentinel program. There's a lot of words here, so let me boil it down to say that our marching orders were to do seven things: one, create a coordinating center; second, to build a distributed data system; the third was to engage three or more health data environments; the fourth is to create a system of governance that would sustain this activity; the fifth was to build a secure communications facility; the sixth was to develop epidemiologic and statistical methods to the extent that they're needed to make this work; and then to do, to evaluate topics that FDA identified for us as being important ones.

So let me give you a progress report on how we're doing in a year later.

We've stood up a coordinating center that has an operations center in Boston and a planning board that is distributed, has membership from all over the partner organizations and others, including a patient representative. And I'll mention it particularly that a project operations committee has done yeomen work in creating policies and principles for us, and our privacy panel has provided terrific guidance for us.

We organize our work according to data methods and protocol core, and each of those has work groups that are stood up and do work on specific topics as needed. So those are sort of ad hoc organizations groups that do the real work of the Mini-Sentinel.

The governance policies that we've developed so far focus on seven areas. I've listed them here but I'm going to highlight the first three. The first was the decision by FDA to consider the work that we're doing to the part of FDA's public health practice rather than research. And it's a decision that followed a substantial amount of thought and consultation and work and that has very important implications -- partly they're operational implications -- for what it takes to do work. But, more importantly, I think in really firmly establishing the kind of activities that the Mini-Sentinel's engaged in as an activity that is addressing an important public health priority rather than simply generating new knowledge.

The second thing that we have spent a lot of time on is the sort of the theoretical underpinnings of the distributed data system, and that is the principle of having as little of protected health information leave its existing home as possible. And so articulating that in a way that is flexible enough so that data can move when it has to, but doesn't move when it doesn't have to was also important work.

And the third policy is the fact that everything we're doing is work that we

expect to appear in the public space in a timely way. One of the unusual -- one of the surprising things about our initial interactions with FDA was the fact that not only did we have to not have to negotiate for the right to publish our findings, and that is sometimes an issue in the work that we do with federal agencies, but we actually had to have a conversation about whether it would be possible to hold off on making certain things public so that we could publish them in the peer view literature. And it's a first for us.

Kristen will talk about the work that the privacy panel has done in thinking through and articulating principles on privacy. There's a whitepaper that I'm sure she'll refer to that's available on our website. This is back to 2010. We were hoping to be able to make available administrative and claims data for 60 million people and listing the other things here. We spent all of this year working on the administrative and claims side since we had to start somewhere, and that's the largest amount of data.

In fact, Lesley will show you that we now have data on 71 million people. We think those are -- when Mark talks about queriable data, those are the data that are queriable for FDA. These are our distributed data partners. We were supposed to have data from three. In fact, the data, the 71 million come from 15 organizations that are part of Wellpoint, Kaiser, Humana, HMO research network. Aetna is joining the Mini-Sentinel team. Vanderbilt will also be data provider. There are also partners that are not data partners but bring content expertise, and I've listed them here.

Mark's already showed you the distributed analysis framework that we use. I'll only point out that part of the special sauce is the Mini-Sentinel portal which uses software that we've developed over the past several years using support from AHRQ which has staked out the space distributed analysis and has allows us to make progress much more quickly than we otherwise would have. This is a team that Jeff Brown has led

that's built and made operational this portal.

We have secure communications facilities, FISMA compliant file transfer capability. We also have a public website, minisentinel.org, where most of the things that we're talking about either are now or will be available fairly soon. So I invite you to come visit the website. The kinds of things that are on it are we'll put the results of our completed evaluations. We have information about every one of the ongoing evaluations that has been sort of formally approved. Our methods, tools, policies, procedures, protocols, computer programs, will all be -- the ones that are finished enough to show are there.

We've put a substantial amount of work into data, into methods development. We're not going to be able to spend time this morning saying much about the methods develops that we've been doing, but that has been both epidemiologic methods development, developing a taxonomy of study designs that might be used for different kinds of questions that FDA is interested in and different kinds of data resources that are available.

We also have been doing some work in getting the best understanding that we can of the existing knowledge about how to use electronic data, and we've been doing a substantial amount of work in novel statistical development to address some of the major gaps that we know we're going to have to deal with in order to make the best use of these data.

So back to Janet's slide, I'd say we've done -- we've done pretty well on six of the seven things that she gave us to do. So as the 2003 Red Sox would have said, it's time to cowboy up and actually do some safety evaluation. So that's the work of this coming year, actually learn something that will be useful for clinicians and for patients.

Bruce is going to describe the protocol that we will be launching fairly soon to evaluate acute myocardial infarction in relations to orohypoglycemic agents, but we'll also be working with FDA to evaluate safety issues, new safety issues for drugs that have been on the market for awhile and to evaluate the impact of FDA's regulatory decisions on the use and health outcomes of products that are the targets of those decisions.

We're also -- we're also going to be working with the Center for Biologics on, now on assessment of effects on some vaccine safety issues. There's a prism project that Judy mentioned which was an ad hoc evaluation of H1N1 vaccine safety is now formally part of the Mini-Sentinel program, and we are delighted.

Last year I thought that our situation was like this: engaged in a good line of work and enjoying the things that came down the pike. I'd say this year we're realizing that we're really dealing with heavy machinery and there are a lot of moving parts. So let's -- that doesn't look like Lesley there, but running the data core is not a job for people who don't know how to stay out of harm's way.

Last year I listed these eight challenges as being things that we needed to be mindful of, and this year I'd say it's the same eight challenges and the same two that are at the top of the list: That is, on the one hand we appreciate that it is important to have the capacity for timely evaluation of the data that are available because it's important to now that products are safe if they're safe, and it's important to know they're unsafe if they are unsafe.

On the other hand, we recognize the tension and the importance of avoiding false alarms that can have an enormous negative impact. And so building the infrastructure and the capability of doing these studies is an important piece of work, but

the leitmotif that governs all of this is making sure that we achieve the right balance of speed and care, and that we avoid saying things that are really misleading.

So I've already shown you that minisentinel.org is a living, breathing website, but one day while I was thinking about something else I typed in minisentinal.com, and you actually get someplace. And I'll just point out that I don't know who owns minisentinal.com, but you can buy it. So if you take a market-driven view of the world and ask how are we doing, I'd say a URL that you could buy for max $15 last year now appears to have a market value of $2,000, which is a return of investment that's pretty good, so.

SPEAKER: You'd better buy it now.

DR. PLATT: Right. So we have yet to do the most important work that Mini-Sentinel has to do. On the other hand, we are delighted to have made as much progress as we have, and looking forward to continued -- continued work here.

Thank you. (Applause)

DR. CURTIS: It's great to be here today to share with you some of the accomplishments of the data core over the last year. Really, I believe over the last year we've created a really productive and actually quite fun collaboration among different data environments, institutions, and we've built an exciting and I think unique resource as well.

Today what I'll do is talk about the process that we used to create the Mini-Sentinel common data model and how we actually developed the distributed database. I'll also touch on the core infrastructure that's been built -- Rachel alluded to this a little bit just a minute ago -- and then talk about how we'll be generating useful information for FDA.

So a common data model, as Judy mentioned, is essentially a commonly defined data structure with specific data definitions to accompany that so that all partners or all institutions in the distributed environment can transform their data in a similar really identical way. In creating the Mini-Sentinel common data model, we began by developing some kind of ground rules or guiding principles for the work that we would do. We did a careful review of existing data models, and then we went through a fairly detailed process of revising and revising and revising draft data specifications.

Now, when I talk about laying the groundwork, we really did do that by creating these kind of common understandings, guiding principles that we would use throughout our work together. There are 11 guiding principles in all. I've highlighted three here that I think really are both broadly stated and I think nicely articulate the kind of underpinnings of the work that we're doing.

Simply put -- you could read them here, but simply put we value the data partners and the expertise and experience that they bring to the table. We are committed to creating a distributed database and environment that is really quite efficient. And, finally, we're committed to creating a distributed database that meets the needs that it's supposed to meet but is also flexible and able to develop over time.

We did a fairly thorough review of existing common data models because we didn't feel the need to reinvent the wheel, and we certainly didn't want to make mistakes that had already been made before, or we wanted to learn from everyone else. Included in that review were some of the data models that you've heard about today -- prism, OMOP, the HMORNs, virtual data warehouse, the vaccine safety data link and several others, and from that review several kinds of lessons or themes emerged.

First, we were reminded again and again that it is feasible for many data

partners to assemble these patient-level files according to some common data specifications. And while doing that they can also retain complete control over the use of their data. As you've heard already, that's really, really an important point, but while they do that they can still work toward common objectives.

We were also reminded that coding varies by data partners' coding schemes that are used to vary, and it's really important to understand those differences and again to keep those data partners and the people who truly understand those differences best at the table for ongoing dialogue.

And, finally, we concluded at the end that all of the analytical imperatives that have been given to us could be met using this distributed approach.

So, as with any development process, we began with a good old straw man, the common data model that really required what we thought would be minimal transformation so that we'd maintain the granularity of the source data and also leverage this prior experience. We spent a fair bit of time reviewing and talking to data partners about their experiences with other common data models and wanted to make sure that we put that experience to good use.

With each iteration of the common data model we engaged the data partners in a discussion about that data model that we had share with them, and questions like: Can you implement this? Are these definitions? Are the tables, do they include -- are they specific enough? Are we specific enough in our direction to you so that you can transform source data in a common way? What are we missing? And are these requirements consistent with what you expect? And, of course, this is a partnership, and so this process actively engaged and involved FDA along the way as well.

Version 1 of the common data model, as Rich said, rests on administrative and claims data and has five major data areas. There's an enrollment table. We include information about demographics, outpatient pharmacy dispensing, utilization, and mortality. Now, although all of these data partners had some experience with common data models, the work of transforming this initial transformation was really a major undertaking for everyone. Each data partner translated its local source data to this common structure and in the process documented exactly how they had done that. So data element by data element, table by table, telling us how source data were transformed into this common data model.

As with everything that I've talked about today, the work took place through a series of weekly conference calls, countless e-mail exchanges, and many, many, many one-on-one conversations. Then the transformed data were characterized using some standard programs that the operation center had developed. Now, I want to reiterate that at all times these data remained behind institutional firewalls, so we used this distributed approach that's already been described to gather information and to characterize these data.

Overall, the Mini-Sentinel distributed database spans from 2000 to 2010. Different data partners have data going back to, you know, different beginning dates. Collectively, there are more than -- nearly 120 million records in the enrollment table the vast majority of which have both medical and drug coverage. There are more than 70 million unique members included in the enrollment tables, and of those 22 million were current as of January 2009 with both medical and drug coverage. This amounts to about 170 million person years of observation time with an average per person observation time of about 28 months.

Slightly more than 50 percent of the enrollees are female and about two-thirds are between the ages of 20 and 65. That's about 45 million people, so for reference the young -- the youngest group here from 0 to 52 weeks, for example, there's about 230,000 people, and the very oldest group, the 85+ group, as about 3 million enrollees there.

The operation center has done a tremendous amount of work over the last year building the core infrastructure that supports this distributed system. I mentioned the standard programs that had been developed to characterize the data. A library of programs also exists to check the quality of the data that are being created or that have been transformed.

We also undertook a formal assessment of the data partners' technical environments which really expanded beyond just technical issues to really try to identify barriers, opportunities, and even non-technical issues that might come into play. With the first transformation complete, preparation is underway now for the beginning of quarterly refresh cycles to the Mini-Sentinel distributed database and, along with that, an empirical assessment of data latency. And, as Rich mentioned, the secure web portal for distributed analyses is a huge accomplishment.

So to return to this picture one more time, just to sort of reiterate how the pieces fit together and what the data core as done and what the data partners have done, local data have been transformed into -- or source data have been transformed into these local data sets that you see described here. The infrastructure is in place now to begin the querying of these data, and we've also developed, I believe really importantly, an approach to not only -- not only fields the kinds of queries that will be necessary for a full-blown surveillance program like the one that Bruce Fireman will be talking about later this

morning, but also to respond to the kind of rapid questions, rapid queries that come up as questions arise.

To do this Jeff and his group have created really a library that will continue to evolve of modular programs that can answer sort of specific and common feasibility type questions. I've listed them here, and you'll see that they really will be quite useful for those kind of quick questions that arise. So the first looks at drug exposures for a specific period, how many exposures were there over this time period to a given drug?

This second expands that a little better, actually narrows that a little bit by saying tell us about drug exposures among enrollees with a specific condition.

The third begins to put together exposures with outcomes in a very simple way summarizing those results across the partners.

And then the fourth explores and summarizes concomitant exposure to multiple drugs. We're very excited about the progress that's been made but certainly understand that a lot of work lies ahead. And thanks again for the opportunity to share with you what we've done. (Applause)

MS. ROSATI: Well, good morning. It's really a pleasure to be here. I'm Kristen Rosati from the law firm of Coppersmith, Schermer & Brockelman. I am in Phoenix, and it's really been a pleasure being involved in this project. I do a lot of work across the country in using electronic help information for research and public health and other purposes that aren't directly related to the treatment of patients. And this is by far one of the most exciting projects I see happening across the country because there's a real chance and a likelihood that there'll be real impact on the health of Americans.

So the FDA and the Mini-Sentinel folks are building this incredible public resource using electronic health information, and one of the really important things that

I've seen is that the FDA and the Mini-Sentinel project personnel are incredibly committed to the privacy of that health information. And I think this is essential to build public trust in what the FDA is building here. I think the public really supports the use of health information as long as it's kept in a secure private way for purposes such as research and public health activities that will increase the health of the public. So I've been very pleased to see the real sincere commitment to privacy in the project team.

As you'll see and as you've already seen the architecture of the Mini-Sentinel project itself really is committed to privacy because it's a distributed data network, as I'll talk about, complies with federal law and, more importantly, it goes beyond legal compliance, and the Mini-Sentinel project team has adopted policies that reflect what are called "fair information practices," which is really the bedrock of a lot of federal and state laws and good privacy practices about how to use health information.

I've had the pleasure of working with two incredibly smart people on the privacy panel for the Mini-Sentinel effort. One is Deven McGraw, who's the director of the Health Privacy Project of the Center for Democracy and Technology. I know Deven's here, raise your hand, we have to point you out. Deven's really a committed advocate for consumer interests, not just the interest in patient privacy which, of course, is essential to what we're doing here, but also consumer interests in building these resources so that we can leverage these wonderful electronic health information resources we're building across the United States.

And also, Barbara Evans, who's an associate professor at the University of Houston, who has really brought an important perspective to the privacy panel. And we've been working together on evaluating the legal compliance for the Mini-Sentinel network and also helping build the privacy policies to reflect those fair information

practices.

Now, you've seen this before, obviously. If there's one thing you're going to get out of today's conference is that you will understand that the Mini-Sentinel is a distributed analysis -- distributed network. And that's really the key to great privacy protection because the individually identifiable information, which is really what consumers and patients are concerned about protecting, stays behind the firewalls of the data partners. And so a distributed data network used for analysis, whether it's for these public health activities or for research perhaps in the future, really protects individual patient privacy because the data source hold onto that individually identifiable data.

So they maintain the physical and operational control over that source data. The put it into that common data model so that you can do good analysis over many different points of data sources. The operation center or the FDA send standardized queries into the data partners; the data partners scan it against their data -- you can tell I'm not a bioinformatician, but I'm perhaps talking in a way that the consumers can understand -- and then the data partners execute those queries against their data and then share summary results back to the operation center.

Occasionally, that summary of the summary results aren't sufficient to do the analysis, so the data partners may occasionally be asked to provide patient-level data to the operation center to do a good discrete analysis of a particular drug safety event where the data partners strip all of the individually identifiable information out of that patient-level data before sending it to the operation center or the FDA. So that's really key to continuing to protect patient information even when that patient-level data may be necessary to do a more particular analysis.

Now, occasionally, the data partners who are doing the analysis with

their common data model may not have the original source data. Health plans, for instance, are working from their health claims databases, and occasionally it may be necessary to ask for a patient medical record from the original source data to confirm a drug safety signal, for instance to evaluate when a particular drug was prescribed or administered to an individual, whether there's any other clinical indications for that patient that would count against that drug causing the actual problem.

In those circumstances, the data partners may ask for individual information from the data sources, but the important thing there is they only ask for what they need -- that's called a "minimum necessary standard" under HIPAA -- and they only use that information for an analyzing the drug safety event, and that data is never used for any other purpose. So the policies that have been adopted for Mini-Sentinel, even when individual information is required to do the analysis, are very respectful of the patient privacy.

From a legal compliance perspective, HIPAA is the primary source of what we look at when analyzing the use of protected health information. And HIPAA permits the use and disclosure of health information, even individually identifiable information, for public health activities and to a public health authority. FDA itself, obviously, is a public health authority, but public health authorities can also include others that are contracted with the FDA to do an analysis for the FDA. So the operation center for Mini-Sentinel as well as the subcontractors that contract with the operation center are all treated as public health authorities for HIPAA compliance purposes.

As Richard mentioned, these activities are public health activities, public health practice and not research, so the approval by an institutional review board is not necessary which is important for making sure that this analysis is a streamlined process

when you're thinking about all the different data sources that we'll need to touch as Sentinel gets off the ground and develops further.

Now, there are a couple of other sources of law that data sources always have to think about when participating in any of the public health activities or research. One of them is what are called the Part 2 Regulations, which are the federal substance abuse treatment regulations. It's unlikely that these will be affected by Sentinel because that sort of regulation just protects information that identifies someone as a substance abuser, and because only data is presented in summary format that is not individually identifiable, it's very unlikely that those regulations will be triggered.

State confidentiality laws also play a part. There's a plethora of laws out there that data sources have to deal with, so each one will have to analyze their own state laws to make sure that there's no additional barriers to participating in the Sentinel Initiative and the Mini-Sentinel: things like genetic testing laws, mental health laws, communicable disease and HIV protection laws. But most state laws -- and this is just a general statement -- but permit disclosure of health information for public health activities. Most state legislatures realize that there's very important public purposes in addition to protection of patient privacy. So in large part, state laws will not be barrier to others or to the data sources participating in Sentinel I either.

But going beyond legal compliance, I had mentioned that Sentinel and the Mini-Sentinel project has adopted policies that reflect fair information practices which go beyond what the basic baseline is required, by HIPAA for instance: things like ensuring data integrity and quality, collection and use limitation. So data is only collected for a particular purpose and only that amount of information necessary for the purposes collected.

And the consumer participation, openness and transparency, the FDA has been fabulous at making this process very transparent to the public and to consumer and to involving them in the decisions about how health information is appropriately used. Security safeguards and controls and accountability and oversight are essential.

Now, here's just kind of a quick recap of what those Mini-Sentinel privacy policies reflect: The keys here are that consumers and patients are not identified in any information sent to the operation center or the FDA. So again the individually identifiable information stays at the data source.

Second, any information collected for Sentinel purposes, whether it's identifiable or not, is only used for Sentinel purposes, so it is that collection and use limitation principle that is so essential to fair information practices.

And, finally, the information is secure. Those are really the bedrock principles that are reflected throughout the policies for the Mini-Sentinel project.

So as a privacy attorney looking at how this has been structured, I think the public should be absolutely assured that the FDA and the Mini-Sentinel contractors are committed to making sure that the system is structured and the policies are pursued in a way that really respects individual privacy and really makes respectful use of the health information that is so important to make this project work.

Now, thank you very much. I look forward to your questions in a moment. (Applause)

MR. FIREMAN: Well, good morning, everybody. This is going to be an overview of our plans for surveillance of acute myocardial infarction in users of anti-diabetes drugs. These plans have come out of a very collaborative and deliberative process that's had lots of input from a large number of researchers at the data partners,

at academic institutions, at FDA. And it's been an enjoyable process, but a careful and deliberative one. The write-up of our protocol and our deliberations is available on the website that Rich mentioned, and I invite you all to get more than this over, you know, more details there, the write-up that was led by Joe Selby, a diabetes researcher at Kaiser Permanente.

Our aims are to develop and assess a framework and infrastructure for monitoring drug safety in large populations using, as you've heard over and over again, distributed databases. And for this pilot effort we're going to be monitoring acute myocardial infarction in users of anti-diabetes drugs and, more specifically, we're examining the association of heart attack risk with saxagliptin, a recently-approved DPP-4 inhibitor used for treatment of diabetes.

And as Rachel mentioned earlier, a big advantage of looking at high-tech risk in saxagliptin users is that there's going to be a randomized trial, and as we're -- of CVD risk in saxagliptin users, and so as we're developing and testing and evaluating our methods and our data and our infrastructure, hopefully we'll have results from this trial to compare with.

We have a big population with type 2 diabetes that we're going to be examining. We're focusing on adults who have had a diabetes diagnosis and an oral anti-diabetes drug during a 12-month baseline period. That's who we're going to be doing surveillance on to see whether they meet our entry criteria. They have to have been member for 12 continuous months in a health plan associated with one of our data partners.

There is going to be very few exclusions from our study population. This is a broad population-based study. We will be excluding patients with type 1 diabetes

and excluding patients under 18 and patients who have been taking only insulin because they're likely to have type 1 diabetes. And we're also excluding people who have had a recent heart attack within 30 days of starting one of our study drugs because their risk of an adverse event is extremely high and very hard to quantify and adjust for as we're making comparisons across our study drugs.

The study period we'll be looking -- we'll be doing active surveillance on goes from July in 2009 when saxagliptin was licensed through June of 2013. We'll be looking at baseline data going back further, though, you know, for adjusting our comparisons we'll be going back a few years. And all of our data partners, as you saw earlier, have data that permit that.

In our study population now are 1.3 million patients with type 2 diabetes, and over this study period we'll be accumulating 5.2 million person-years that we're going to be monitoring for AMI. And given our baseline rate of about nine heart attacks per thousand person-years of follow-up, we expect about 47,000 heart attacks in this study period during this period of active surveillance.

So we're going to focus on a comparison of new users of saxagliptin with new users of -- for comparative drugs. And these are the comparators: saxagliptin, pioglitazone, sufonylurea, and long-acting insulin. Follow-up is going to begin at the first prescription for one of these study drugs and end when the user quits or switches drugs or leaves the health plan.

I want to -- this new-user cohort design has a lot of strengths because the baseline period and starting follow-up at new use permits the comparisons to be balanced and adjusted for possible differences between the users of the different study drugs with respective possible confounders. By restricting to the new users it means that

we're not going to be making inference on the drug, heart attach association either from prevalent users of these study drugs, or from within person on/off changes. People go on and off and switch drugs, and we'll be investigating some of these methods in other settings but not in this, in these plans that I'm discussing here. And that's because we feel we can address possible biases from unmeasured confounders and from measured confounders better in, when with a new user design.

Our primary outcome, as I mentioned, is heart attack. It's a good place for us to be starting because this is a very important event that's of great interest to the public and is well identified in our databases with numerous studies, at Kaiser Permanente and elsewhere, have shown very high positive, predictive value for heart attacks identified by these means and these databases.

Our secondary outcome is the broader classification of acute coronary syndrome. I want to mention that we have two main measures of our outcome which we'll be following over time, and by "time," I mean time on study drug as well as calendar time. And they are the relative risk and risk difference that might be associated with one study drug versus the other. One's a little more tractable and, in many of our statistical models, the -- and more reliably measured -- the relative risk; the other is important for weighing the harms and benefits, and they're closely related.

We're going to be adjusting for a number of possible confounders including prior cardiovascular disease, comorbid conditions, patient demographics, other drugs that patients are using, the history of patterns of use of health services. And we're going to pay very careful attention to adjustment for differences in our practice settings and data, data management for in code -- possible coding differences by looking carefully at differences by site and health plan, and also differences over time. That's time-over on

drug as well as calendar time.

We're going to be considering several adjustment strategies in methods. As I mentioned before, we're going to be restricting our comparisons to new users. We're going to be stratifying carefully for prior cardiovascular disease. We're also going to be stratifying by site, and we're going to be adjusting by covariant adjustment for these other factors that I outline above.

We're going to be testing and evaluating and using gaining experience with several alternative methods of adjusting for these possible confounders, and which we're adapting to this distributed data environment that you've heard a lot about today because we're not dumping and pooling all of the data together. So we're going to be looking at the propensity scores and disease risk scores and weighing some of their advantages. Both of these we've developed some methods for using them in the pool of data with making -- there's a number of advantages and disadvantages which I see here.

Since I only have a minute, you all can -- we can -- of each of these which I could talk about later -- I want to emphasize that this is sequential surveillance. It's ongoing. We're going to be looking -- our first analysis is planned in a couple of months, and that will include all of the experience in this, and our data partners that's been accumulating since the licensure of saxagliptin. We plan nine coordinated analyses of the accumulating data with the final analysis in June of 2013. We're going to be using sequential statistics that are adjusted for multiple looks. Each look is going to include all of the data, but we're going to be paying careful attention to the multiplicity issue.

I want to say that -- a few remarks about the size of the relative risk that we're going to be able to detect or rule out. And assuming that we accumulate 23,000 person years in saxagliptin users and a similar amount in matched users of a comparator,

and expecting about 9 heart attacks per 1,000 person years, then we're going to have about 80 percent power to detect a relative risk of 1.3, which is quite as bit of power.

And I have signals don't arise the confidence intervals that we're going to be estimating will be informative about the size of the relative risk and risk difference that can be ruled out, and the amount of reassurance that's appropriate, given that we've been looking and haven't seen anything.

And this surveillance is designed to be worthwhile even if saxagliptin isn't used much because comparisons of heart attack risk in the users of any diabetes drugs can yield worthwhile reassurance or safety signals and lessons about statistical methods, and evidence about the value of Sentinel's data and infrastructure regardless of saxagliptin uptake.

And so in summary, this overview is just let me know that Mini-Sentinel has developed plans to examine heart attack risk in saxagliptin users versus users of four comparator drugs. We're going to be assessing the feasibility and value of heart attack surveillance in users of anti-diabetes drugs using the distributed databases, and we're going to be evaluating methods for monitoring drug safety in these large dynamic populations.

Thanks very much. (Applause)

DR. McCLELLAN: Thanks very much for all of the presentations.

I want you to hold your questions, or rather use the next few minutes to think of some really tough questions for all of the panelists.

We're going to take a short break now. I'd like to keep it to about 10 minutes or so to just stretch your legs and so forth. And we are going to be breaking for lunch after this panel discussion. Then we're going to reconvene in here with these four

panelists plus our FDA leaders to discuss Mini-Sentinel.

One other thing for those of you who are in the overflow room, there are some additional seats in this room, and we will definitely try to make room for you if you'd rather sit over here. So see you all in about 10 minutes.

(Recess)

DR. McCLELLAN: Everyone please head back to seats so we can get started.

All right, we're about ready to start. I know this was a short break. We do have lunch coming up soon, but I wanted to make sure we had plenty of time for discussion. Now, you all have gotten a lot of information this morning on all of the progress and the Mini-Sentinel Initiative and how it fits into the larger strategic goals and implementation framework that FDA is trying to implement. So, all of that on the table now for discussion.

Before opening up to comments I just wanted to check with Rachel Behrman to see if she had any additional perspectives or comments after hearing from the Mini-Sentinel presentations, anything else to add or clarify.

DR. BEHRMAN: I guess two points. Should I speak to the diagram in question or --

DR. McCLELLAN: Go ahead and talk about --

DR. BEHRMAN: Apparently there was some concern expressed of whether diagrammatically -- and we have struggled mightily with diagrams over the years -- whether diagrammatically it's just the FDA has direct access to patient medical data, which we do not -- that's point one -- at least through Mini-Sentinel. I'll keep on our attorney, who's here, who has been instrumental in helping us articulate this clearly under

a public (inaudible) authority, sometimes we do have to go out and seek patient-level information. But that's no different than what we do now.

I thought that the overview this morning was a pretty excellent demonstration of again what has been accomplished. And to paraphrase something Rich wrote about a year ago that we we've turned, and again through this collaboration, through hard work and a lot of careful thinking, we've turned, quote -- or paraphrasing, a few words in the FDA Amendments Act into a vibrant, productive program that's actually producing information. I think to do so in a short period of time really speaks to the commitment of everyone involved, and on behalf of the agency I'd like again -- once again, just like to thank everyone for that commitment.

DR. McCLELLAN: Thank you. Let me remind people that there are microphones in the back of the room. It would be great if you have a question that you could go there to ask, and I want to -- and get -- encourage anyone who's sitting in the overflow room to participate as well. So, please feel free to start with the questions right now.

DR. RACOOSIN: Mark, could --

DR. McCLELLAN: Yes --

DR. RACOOSIN: Could I just --

DR. McCLELLAN: Judy, you had a clarification first. Go right ahead.

DR. RACOOSIN: I just wanted to respond to the -- one of the presentations this morning.

You heard about the detailed plans for the evaluation of saxagliptin and kudamie and the comparison to the other diabetes drugs. I think a tremendous amount of work went into planning that protocol, and I think it raises one of the issues that we'll

be continuing to grapple with, which is how do we scale up, if you will, because there are many questions that we have. You know, with every newly approved medical product, there are safety questions that we're going to want to evaluate, as well as questions that crop up, you know, periodically during the marketing of a product. And so I think that's something that we will be focused a lot on in the coming year -- is to think about, you know, from what we've gone through with that first process of planning a protocol for an active surveillance evaluation: How can we streamline the process for developing additional protocols as we want to expand, you know, to look at more questions.

The modular programs that Lesley mentioned at the end of her presentation are going to be key, because they are programs that are ready to fit in the various bits of information that we need to -- that would help us to narrow it to the specific question, and I think the process we're going to be thinking about is, you know, how to go from the modular programs to the more complex analyses, making sure that we have -- get useful and actionable information out of those evaluations.

DR. McCLELLAN: Okay, Rachel?

DR. BEHRMAN: And just to expand on that, in addition to being able to be scalable and timely and nimble and respond to urgencies and emergencies, this also speaks to the strength, the fact that this was not developed in isolation but we really took advantage of all available national expertise.

One piece we alluded to this morning and haven't explicitly said, so I'll put it on the table, is how to better, more effectively involve regulated industry in those discussions. But they're obviously a key stakeholder, and there are some complexities involved, and the governing system certainly at the moment fully -- as it is fully financed or -- so financed -- the level its financed by the Food and Drug Administration raises

some questions about how we are going to incorporate, if you will, industry studies. But I think as part of the national research, that's something we're going to have to grapple with and solve.

DR. McCLELLAN: Mm-hmm, and that's a good topic for further discussion. I wonder if any of the panelists had any further comments that they'd like to make, again kind of sticking with the topic of the saxagliptin protocol -- how that was developed, kind of lessons or implications for doing this in future applications of the Mini-Sentinel or the Sentinel system?

MR. FIREMAN: Well, it was an enjoyable collaborative, deliberative process, and so we had -- my input from a lot of top people -- as I said, I think the issue that was raised about choosing comparators was an interesting one. We wanted to be able to make inference about what would have happened to saxagliptin users had they been taking something else. But there are a lot of alternatives that are out there in clinical practice. And we think that something can be learned from each of them, so we -- after a lot of deliberation, we started out with a couple of comparisons. We expanded to four. And we think -- the reasoning and deliberation that went into that I think was helpful, and our deliberations are, as I said, are, you know, summarized in a useful document that's available on the website that Rich put up there.

All of the issues in terms of validating the data, adjustment for confounders, doing appropriate statistics as we look at accumulating data over time during the surveillance period, interpreting the data and not just when we're detecting signals but how much reassurance is appropriate when we don't detect signals, how much reassurance can be derived from the statements about how big of a signal we want to notice; and, you know, had there been something out there. So, I think we put a lot of

thought into it but there's a lot more left to learn.

DR. PLATT: So, I take -- there are two ways Mini-Sentinel will make progress. One is by taking what we've learned directly from the development of this protocol and applying it to other questions of interest to FDA. So, given the investment, it's well over a thousand hours of thoughtful clinician/epidemiologist/data partner time. It will take a lot less work to build the next protocol that looks for myocardial infarction in relation to any other therapeutic agent. And similarly, we've thought through a lot of the issues around studying the outcomes of diabetes therapy. So, if you ask where would the quick winds be next in terms of scaling up, it would be to start to expend what this process has learned to those kinds of settings, and there may be important ones for FDA to consider, whereas it'll be a lot of sitting around the table and thinking again when FDA has an interest in studying pancreatitis as an outcome or acute liver injury, because those will all take a similar kind of convening of FDA experts and clinicians and epidemiologists with data experts. So, some of this can go fast, and some of it will be a hard slog.

DR. McCLELLAN: Thanks. Further questions?

MR. MINES: Yes, thanks. I'm Dan Mines from HealthCore in Wilmington, Delaware. Thanks for a really nice presentation.

My question has to do with the saxagliptin study, and I'm trying to place it in terms of the categories I had in mind in terms of evaluating drug safety questions. Traditionally we think about signal detection, maybe signal strengthening studies, and then full-blown hypothesis testing studies. As I heard this study described, it sounds to me a lot like a full-blown pharmaco(epi) prospective cohort study with preplanned interim analyses. Is this what we mean by active surveillance?

DR. PLATT: I'd say the boundary between sort of signal refinement and

full-blown epi studies is a fuzzy one. But our take is that we're in an environment where FDA has reason to want us to evaluate a specific outcome of an exposure, and that takes us from signal discovery into the refinement area, and we're specifically not developing this as a full-blown epi study. To the extent that we can build into the refinement process activities that ordinarily have been characteristics of studies that are assessing causal relationships, we see that as a good thing. But this is really at its heart a signal refinement activity.

DR. BEHRMAN: Can I address a point as well? That, in a sense, doesn't matter so much to the agency what you're asking. In other words, we're trying to learn how to develop Sentinel, and any activity we do will teach us a lot about governance, communication, processes and procedures, (inaudible) development, and so forth. So, on one level, the question itself and where it fits in the paradigm, which I personally leave to the continuum, is less important this early in the game than the lessons that we've learned, and we learned a lot of lessons. Those of you who were at the Brookings roundtable where we talked about this -- where we said, ooh, look; we forgot to post this before it was mentioned publicly. That's an important lesson for us to learn, because, in retrospect, we want it posted and make sure that that the division in the company was aware. We were still trying to scramble and figure out who the sponsor was. So, we -- the little lessons and big lessons we learned. So, where it fits in the spectrum this early in the game is not that troubling to us.

DR. RACOOSIN: I think we are grappling with that question, though, and so by doing this and going through the process -- because we have had an expert panel on signal refinement, and one of the questions is well, where does that end and how can we produce actionable information in an efficient way. And so -- but we need a

place to start, and so we have a very, you know, productive process in developing this first protocol, and I think it -- you know, as Rachel said, you know, the lessons learned is a big part of this. So, now that we have -- is how can we think about adapting it for other products that we're interested in assessing MI for and adapting the methodologies that have been developed for it and evaluating the propensity score matching, the disease risk score stratification, and thinking about how these can be combined in future evaluations now that we've done the heavy lifting of creating it for this protocol. So, I think it's a key question as to how we can adapt these in the future, but we have a very, you know, well-developed protocol to start from as we move in the directions that we need to.

MR. MINES: Thanks.

DR. McCLELLAN: Thank you.

MR. HARE: Hi, there. I'm Jonathan Hare from Brazilian Network Systems.

First of all, I'd like to applaud the work you've done with Mini-Sentinel. It's seems a really appropriate and pragmatic way to get started. I do -- I would observe that there seems to be in the design of it some tension. It reflects some tension between the patient safety objectives and the need to preserve privacy and also respect the concerns of the various data partners. For example, the fact that data is analyzed at source and only the identified records are sort of aggregated. You lose the ability to get sort of the full longitudinal record from disparate sources for the same patient -- things like, for example, you actually want to know if they have behavioral health issues. If they're on -- you know, abusing drugs or alcohol in combination with certain drugs and other risk factors, you actually want to know that. You lose the ability to confirm

suspected results. You get, you a hundred million patient lives out there, you're going to detect all sorts of apparent risk factors, many of them real, many of them false. So, you lose ability to confirm from the patient or from the treating physician what are real events, and also you lose ability to give sort of personalized assistant support to the patient and to the clinicians, like, you know what should this patient be worried about.

So, I have really two questions. One is: Is my sort of assumption accurate that the design was, you know, sort of a concession to the constraints of available technologies to preserve, you know, basically deal with those different competing issues? And, second, when you go beyond Mini-Sentinel, do you see -- do you anticipate efforts to resolve the underlying tension? You know, how do you connect dots without filing 5(c)? How do you respect the rights of the data holders which we rely upon? And how do you sort of close the loop with the patient and caregivers so we really get the result we're all looking for, which is improve patient safety on a national scale?

DR. PLATT: I'd say our take all along has been that the principal needs have been to develop acceptable governance structures for what we're doing. The technical issues are not small, but they are small compared to getting to sort of a shared space where all parties can be fairly comfortable. In this coming year, we're going to be starting to test methods for doing linkage across data sources so that we can start to construct longitudinal records when we need to do that. And for that, as well, our take is that the technology will be important but the part that's going to take the most time and need the most care will be establishing rules that everyone is comfortable with and that we can post on our website and have all of us whose data will be linked across sources be satisfied with as well.

DR. McCLELLAN: Can you, I'm wondering, maybe clarify that --

Jonathan also brought up this confirmation question, so do you see something in the data? What about -- what capacity's in place to go back and verify the clinical accuracy of those administrative data or other findings?

DR. PLATT: All the data partners have access to full-source data when it's necessary. Kristin just described some of the issues about the -- sort of the legal underpinnings of that. One of the great strengths of this overall framework is the ability to use coded electronic data to do the really heavy lifting, be able to understand almost everything you need to know about millions of people and then to review the actual records a few hundred people when that's necessary. That's largely a manual process these days -- by and large the target is hospitalization records, and those -- almost none of those are available in electronic form, so that's -- that becomes a slow process. But it's one that everyone of our data partners has a substantial amount of experience.

DR. McCLELLAN: So, for example, in the saxagliptin site that you were talking about for patients that are suspected of having -- or that appear in the electronic data have MIs, there will be some kind of confirmatory process.

DR. PLATT: Actually, the plan is no, is that right, Bruce?

MR. FIREMAN: Well, there -- one of the advantages of starting with MIs is, unlike some other outcomes that we could have started with, there's already been a lot of work and a lot of study in our data partners, some of which I've been involved with at Kaiser Permanente validating the positive predictive value of the hospital discharge diagnosis of a MI, and so our choice of codes and criteria for including heart attacks, you know, has been based on that work.

But I will also say that in responding to the question that building infrastructure is gaining -- you know, we'll be gaining a lot of experience with this back

and forth process with the distributed data so that we'll be able to use the richness of the data that's available at each of the data partners, and it's going to get richer as we get -- more and more people have EMRs -- electronic medical records -- and keep the information local, keep privacy respected, but extract all the information that's useful for inference about the safety of the medical products. And so that we'll be going back and forth and there will be -- our analyses are stratified typically by site and health plan so that if there are coding and diagnostic and practice differences across these sites and we see an unusual number of them coming from one place, we can go back to that site and say hey, what's going on here during this six-month period when we see an unusual number of events and can go back and forth with people who are familiar with the courts and limitations of their own database and their own setting and do some of the validation that you're envisioning.

DR. PLATT: Having said that, FDA's taken a belt-and-suspenders approach. Although the data are fairly compelling that the codes for acute myocardial infarction actually represent acute myocardial infarctions, they also asked us to pull a hundred records and have them adjudicated by an expert panel, and we're about 80 records into that hundred-record validation. So, we'll have separate information telling us what the conformance characteristics of these codes are in the Mini-Sentinel distributed database.

DR. RACOOSIN: And I think a second goal of that project is to establish that process within each of the data partners so that when we in the future want to validate a particular outcome we already have procedures in place that have been tested so that we can efficiently get to those charts and validate them.

MS. ROSATI: I think one of the other important point to pick up on there

that he had mentioned is that by using a distributed data network, we were using summary aggregated data. It's difficult to communicate with the patients about the outcomes. Well, I think one of the intents here is to make sure that that communication process with physicians and patients is a controlled one so that preliminary data is not communicated, because it can cause false alarms that alarm the public and potentially cause them to get off drugs that would be very important and beneficial to their health. And so the fact that the communication and decision about the drugs is removed from the data partners I think is probably over the long term a very good policy decision.

DR. McCLELLAN: Thank you.

MS. JONES; Judith Jones, The Degge Group and long time ago FDA Safety.

I first wanted just to congratulate the effort. It's very exciting to see this come in to fruition, and I'm a perpetual optimist, so I think this will work and be demonstrated.

And so the question I have is looking to the future. FDA at any point in time may have 50, 100, or more signals that they could evaluate realistically in this data. Is there going to be, on the short term, any priority for perhaps the 20 that have been validated and then, a longer term, any notion about how this will be utilized and what the priorities will be? Will it be public health populations, severity, or what? It's a hypothetical question, but it would be interesting --

DR. BEHRMAN: I guess that's mine. Each center is -- this is a resource that's going to be available to each medical product center, and each center will -- setting in place, processes to tee up the priority list. We already have that problem. Again Sentinel is another -- already a new tool to help address the issues. We have -- always

have, I guess always will, if you will, more work than we can handle and resources that are always an issue. So, the notion of how to prioritize is based on many of the factors you mentioned. We've written guidance, for example, in the warnings/precautions guidance when we talk about how to prioritize what's put in labeling. We go through basically those elements, and we talk a lot about the impact on the population, and that has to do with severity, size of population, and I believe impact. So, all those will fix into our thinking.

Judy, you want to answer that?

DR. RACOOSIN: No, I just want to emphasize that the -- you know, as Rachel said, the use of an act of surveillance evaluation is one more tool to help us better understand what the particular safety issue is. And each of the centers already has in place procedures for identifying and prioritizing safety issues, and so, you know, this is an additional tool that's being incorporated into those procedures. And so it's really on a center-by-center basis by which they are determining how they want to enhance their surveillance capabilities with this tool.

I want to go to the side microphone over here. I'm trying to keep all these in order, but -- I'm doing my best.

MS. PENDERGAST: I, too, would like to congratulate on the progress that you have made.

I have a question.

DR. McCLELLAN: I'm sorry; can you identify who you are?

MS. PENDERGAST: I'm sorry. Mary Pendergast. I'm a lawyer in private practice.

My question goes to the results of this study whenever they occur.

Unless all the drugs have the exact same risk of MI, there's going to be some stratification among the drugs. Do you know now what you're going to say depending on what those risks are? I mean, is the answer going to be drug A has a higher relative risk than drug B? Or is -- how are you going to describe what you find?

And the my second question is if this is technically signal refinement -- you're saying we see a signal of a higher risk of MI with X drug -- do you know now and can you tell industry now what their next step is to resolve the question of whether or not it's a true or a false signal?

DR. BEHRMAN: I think that's mine. We are a data-driven agency, so we will look at the data and make the necessary regulatory decisions and then take the necessary regulatory action. And as an ex-FDA are you -- I think you know that, so if the data are sufficiently compelling that we believe that we need to change labeling, we will do so and will do so for the products that need their labeling change. If the data are compelling and we believe there's a class effect, we will initiate class labeling changes. It all depends on the data. And as Judy has emphasized a number of times, a Sentinel finding is one piece of the puzzle and it will be evaluated in the context -- by the way, by the medical practice center and the appropriate review division, not by the core Sentinel team that's responsible for organizing the initiative. We're not responsible for the review of the data. These data will be handled just the way we handle any other data. It's another piece of the puzzle.

MR. KRALL: Ron Krall from Penn Center for Bioethics and also a member of the OMOP Executive Board.

I have a question about the saxagliptin study, which really stems from the results from OMOP that we saw yesterday. I think it was striking to many of us that

the estimates of relative risk that we saw yesterday could vary tremendously based on the design choices that are made for the settings for different analytical methods that are applied to these kinds of analyses. To what extent do you --

DR. McCLELLAN: Excuse me, Ron, can you, just for benefit of the audience that wasn't here yesterday, maybe expand on that a little bit on what you mean when you say the differences in methods and implications for differences in relative risk?

MR. KRALL: It would probably be good if one of the principal investigators actually did that, but I'll summarize it briefly. What OMOP has done is carry out a set of experiments using drug health outcome of interest pairs and systematically explore the effect of studying the associations between the drug and health outcome pairs in different data sources using a variety of analytical methods and in those analytical methods a series of choices about how those methods are actually implemented. And the kind of bottom line of those results -- and I invite all -- certainly Judy to comment on that -- is that there's a lot of different -- you got a lot of different results based on the choices you make. And the question -- so that's -- that was kind of my takeaway from yesterday.

And the question I wanted to ask you is to what extent do you plan to explore the effect of the choices that you'd make in both design and in implementation of methods of analysis in the study of acute MI and the four oral hypoglycemic drugs?

DR. RACOOSIN: So, just to clarify one thing about Ron's description of OMOP experiment. The drug outcome pairs that were selected are known associations based on the medical literature, and so by testing the methods and the range of parameter settings on each of the methods on these known associations, there's a capability of measuring whether the method actually hits the mark. So, I think given the

results of the OMOP work, we are going to need to think about how to apply those lessons learned to the act of surveillance evaluations moving forward. I think we are very close to having just learned a lot more about the results of the experiment, and so as we move forward we'll need to consider how recognizing -- how all of those choices are made in the analysis, how those potentially impact what the results will be, and to think about how we can do that in an efficient way but recognizing the importance of questioning those choices and the ultimate -- how the ultimate result comes out.

MS. ANDREWS: Hi. Elizabeth Andrews from Research Triangle Institute, also a member of the Scientific Advisory Committee for OMOP.

I, too, am just floored by the progress that's been made, and partly because of the observations that were just discussed, I'm really delighted to see that this first example is learning from the lessons of many years of structured epidemiologic study, so I'm glad things are looking more like studies than they might have otherwise.

My question is about the governance structure that you put into place in which the decision has been to consider this not to be research but active surveillance. And you have the advantage of not going through the IRB review and approval process at each site, which can be -- while it can be very effective and necessary for human subject's research can also stand in the way of getting early results to pressing public health questions. So, I applaud you for doing that and I'm wondering how that lesson can be implemented for studies that are not directed by a public health agency. So, as I understand it, the Sentinel Initiative has been granted a unique status as a public health activity. Can that be done for studies that are sponsored by other organizations?

DR. BEHRMAN: I guess -- is that mine?

MS. ROSATI: And I'll follow after you.

DR. BEHRMAN: Okay. I don't think we've been granted -- we haven't been granted special status. We are a public health authority doing our job, and it's not research and we just had discussions at the OHRP and they confirmed that. I think there's, as we all know, a national discussion going on about what is research and what is not research and that this -- the notion that one creates general, logical knowledge, therefore it's research, seems to me counterproductive. But you've asked a very important. As we start to think increasingly about a national resource and other activities and who is conducting those activities and what questions they're trying to answer, it becomes very complex. If the Saxa study had been conducted by the drug manufacturer, would the positive procedures have been different? If we found a way to incorporate the manufacturer into Sentinel such that because -- and it was a post-marketing commitment we were directing, does that change its status. And now I will turn to the attorney.

MS. ROSATI: Picking up from what you were saying, you know, the distinction between public health surveillance activities and research is a very thin one, and there's lots of activity going on across the country to figure out exactly what that distinction is. OHRP, my understanding is, working with the CDC quite carefully to develop guidance for us on what that distinction is, which should be helpful. But, clearly, the kind of private industry to, you know, non-federal agency directive activities need some guidance out there, and we're just really crying out for that, because as you point out involving local institutional review boards is not a very -- it's a pretty unwieldy way to do the same type of research across the country, and we either need to provide really specific guidance for IRBs so that they review the study the same way, because if you variate across sites you can end up with a study that has less validity at the end. While we need to create a national institutional review board perhaps to review these big data

studies because local IRBs are not very well -- are not usually trained adequately to judge big data research. They're usually clinically trained, do a very good job at thinking about patient rights and interventional studies but often don't know much about the issues related to the big data research. So, that's -- you've really hit your -- hit the nail on the head in terms of what we need to do next.

MS. ANDREWS: Right, thank you very much. I hope that does stay high on the agenda for the next year or so.

DR. DeCHERNEY: I'm Steve DeCherney. I'm a professor of endocrinology and diabetes at the University of North Carolina in Chapel Hill, and so I had a methodological question about your study.

While it's clear that a very low blood sugar reaction can precipitate an MI -- no question -- there's also a fair amount of literature that suggests that the coefficient of variation around ambient glucose levels also contributes to the complications of diabetes, including the acute events. And I just wondered methodically how you take into account a drug that may actually cause less fluctuation, which actually may make it a safer drug than one that causes an acute drop in blood sugar.

MR. FIREMAN: Okay. Well, we will notice if this -- if one or another of our study drugs is safer, and so if the risk is lower after adjustment for whatever we can adjust for, for the co-morbidity and other covariate information that I outlined there. Now, lab values and other detailed clinical information we may be able to incorporate eventually down the road in Sentinel. But right now clinical lab values would have to be part of some kind of follow-up study. But were you asking can we notice, with our design, benefit as well as harm? Was that your --

DR. DeCHERNEY: No. I'm assuming you have access to hemoglobin

A1C data, but what you may not have are ongoing glucose logs or downloads from meters or those sort of things. I just wondered how you were going to take into account -- I mean, a very simple case is a patient who has a hemoglobin A1C of 9 who suddenly has an MI. Is that a different case related to a drug? Is that a different case than somebody who had a hemoglobin A1C of 6-1/2 and has an MI if you didn't know what those fluctuations were prior to the event?

DR. PLATT: That's really beyond the scope of this protocol. This is -- this protocol doesn't attend to mechanisms to explain the observed results, and that would be a good example of the kind of follow-up full-scale epidemiologic study that would be needed in the event that there was some difference between saxagliptin and one of the comparators.

DR. McCLELLAN: Is that something that's contemplated being handled in Sentinel-type framework at some point? You all have emphasized the dynamic nature of the data that are available. If, you know, additional -- you know, you could see at some point in the future, and I expect some of the Sentinel data holders right now have lab results over time and maybe even if they've got full electron record systems, the logs of glucose readings for patients and it seems like the potential is there. I don't know --

DR. CURTIS: Certainly.

MS. ROSATI: Yeah.

DR. CURTIS: Yeah, and over the next year, we're actually working now to sort of expand the common data model to include selected clinical laboratory data and vital signs from some of the data partners. As you can imagine, if it takes several months to create a common data model that is robust and a robust distributed database of administrative and claims data, it's a mountain to go up the clinical data, into the clinical

data realm. I think we're doing this in a way that makes sense. We're beginning with sort of -- in a manageable fashion. But when you start talking about bogs, things that are measured repeatedly over time, and then think about how to put that into some sort of distributed data environment, eyes get glassy quickly. So, I think there's a lot of important work to do. We're starting on that, and we'll look to continue in that direction.

MR. FIREMAN: So, since Lesley's responsible for it, she's been appropriately cautious. So I'll have to say that we've made a commitment to FDA to have consolidated hemoglobins and certain other lab test results available for use by this time next year from part of the population. So, we should be able to do a deeper dive using those kinds of data.

DR. McCLELLAN: Well, in taking it to the different version of Rachel's point earlier that this is a piece of all the evidence that's being developed (inaudible) involved, it might be difficult both from a data availability standpoint and another standpoint to have lots of sites doing these kinds of particular detailed clinical studies. You know, one does wonder whether having a network like this makes it easier to do complimentary studies or extension studies. You know, maybe you're not going to do this kind of glucose log analysis on particular drugs at every site, but if you really want to investigate further against more insights as to why you're seeing certain bottom-line patterns in terms of safety risk for particular drugs in the overall network, it seems like it might be something that could be a extension piece for certain sites or part of a more complimentary research or, you know, underline the causal -- analysis of the underlying causal mechanisms.

DR. RACOOSIN: I think one that is -- the way things are structured right now is that these active surveillance evaluations are part of the Mini-Sentinel and/or other

active surveillance pilots, but as things are structured right now at FDA, each of the centers has contracts with various databases for conducting formal studies. And so right now the way things are structured, something like that would move into the center who has the question to develop and -- not to say that there isn't much overlap between the Mini-Sentinel data partners and each of the databases that the centers have contracts with, but just logistically it's not currently part of what we're envisioning as part of Sentinel.

MR. FIREMAN: While I share that vision and also note your caution, I just want to say that we do have clinical experts working with us at the different sites -- endocrinologists and diabetes experts -- and so we'll be thinking through ways in which bias might arise from some of these sources, and the main issue here is are the people who are becoming new users of one or another of our study drugs likely to be different in some unmeasured way related to some of the clinical measurements that we don't have access to. So, we'll be thinking about that and cautious about the limitations of our work, you know, as these considerations may arise, and hopefully in the future we'll have more data to address them directly.

DR. LIPKIN: Yes. I'm Paul Lipkin. I'm a pediatrician with a special interest in special populations, and I'm a health policy fellow with the Robert Wood Johnson Foundation.

When this clearly very rich database with tons of important information that could be gleaned from it -- however, when I look at the population distribution curve, my eyes focused to the left, which is young children, but at the same time to the most elderly, and the numbers of people represented in your samples at this point are really quite thin at either ends of the age curve. Question in my mind therefore is do you think

the Sentinel Initiative will be able to adequately look at these special populations, particularly because they are often the most vulnerable medically?

DR. CURTIS: I can take that and then add to it. I mean, ultimately, yes, the goal is to have a robust system that serves the entire population of this country. That said, we have to start small, start with what's easiest, if you will, and cheapest to get and then learn how to do it well and expand carefully. One reason we've made as much progress as we have is we've been very careful and judicious and have with a laser-sharp focus. So, the answer is absolutely yes. How quickly will depend on resources and the availability of the data. I was thinking back to one of the questions that was asked in terms of looking at information longitudinally, and if only the current state of data standardization was such that we were limited by our governance and our ability and our resources -- in fact, we all know that the state of data out there is not what it should be and the populations you're talking about are often either underserved or hard to get hold of. So, that is the intent. We will get there. How quickly we'll get there is a question that's extremely hard to answer.

DR. McCLELLAN: Well, now, one piece of --

DR. RACOOSIN: Can I just answer that?

DR. McCLELLAN: Go ahead.

DR. RACOOSIN: Is that we do have our federal partners collaboration, which includes Medicare, Medicaid, populations, as well as the VA and the Department of Defense, and so we have been able to -- you know, the data that Leslie presented is -- you know, the groups captured within the Mini-Sentinel population, but in addition to that in our federal partners collaboration, we are accessing, you know, many older people in this country as well as within the Medicaid population we can access younger people who

are in the lower economics population.

DR. McCLELLAN: So, that was -- my follow-up question was, I mean, look, you're not going to be able to get to a representative sample in filling out the vulnerable populations, either higher age ranges or the lower ranges, without including federal program beneficiaries of Medicare and Medicaid, and since there are so many activities ongoing now with the FDA's Federal Partners Program, it may be worth spending another minute on that. And then my question was how does that -- how does the analysis that's going on in that work match up with the analysis that's envisioned with the Mini-Sentinel and further Sentinel efforts that are relying on private sector partners?

DR. CURTIS: Right. So with our federal partners, there's really -- prior to the Federal Partners Collaboration, there was established the Safe RX Project, which is a project between FDA and CMS that was launched shortly after the Medicare Part D data became available for research purposes. And so through that Safe RX Project, within FDA across the medical product centers there are a number of projects going on involving Medicare and Medicaid populations that are both formal, pharmaco(epi) types of projects as well as active surveillance-oriented projects. So, that is ongoing.

And then around a year and a half ago we launched the Federal Partners Collaboration, which brought in, in addition to the Medicare and Medicaid populations, the VA and DoD. And so we have been able to look at some questions that have arisen that are of interest of the three organizations, and as we get -- and some of this work has been published or presented already, so some of the work that Sieber has done with flu vaccine surveillance for Guillain-Barré syndrome, et cetera, things -- those kinds of active surveillance efforts have been presented in pharmacoepidemiology forums. And we've additionally presented results of some of the methodology work that we've done to try

and understand how easy is it to use Medicare data for the purposes of active surveillance evaluations. And in some of the projects that are being worked on now will be presented or submitted for presentation at upcoming meetings. So, while I'm not going to get into specifics of projects right now, I think the goal is certainly to address questions that are arising in these populations that are of interest to a range of federal partners.

I think the question that you raise about how does that coordinate with Mini-Sentinel -- I think certainly there are some questions that would be useful, especially once we have developed the protocol in the Federal Partners Collaboration to also implement it within the Mini-Sentinel so that we can get broader input into whether these issues are real problems.

DR. RACOOSIN: Well, Mark, if I could just -- I mean, one can envision at some point in the future there's the Sentinel, which is the national program, and the agency -- the various pieces that are informing building that will somehow coalesce, but we can't predict precisely how that will happen. But full lab studies at that point will probably be done under that umbrella as would capturing the rest of these populations.

DR. McCLELLAN: And broader distributed network.

Ron, your first question was a good question, so you can ask another question. I just thought I'd get a sense of like who -- Paul, any other questions there? Okay, so we'll finish with these two and then break for lunch.

MR. KRALL: Thank you. I'll try not to ask a good one so that I get to ask a third.

I ask this actually as a member of the OMOP Advisory Board or, rather, Executive Board.

You guys had many Sentinel and, ultimately, a Sentinel or on the sharp end of the stick OMOP has been conceived of and implemented as a research project. My question is to what extent have you been able to take advantage of the tools, a common data model, the data characterization tools that OMOP developed, and if you had advice for OMOP today about what its focus should be over the next two years in its research program, what would that be?

DR. PLATT: So, we've been -- I'd characterize us as OMOP's most interested consumer. And so we've been watching with terrific interest what's going on. Since yesterday's sort of the first time the full sort of breadth of the findings have been available, we're ready to sort of dive in with OMOP to sort of talk about where are the lessons that we can adopt and to plot a shared strategy.

After this meeting ends but before we all go home tonight, we're sitting -- 10 or 12 of us are sitting down -- Mini-Sentinel, OMOP, FDA -- to talk in some detail about starting to build the shared agenda for this coming year. So, it's clear that OMOP has so much -- has so many results. I think our next job is to figure out which of those results is relevant to the work we're doing -- and to this protocol in particular, because -- so for those of you who weren't here, if you had to say one thing about the OMOP results, it's some methods seem to work in some environments sometimes, and I think what we have to do is ask in the environments we're working in for the questions we're asking which methods are most useful. So, I think the next order of business is for us to start doing that deep dive with OMOP to try and make sure that if there are flashing red lights we stay away from them, and if there are particularly appealing approaches that we implement them.

DR. McCLELLAN: Paul.

DR. STANG: Mine is just a quick question. It's --

DR. McCLELLAN: Identify yourself.

DR. STANG: Sorry, Paul Stang, Johnson & Johnson and OMOP.

It's more opportunistic, so, Bruce, if I understood your presentation correctly, you're essentially concurrently able to do observational analyses as a large clinical study will be ongoing. And I don't know the details of the large clinical study, but it appears to me that you also have the opportunity to take the inclusion/exclusion criteria being used in the large clinical study and apply them to the observational data and look to see the extent to which they are concurrent with each other and maybe inform ways that we can do better at interpreting why observational studies may or may not always be consistent with findings from large randomized studies. It just seems to me it's a unique opportunity, because they're happening at the same slice in time, which is not usually the case. Usually the clinical trials or something has happened in the distant past. So, I'm just curious if that's come up in any of the discussions.

MR. FIREMAN: Well, as we were talking about earlier, we at Kaiser Permanente anyway, because we have electronic medical records we can -- if signals arise or findings arise or disparate results like what was referred to before from OMOP when we use one method we find one thing, when we use another method we find something else. We do have the capability to look at much richer clinical data that might be helpful, and I know you have experience looking at some of our data on, what, EKGs I think.

DR. STANG: Right.

MR. FIREMAN: And so we have, you know, a lot of data online that we could amplify this. But what we're planning here, in the plans that I presented here, we're

relying on data from Kaiser that's comparable to the claims-based and administrative data that's in the other databases and these supplementary efforts -- which I think are very intriguing that you've mentioned and that arose a few minutes ago in discussion -- I think there are intriguing possibilities, but they aren't yet planned out in (inaudible) our protocol.

DR. STANG: Okay, because I was thinking --

MR. FIREMAN: What's the promise of --

DR. STANG: Well, I just think it's an opportunity to take what -- I'm oversimplifying, I'm sure, the clinical study, but their inclusion/exclusion criteria in the clinical study, many of which I think could be applied to the observation -- there were 23,000 or so people that I think you're going to identify to look at the relationship in this case between observational data and clinical studies. It's -- to me, it just seems like a pretty unique opportunity that you might want to discuss. I think it could be pretty cool to do.

Thanks.

MS. ROSATI: Just in time for the year 3 work plan. Thank you, Paul.

DR. STANG: Well, I figured why not.

DR. McCLELLAN: Good idea, thanks. Any final comments from the panelists on any of the issues that have been raised?

All right. I'd like to thank you all very much for driving a very interesting discussion. We are now breaking for lunch, and a reminder that lunch is on your own. In the packets, there's a list of local restaurants that are close by. In addition, our host here at the hotel wanted me to let you know that there is a lunch special upstairs -- soup and sandwich $10, and that'll be quick. We are going to start again promptly at 1:15, and in

addition reprints of that *New England Journal of Medicine* article are at the tables. If you don't have a list of restaurants in your packet, those are at the tables as well. Thank you.

(Recess)

THE BROOKINGS INSTITUTION

THIRD ANNUAL SENTINEL INITIATIVE PUBLIC WORKSHOP

Wednesday, January 12, 2011

PARTICIPANTS:

Session II: Perspectives from the Stakeholder Community:

MARK McCLELLAN, Moderator
Director, Engelberg Center for Health Care Reform
The Brookings Institution

DIANA ZUCKERMAN
President
National Research Center for Women & Families

MYRL WEINBERG
President
National Health Council

DANIEL TROY
Senior Vice President and General Counsel
GlaxoSmithKline

J. LEONARD LICHTENFELD
Deputy Chief Medical Officer
American Cancer Society

BRIAN GALLAGHER
Senior Vice President of Government Affairs
American Pharmacists Association

* * * * *

P R O C E E D I N G S

DR. McCLELLAN: All right. As I said, good afternoon and welcome back. I hope everyone enjoyed their lunch break. And we're going to pick right back up with continuing to discuss some of the important issues of where we've been and where things are headed with the Sentinel Initiative.

In this panel, we're going to hear from a number of stakeholder perspectives, and I'd like to do this with a couple of key ideas in mind. First is, what's some of their thoughts and ideas about the most important challenges and how to address them facing the Sentinel Initiative and post-market safety evidence more broadly; and second, we're looking for some perspectives on their opportunities for further participation in the development of this system going forward.

I'm very pleased with the knowledgeable representatives that we have together this afternoon from a wide range of perspectives. They include Myrl Weinberg, the president of the National Health Council; Diana Zuckerman, who is president of the National Research Center for Women and Families and a member of the Reagan-Udall Foundation Board; Dan Troy, senior vice president and general counsel with GlaxoSmithKline and former general counsel at FDA; Leonard Lichtenfeld, the deputy chief medical officer at the American Cancer Society; and Brian Gallagher, who's senior vice president of Government Affairs from the American Pharmacist Association.

And what we're going to do here is similar in format to what we did with the first panel, but without that break in the middle. We're going to hear some opening comments and perspectives from each of our panelists, and then we're going to open this up to a broader discussion and questions involving all of you. So please be ready for your participation in just a few minutes. In the meantime, I guess I can start right here at this end, Myrl, do you want to begin?

MS. WEINBERG: Sure, if I can get out. Well, thank you. I wanted to take just probably 30 seconds to make sure people are familiar with what the National Health Council is. The National Health Council is unique, it's a non-profit umbrella organization and we are unique because we have about over 100 health related national organizations and companies in our

membership.

Our primary constituency are about 50 patient advocacy organizations representing 50 different chronic conditions, diseases, disabilities like American Cancer Society, Alzheimer's, diabetes, American Heart Association, as well as many others, and so it's really their voice, a united patient voice, that we bring to these systemic discussions.

We don't do condition specific work, but together with them, we try to resolve issues and help improve health care and the medical research in the country that would benefit all people.

So I have three points I wanted to briefly make today. The first, and fairly quickly, is to reinforce some of what Kristen said about the privacy concerns that she addressed this morning.

A few years ago, the National Health Council, in partnership with another of our members, AHIP, or America's Health Insurance Plans, sponsored multiple meetings between representatives of patients, organizations and health plans. And during these meetings, the purpose was, the health plan representatives shared information about their proposed or implemented electronic personal health records, and the patients, in response, shared their views on this then new technology. It became clear that EPHR's described by the health plan representatives did not include several functionalities that were critically important to patients. And specifically, the patient group representatives identified five functionalities that were missing. I just want to let you know what one of them was. One of them was the ability to use the data for research.

What we have found in multiple ways is that patients with chronic conditions are generally not as concerned as sort of your more average healthy consumer with the privacy concerns especially as it relates to their health information. Their concern is that their health information and their data is used for research so that they have better information, their families have better information, and the nation has better information to improve health care for everyone.

So our suggestion and recommendation, and certainly FDA has heard this

before, is that we encourage FDA not to allow privacy concerns to inappropriately impede the progress of the Mini-Sentinel.

I'd like to turn now to the area of communications. I think we heard this morning from Mark and from others that moving forward, when and how and what we communicate about the results from the Mini-Sentinel, and ultimately from Sentinel, become more and more important. We did research in the areas of what patient's perceptions and concerns were about benefit risk, among other areas, and so I wanted to share some findings from that research.

We found that patient's assessments of benefits and risk is very complex and usually involves both emotional and analytical factors. Second, we found that most people have incorrect assumptions about the benefit/risk correlation. They believe that as the benefit goes up, the risk goes down.

And most importantly, patients expect full disclosure about risk and benefits, but they also believe that all risk is knowable at the time of approval. And finally, patients view any limitation to accessing a drug they found effective for themselves as a violation of their right to make personal health decisions.

So what we've drawn from this, I have really sort of two recommendations. First is, how do we address communicating the uncertainty of the findings, because we know they won't be clear at all times. And in thinking about this, we're suggesting that, first, we all need to think about the underlying problem, which is that many people believe that all of the risks are knowable at the time of approval. If they don't have an understanding about the real situation upon approval, then the results of the Mini-Sentinel may not make sense. So we're suggesting that there be some real research conducted and some resources put into careful message development and testing to address that issue and then move on to the more specific challenges of really communicating well about the unique findings of the Mini-Sentinel Initiative.

One of the things we're recommending, and have, and probably is in process, is that there be an objective framework for assessing risk developed, so that you would have some idea of where on the spectrum of patient consumer use does the signal fall, how do you stratify the magnitude of risk and the likelihood of risk of treatment compared with other treatments or no

treatment at all, and what are the potential impacts of the communication on the patient centered outcomes, their health status, their quality of life and functional status.

And I don't have time, but maybe someone else will address, there are very big differences in the sub populations of patients, those who have an attitude of taking a product with side effects, who are fairly healthy and think it's not worth the side effects, and those whose life depend on the product and they don't care much about the side effects, they just want to live a better life longer.

So we also feel that this framework can be used to determine the point at which we disclose the risk, whether it's signal detection, signal (inaudible) or signal validation, and those would be different in different circumstances, the manner in which you disclose the risk, and to determine the role of the various providers and stakeholders, and from my perspective, especially patient organizations and their representatives.

So the final recommendation is, given some limitations that FDA has on the communications that it is able to create, we're suggesting that there be a more formal way to take the basic messages that FDA will create and then work with known, trusted, credible sources of information for the specific populations, not just patients, but providers, et cetera.

So using us as an example, the patient advocacy community, messages could be taken to those communities, and they do not have as strict limitations on how they communicate with patients directly. They're able to, from years and years of experience, to know how to communicate, at what level to communicate, through what communication means they should communicate, and use these external groups in a formal partnership way to communicate to the providers, to then communicate to patients, to communicate with patients so that we don't have a breakdown, because when FDA does its communications, it just doesn't get out in an effective way and reach far enough for people to really understand and support the whole Mini-Sentinel and Sentinel Initiative. And I'm going to stop with those three points. Thank you very much.

DR. ZUCKERMAN: I'm Doctor Diana Zuckerman, I'm President of the National Research Center for Women and Families, and I'm here representing the Center and our

perspective really, which is one for patients and consumers and public health advocates.

I should also just say that a big part of our work is at the Cancer Prevention and Treatment Fund, and also we work very closely with the Patient Consumer and Public Health Coalition. And although I'm not speaking for that Coalition today, many of the points I'll be making are ones of great concern and interest to them. And this Coalition was instrumental in helping make sure that Sentinel came to be as a part of legislation, so it's a topic near and dear to us.

I, too, will start out by just saying the National Research Center for Women and Families focuses exclusively on health and safety issues, and our non-profit is independent, and a large part of what we do is looking at programs and policies that can improve the health of adults and children, and that includes men and women and boys and girls.

So today I will be speaking from my perspective, and it does overlap patients and consumers and public health. And I personally am trained in epidemiology in public health, and so I look at this project specifically for the research opportunities.

And I'm one of those people that gets very excited when I think about this enormous, amazing data set or data sets and all the kinds of information that we could get from them. And so, to me, both speaking personally and on behalf of patients and consumers and the public health community, it seems to me that the big question is, what do you do with this information, how do you make the most of this information in a way that is fair and as accurate as possible and as useful as possible, and that's a big challenge. Whenever you have this much information and all these different ways of looking at data, that's always going to be challenging.

I wanted to say I agree with Myrl about the privacy issues. Certainly the people that we talk to, patients and consumers, they're very concerned about privacy, but they – when people know that their information can be used for research and that that research can benefit other people, as well as themselves, that is something that they want to do.

And this is an opportunity that most people don't have. When you're in a clinical trial that can be beneficial to other people, usually not that beneficial to yourself, and what's different about this is that it can be beneficial to everybody, the people whose data are being

used and their family members, and their friends, and strangers that they've never met.

One of the things that hasn't been talked about very much and I think is important is to think about the safety signal. And when you look at the legislation, it was clear that the goal of the Sentinel project was to focus on safety. But I think it's very important to think about safety also in the context of effectiveness and efficacy, because, you know, that's the thing that FDA needs to weigh all the time, and that we, as patients and family members need to weigh all the time. We want products that are safe, but we also want products that work. And we might be willing to take risks on products that have safety problems if they're more effective in other ways. And so I don't think you can look at one without the other, and I hope that's something that will be taken into consideration very carefully.

In some cases, the safety signals might be very similar to the effectiveness signals, and I think diabetes drugs is a good example of that, where a heart disease can be an effectiveness issue or it can be a safety issue, but for a lot of products that would not be true, the safety issues and the efficacy issues would be very different and we might have to look at all of those issues at the same time to come up with some kind of reasonable conclusion about whether a product should be taken off the market, or should have a black box warning, or whether doctors might or might not want to prescribe it for their patients and so on.

One of the issues that was raised today was the issue of the signal that can be – looking for signals, looking for warning signals versus real findings. And I think it's very difficult to distinguish between what is a signal and what is a real finding when you have data sets that are so rich.

And so, you know, in the ideal world, we'd have massive clinical trials that – we like double blind clinical trials, we like to look at data from them, but we're never going to have huge samples, you know, with millions of people or thousands of people where you can statistically control for age and health prior to treatment, and maybe race or ethnicity might be important, many other issues that we would never be able to control in clinical trials because the trials would never be large enough that we can statistically control for in these data sets.

And so for that reason, I think that we can go from signals to findings, or at least

as close to findings as we're likely to get in the real world, and that's important.

Another point I want to make is that most of the talk has been about drugs, and medical devices are a part of the legislation, and a very important part. My understanding is that, unfortunately, we had hoped we'd get data on implanted medical devices, whether heart valves, or knees, or hips, that's going to be very difficult to do for past data because of lack of a registry, and claims data may not have information about exactly which hip replacement was used or exactly which heart valve.

But it still should be possible to get some very good data in the past on some implanted devices, specifically ones where there's only one on the market, and so you know which one you're looking at rather than many different ones. But also, in the future we need registries and other mechanisms to that we can get that information.

And then finally, I just want to talk very briefly about communications, which has already been mentioned. Let's face it, the FDA isn't really known for great communication skills with patients, I think everybody would agree to that. They're going to have to do a better job on that if they're going to successfully communicate information from Mini-Sentinel or the Sentinel project to patients, and to providers, and to, you know, any interested parties.

So the FDA is going to have to do better, they're going to have to – with others, many of us in the room, we're going to all have to do a better job of explaining to patients how to look at safety information, how to look at effectiveness information, how to put those together, because as has been said, people want to live longer, they want a better life, they may not care about adverse reactions unless it happens to them, but living longer and with a better quality of life and the risks all go together, and patients aren't very good a lot of times at weighing those, and unfortunately, doctors aren't very good at communicating those issues to patients.

Many of us in this room are going to have to work together better with the FDA and independently to get this information in a way that's useful and truly helpful to patients and consumers.

And I guess, in closing, I just want to say that, you know, it's a pleasure to be here and I'm very happy to have this opportunity, and I really am very excited about Mini-Sentinel.

I think it's a wonderful, wonderful resource, and let's make the most of it, and let's not get too bogged down in some of the definitions, but also be very careful about how the information is used. Thank you.

MR. TROY: I'm Dan Troy, I'm always short, I'll try to be brief, and I'm actually going to speak from here for both reasons. I'm very grateful to be here and to see old friends and colleagues like Janet and Rachel and Mark. I'm supposed to be speaking for industry, for the pharmaceutical sector, and I'm going to be very clear, I don't even speak for GlaxoSmithKline. My views here are my own, and as you're going to hear, they're not particularly original. I feel very much in a room of scientists, epidemiologists, PhD's.

As a lawyer not speaking about law, I feel very much like a poser, so I'm mostly going to amplify and pick up on some points that have already been made. But one point that I think that has not really been focused on is that, as is often the case, Congress has created and sort of imposed on FDA what are, let's be honest, essentially unreasonable demands.

I mean if you're in Congress, it's very easy to state goals, oh, we want an active surveillance system, we want it, you know, very fast, and by the way, we're not going to give you enough money for it. But as this entire effort and this symposium shows, it's far more difficult and far more complicated than the statute makes it seem. And so in light of that, actually the achievements are genuinely, you know, absolutely, as people have said, remarkable. But again, as others have said, we really do need to very much manage and communicate about what this system can and can't do. Query, whether when Congress used the word "active", whether it meant a query based system, where FDA would be asking questions rather than the information would just magically appear.

Because, again, to be honest, politicians, the press, and particularly plaintiffs' lawyers, the vane of my existence, have a very powerful incentive to over simplify. But again, we hear no better, we know that this is not a magic bullet, in part, because of symposiums like this one and, in part, because so many of you know so much about this, so as has been said already by (inaudible) and Myrl, we really need to work together to communicate about what Mini-Sentinel and eventually Sentinel can and can't do, and I think that's going to be a continuing challenge.

I mean the – I'm perhaps the most ignorant person in the room, so I can say it from the ignorance perspective, you're like, well, why not, why can't we just get this data and find out instantly about why all the, you know, all this information is, you know, what all this information is, and you know, as was said, there are many people who think that the full amount of information is known about drugs when they're approved, but certainly people think that there's a way of finding out everything that there is to be known about things after they're approved, and, in fact, as, you know, as we see, that's really a challenge.

Now, to the extent that the FDA has a strategy to achieve a goal of what might be the next generation, genuinely what might some think of as active surveillance system, I think it would be interesting to – for the FDA to communicate about that. So I guess I'm sort of asking what essentially comes next, although I recognize that, again, even just achieving Mini-Sentinel and then Sentinel is a very substantial challenge.

The second point that, again, has been picked up on a number of times is, we need to ensure that Mini-Sentinel or Sentinel does not need unwarranted regulatory actions or pronouncements that harm the public health by unnecessarily harming people and alarming people and creating unnecessary liability, but that's going to be really hard because the incentives to communicate prematurely are very profound. I mean Doctor Platt said that we need to ensure that there's a balance. But let me give you one sort of practical example from the real world that I live in. Let's take this (inaudible) analysis, which I guess – was it said there was going to be a quarterly analysis? Well, is that quarterly analysis going to be made public? I would hope not, because, you know, talk about the small numbers, well, first, I should be on this drug, no, I shouldn't be on this drug, yes, I should be on this drug, no, I shouldn't be.

Well, what if Congress decides that it wants to see that information? What if I don't want to give plaintiff's lawyers any ideas, but they don't need me to give them ideas. What if they decide to subpoena the FDA and they want to get that information? It's information that's been paid for by the public. But as you, you know, might imagine, that would just, you know, kind of wreak havoc on a variety of things.

And so I think that we have to – again, FDA does have to come up, as was said

earlier, with a communication strategy, and we need to continue to reemphasize, as Rachel said a number of times. It's a tool, it's not definitive. The reality of the observational data, and I think there was a great discussion that I've at least been briefed on by (inaudible) yesterday, is the presence of false positive and false negative results depends on the rigor of designs to account for biases, and, you know, there's no doubt that the distributed data model has potential to produce false positives even with the very best methodologies. That doesn't mean that it's not the right thing to ultimately do, but we have to continue to emphasize, as Rachel did, as others did, that this is a tool that's going to augment things, and not as I'm afraid some people will have a tendency to over simplify, to replace.

And I think all of this feeds into, again, a point that's been made before, a need to be just as transparent as possible.

Now, we at GSK are very appreciative of the opportunity to play a role in OMOP My colleague, Patrick Ryan, plays an important role in OMOP. And we also really appreciate the discussions we've had with FDA about potentially using either some Mini-Sentinel data centers or the coordinating center about a study that we're – that's under discussion.

But there is a need for, I'd suggest, more transparency, and dare I say it, more involvement by industry not for us to own or control anything, and obviously there's a very interesting question that was raised about, well, if industry is getting involved, then all of a sudden does this become research and no longer public health practice, and then you have to go through all sorts of IRB approvals, but to enable us to give input into a variety of things.

So unlike OMOP right now, we don't have visibility into the research protocols, the data modules, the data base evaluations, the quality assurance tools, the analytical programs, and we think that, again, having a seat at the table and having some visibility and input into this, we can be helpful.

You know, some have talked about the value of collaboration, and we agree with this. So, for example, people in the industry just have more experience with their compounds than pretty much anybody else and query whether we should have some input into the queries about the compounds with which we have more experience than anyone else.

I mean people in, not me, but the people in our organization understand, probably more than even FDA gets the opportunity to do, about co-medication issues, and patient populations, and the limitations and the benefits of the studies. And so I think that industry can actually play a role, not control, in formulating the queries. I also think that the more we know about the Sentinel system, and we understand there are limitations on what can be done both within law and practice, is to ensure we don't create our own inconsistent Sentinel data bases, because we don't have visibility into the methodology, I think that would be counterproductive.

And finally, as Myrl Weinberg and others have said, we absolutely need to ensure that we understand when and how FDA is going to use this data to communicate to the public so that we can coordinate and harmonize our own communications about our medicines.

And I would strongly suggest and appreciate FDA thinking about this now rather than when the time comes, because it is going to be, you know, a difficult question about the point at which you communicate. And we, as always, appreciate FDA guidance about this topic with as much specificity as possible; again, Myrl talked about some of these things, thresholds, timelines, et cetera.

We understand that the centers already have priorities, but the more communication that we can have to understand what those priorities are, the better. So to close, this is a very important initiative. As is often the case with FDA, I say this as a former FDA-er, proudly, I'm proud to have been a former FDA-er, I'm not proud that FDA is often under funded by Congress, and therefore, necessarily understaffed. Now, that's, by the way, not an offer for the industry to pay for this with different funds. But we should all call on Congress to allocate more resource for this even in this troubled vegetary time. So thank you very much.

DR. LICHTENFELD: Unlike Dan, I'm tall and I talk too much, so I'm going to (inaudible). My name is Len Lichtenfeld; I'm Deputy Chief Medical Officer for the American Cancer Society. And I'm involved and interested in a number of other organizations that have interest in these sorts of areas. But I wish to reflect that, like Dan, I'm speaking on my own, not on behalf of the Society or any other organization.

What I'm going to talk about with you are my reflections on where I see Mini-

Sentinel and what I've heard today. In fact, I have to share with you, I made some notes, and as I made my notes and my concerns and my questions and my comments, almost every one of them has been addressed, starting with Mark McClellan all the way through the panel. So maybe some of this is repetitive, maybe that's a good thing. Let me start off with a different thought, though, because I do come from a background as a practicing physician, I've been involved in the public health arena through my work at ACS. This is really an incredible moment in our time as a country in terms of health care, what I would call a convergence of opportunities, a convergence of technologies, if you would, with the emphasis that's been put on health information technology and electronic health records.

And I have a four plus here after the ONC. I have to give a tremendous amount of credit to the ONC for the work that they've done over the past year. I'm a very vocal critic and have been for decades about health information technology, infrastructure, what we have promised, and what we have failed to deliver, and I have to give the ONC credit for actually delivering on its promise in a timely fashion, in a way that I personally publicly said they would never be able to do, and I had to eat my words, so I'll eat them up here publicly, as well.

But the implication of that, the implication of that within the medical infrastructure is so critically important, what we're talking about here today. Many years ago I heard a lecture where they talked about why we spend so much money in the treatment of acute leukemia in children when it's such a rare disease. And the lecture was titled The Stalking Horse, that is, something that sets a precedent that we can all learn from going forward. And I would suggest to you that we start talking about data bases and making them happen and include 100 million patient medical records, potentially medical records, a public/private partnership that actually has the potential to deliver this demonstrating delivery, that's really impressive and we should not lose sight of that in our conversation.

To give you a sense of where the American Cancer Society is, and other organizations like Harvard School of Public Health, I would add, back in the 1980's, the ACS went out and recruited one million people, and that became what we call our SPC 2 study, and a tremendous amount of information came out of that study, where we collected data periodically

from the patients over time.

And that cohort, unfortunately, is now dying off literally. But we have learned so much from studying those folks, in terms of what it meant for cancer. We learned about obesity and cancer, we learned about smoking, we talked about all sorts of issues, the way statents work or statents don't work to prevent cancer. Harvard has written on vitamin D relationships. But it's so time consuming, it's so difficult to get that information, and you never know, even though you're doing your best data collection prospectively, whether you're asking the right questions.

So when a question came up recently and in full disclosure we have – we do serve as unpaid, and we're not engaged in any financial way with Sanifie in terms of looking at lantis impact on cancer, when that question came up about a year and a half ago, we went to our data base and we could not answer that question from whether or not there was an impact of various instances along the line of what was discussed and I will talk further about in a moment with the proposed study here that was discussed earlier today, not cancer, AMI substitute, the same issue.

But you begin to understand how important this concept is and the potential that this has, the potential this has to improve the public's health. It's not a simple process, and no one should think that it is. And I know there are a number of criticisms of the study, and they're valid criticisms. I'm not an epidemiologist, I deal with epidemiologists, I do quick studies from time to time and comment on them publicly. But I understand, and we all need to understand that this is not simple, but it is, in fact, retrospectively, worldly, a simple beginning to a complex process.

Now, as was mentioned earlier, the lessons we learn today are the lessons we're going to take forward with us in the future. It is important that the group maintains its focus, but I don't think I need to tell them that, they know that, as well.

Let's talk about a couple of current issues. I've heard an awful lot about communication, and frankly, I am somebody who is very much involved in communicating issues to the public. And I usually am the person who comes out and says, wait a minute, that's not exactly the big breakthrough that you thought it was.

For example, last week a company announced that they were investing $30 million in the technology at Mass General Hospital to find the single cancer cell circulating in blood. It was a development contract, folks, it was not a scientific breakthrough. It did not announce new science. I'm not criticizing; the science behind it is elegance science, it is important science. It may be critically important in the future. But the announcement was only by a company saying we're getting start-up capital to another company – to another organization to improve its technology.

So now when we talk about these things, communication is so important, and everybody here is saying we need to learn to communicate. Controlling the message is impossible. Controlling the message is not impossible, it's difficult at best, and it's so critical that that be done properly in this process. And I assure you as we are sitting here today, no matter how much we do to try to make sure everybody gets the right message, it will not come out that way, and how that's balanced is so important.

So you have people like me, I'm not just saying, there are others out there, but people like me who write blogs and say, wait a minute, let's put this in perspective and understand it.

You may recall one of the examples I used and talked about at lunch was, about a year and a half ago there was a report at ASCO about Tamoxifen and SSRI's and the impact SSRI's have in reducing the effectiveness of Tamoxifen. The next day, someone from the agency, I didn't go back to find out who, was quoted as saying, we need to look at this immediately, maybe put our black box warning so everybody knows about it. What was completely ignored on the other hand was another study from medical records in the Netherlands that did not come to the same conclusion.

So here we still are, and that is a real issue, and that is something that people are looking at and are concerned about, not administering it, but making sure that we deliver the right message in this environment is important.

Number two, the FDA enjoys a real advantage by having to – being able to avoid HIPAA. The rest of us live in the HIPAA world. So when you go out to do this type of research, if

it's not – whatever defines – and again, I'm not being critical, I'm just making an observation, whatever defines the value of this research for the FDA is not necessarily the same measures that will evaluate the research or that opportunity for organizations like the American Cancer Society, CDC or whoever, who need to go to every state and get permission from every person in order to, I get a big sign here, I get it, to get that permission. So, you know, the FDA does give a pass that makes the applicability in the larger sense perhaps a bit more difficult. Number three, the diabetes protocol is elegant, and I admire the folks for having put together the paper that I read last night on the plane on the way up from Atlanta which talked about – which actually made that process transparent.

They did in three months what other organizations would take a year to do. It was difficult, it was intense, it showed the decisions that had to be made. It is, as was mentioned earlier, a complex process, and I believe, Judy, you mentioned, hopefully the next time it'll be easier and easier and easier, I hope so, too.

But it's a real issue as you go forward because these are retrospective choices, shall we say, with prospectively gathered data, and asking the right question is so very important in these studies.

But let's remember, this is high level, not granular data, there's a lot more information, like was mentioned today, a lot of information we'd like to be able to have access to that we don't have access to, this is a distributed system, but there's some questions that will not be answered by this type of process, but this is a start, this is a start, folks, and let's remember that.

So where do we go from that looking through the cancer lens? Imagine the potential and the power of taking this technology and moving it into the epidemiology world to understand some of the things we don't know. We do not know about the long term effects of cancer treatment in adults. We do know about it in kids because they've collected the data. We don't know about long term – the epidemiology of cancer. We don't know about biomarkers and do they really make a difference. We don't know do we have systems in place that can, in fact, avoid some of the onerous aspects of REMS programs with opioids if we had real time

background systems.

These are the types of processes that will come out of this, but there are barriers and questions. Data will need to be patient centric in the future, it is not patient centric today, it's system centric, and that's why it has to be distributed, because only the people who have the systems understand how they work. And let me tell you, it's hard to pull the data out of those systems.

What about other large forms of practice, private practitioners, large data banks, the existence and a lot of the vendors? We are working with the Heart Association and the Diabetes Association on the guidelines project, and we're going to each of the vendors to get the information into a format that we can use to evaluate. We should be able to query that system, and the data should follow the patient, not the system holding the data captive from the patient.

Another issue, what I call my Uncle Chester thing. He's a minister, preaching over my wife's grandfather's funeral, he says we bless them that comes and them that goes, he was talking about people who came in the family and people who left, like me, I had come in, somebody else had left.

Twenty-eight months is not long enough. The age distribution is another example of something we need to improve that was pointed out earlier in the questioning. Validation of the data is critically important, and we need to get to a real time system, we're far away from that today.

So where does that leave us? And there are many other things we could talk about, but time doesn't permit. We are early stage and progressing. From my point of view, as someone at the American Cancer Society, where we are involved in this type of process, and others out there who are involved in the research world, and I'm sure that some of them have been engaged in this, as well, it is critically important we bring them into this process in a way that we not necessarily change what we're doing today, but we inform the technology for the future, because it is that future potential that is so important and will give us the opportunity in this country to finally get our arms around what we do and how we do it, and to make sure that what we do really makes a difference in the care we offer our patients. Thank you very much.

DR. GALLAGHER: Good afternoon. I'm Brian Gallagher; I'm here representing the American Pharmacist Association. We have over 62,000 members in all practice settings throughout the country. We support and commend the FDA for the progress that's been made thus far in the Sentinel Initiative. And we believe that pharmacists and other front line providers have a key role to play in that system, in that process.

We have the public's trust and good relationships with patients, and so we can participate and should participate in two ways, on the front side and on the back side, on the front side meaning we need to participate by including information in the Sentinel Initiative so that the Sentinel system becomes a tool for pharmacists and other front line providers to be able to provide information. We participate on the back end by helping patients understand the information that comes out of this, take the medication safely, moderate and temper fears and concerns that patients might have, because like I said, we're in every community. Patients will be coming into pharmacies and talking to pharmacists about the message, so we have to partner with the FDA and the researchers that are going to be generating this information so that we can provide accurate information to patients so that they feel good about the medications that they're taking.

So I guess the first point I want to make is that this is a great opportunity for pharmacists and other practitioners to partner with FDA on educational programs, creating materials for patients so we can help educate consumers and we can get ourselves ready to be able to provide appropriate information to patients.

We probably ought to partner and tie this into the safe use initiative, too, and look for linkages with REMS programs, because a lot of these things sort of tie together.

The second point is, providers, including pharmacists, need data early on, because patients will be asking them questions when a press release comes out or something that there's some tentative data or whatever. If it's cold information, patients are going to be coming in to talk to pharmacists. Pharmacists need to know what the position is, as well as the other front line providers, so we need that information early on.

But a balance needs to be struck, as was stated earlier, between minimizing

false information and providing timely and accurate information that can be given to front line providers like pharmacists in an early and timely fashion.

The next point is that we need to make sure that there's not data overload. Coming from a hospital background, seeing a lot of instances in the ICU's where the buzzers go off incessantly and nobody pays any attention to them. So the information needs to – when it rises to the level that it's reportable and useable, it needs to be put out there, and as it evolves or new information becomes available, it needs to be clarified and brought to the point for pharmacists.

Now, turning to a point that's directly related to pharmacy and doesn't – and concerns some front line providers is the key role that pharmacists in particular can play in this, and one of the key obstacles that we have, and I don't think the FDA has a lot of control over this with regard to Sentinel, but it's something I think we all need to be thinking about to maximize and optimize the ability to pharmacists to play a vital role in this, and that is providing a band width for pharmacists to be able to actually engage in these services.

Often it's presumed that pharmacists can choose simply to participate or not participate in these programs, this Sentinel event, REMS, any other programs like that, and that's simply not the case.

The fact is, it's not really a matter of choice, because, as a pharmacist, given the choice between working with patients on Sentinel initiatives, or REMS, or any other programs like that, providing medication therapy management, pharmacists will tell you, they would much rather do that than count to 30 by five.

However, the truth is that a lot of times pharmacists simply don't have the time or the band width to be able to engage in these type of activities. So what's the solution to that? What we need to do is find new ways to deploy and resource pharmacists so that they can be a valuable resource and provide all the good services that they can in a situation. So how do we find ways to provide additional resources to hire more pharmacists? How do we find ways to position pharmacists appropriately in the health care team? Is that a different practice setting? Do they practice in the doctor's office? Ways to use health information technology and make it

fully available to pharmacists so that they can participate in these programs. Use of a wide array of other technologies to free pharmacists up. We need to create band width.

So, in short, we need to find ways so that pharmacists can do what only a pharmacist is able to do. So we need to make sure that the band width is freed up so that they're able to do that.

The good news is, up until a few years ago, there was an acute shortage of pharmacists, and now, since a lot of schools have come online, there's a lot of new pharmacy graduates that are going to be out there and they're all going to be looking for work, too, so that's a very good thing.

So hopefully all of us can work together to retool the system in such a way to allow pharmacists and other front end providers to more fully utilize and deploy their skills, to help patients take their medications safely, and fully participate in these and other important programs. APHA looks forward to continue to work with the FDA and all the other stakeholders on this highly important patient safety program. Thank you for including us.

DR. McCLELLAN: I'd like to thank all of our panelists for their comments, a great starting discussion. I would like to also remind you that now is the time that we'd like to look for comments from – and questions from all of you. So, as before, microphones are at the back of the room. If anyone is using the overflow room, please feel free to come in to the microphones and make your comments.

Before going to any comments and questions, though, I'd like to ask if any of the panelists have any points or reactions they'd like to add in now based on what they've heard from the others who are present. Okay.

And let me just start off with a question about implications for Sentinel for consumers and patients at this point. I think many of you commented on the progress that – I guess two things, both the progress that Sentinel and Mini-Sentinel have made over the last several years, but also on the complexity of the task at hand and on the information at hand.

This doesn't seem like a particular topic that consumers are very familiar with yet. Is it time to start communicating to them about it, and if so, is that part of a broader set of

communications related to new evidence emerging on products after they come to market?

MS. WEINBERG: I think it is part of the broader communication. And I think that before we go out, it would be great if we could, as I said, have a little bit more organized way that FDA and some of the external groups who have the knowledge and expertise and maybe more freedom to communicate in certain ways to their constituents, actually sit down and talk about what the needs are, various approaches to addressing those needs, and really have a plan of action instead of just going out and starting to communicate when we aren't I think organized about the audience's messages and some of the complexities we need to address.

DR. ZUCKERMAN: I agree with Myrl, but I would also add that patients are just not going to care until it affects them. And so we could explain what the Sentinel project is, but until we have data that are relevant to the particular person, and even with the diabetes data, if they're not interested in diabetes treatment, it's just not going to mean anything to them. So I do think we have to prepare an advance, but we shouldn't expect, you know, a rousing response, and actually I think we should hope not to get one until, you know, until we start providing information. But we should be prepared in advance on how to provide that information in the context of where this information is coming from.

I mean there's just so much confusion. I was mentioning the Sentinel project to somebody the other day who I thought would have a good grasp of it, and he just said, well, you know, are they going to include adverse reaction reports on this.

I mean it was just a different way of looking at it and they just didn't understand what is the difference between a data set like this and an adverse reaction report, and, by the way, went on to say, well, they have to integrate it with adverse reactions, and they have to make sure that all the adverse reactions are included in the data set, and so it's going to be, you know, I think it's going to be tough.

But I think that patients will be interested in it, and I think one of the challenges is going to be that, you know, let's face it, there are a lot of different perspectives in this room and on this panel as to how best to do that, and I, you know, personally am not that worried about scaring patients, I'm more worried about getting them to understand the information. And it's true, they'll

be scared potentially if they don't understand it, but the bigger issue is how to understand it so people can use it and worry less about scaring them and more about explaining it really clearly.

MR. TROY: Well, that's why I actually think Myrl's idea of starting out and, you know, again, FDA has been taking some steps in this direction under Rachel's direction, but there's not enough resource to the agency to really understand how people understand, you know, how patients in particular understand medicine.

And I think, you know, it's easy once you get into the FDA world to forget the level of ignorance that truly exists, and I don't mean that in a denigrating way, but I remember I saw some survey a few years ago, which it gave FDA and the pharma sector an incredibly low rating, and then it said, do you understand that no medicine is approved without two studies done of it, and all of a sudden the approval rating shot up, because people just don't understand even what kinds of tests are done.

Now, again, everybody in this room, it's like mother's milk, but that's why, again, Myrl's suggestion is trying to do some really serious research into what patients understand, what consumers understand, and, as was pointed out, those are two different groups. Once you're sick, you're in a different place than when you're not sick.

And how we can best communicate to them so that when this information comes out, it comes out in the right context, is not an insubstantial challenge and one that the FDA has not traditionally been that expert in or focused in because that's not really been a place where it's gotten enough resource and not really a place where it's put its focus.

It's put its focus on what is the impact of this product in the human body. And the whole developing area of consumer understanding is one that – there's, you know, we just to spend a lot more time on. So I think Myrl is exactly on point.

DR. LICHTENFELD: I guess I'm next in line, so I have to say something, right?

DR. McCLELLAN: Well, you don't have to say something, but you are next in line.

DR. LICHTENFELD: I can always talk, you know, one of my unfortunate trademarks. Let me come back to a point. Number one, I'm not sure if the general consumer out

there really is prepared or cares about something that you don't have a – something to deliver in their hands right now.

Yeah, I think the web site is good and I think that information planted in appropriate media is fine to have a story, but don't expect a rousing interest. You would expect a rousing interest – let's go back to some of the events that have occurred, because the point I think, Myrl, I think you made it, you know, the risk tolerance for drugs, it's fascinating because I had that same conversation way back when the Vioxx thing broke, because it's fascinating to me to see where risk tolerance is relative to expectations.

So you have a cancer chemotherapy drug, and just about, unfortunately, lead to very serious consequences from its administration, but it might save your life, so you accept it, but here's another medication that comes out, and it turns out there's a lot of class effect well around it, that's the moment, and those moments will happen, you'll have a chance to say, listen, we are improving our process to look at some of these issues and to get definitive answers, so that's the tag line to the larger question.

Now, having said that, that's the general audience, but there's an inside the beltway audience, folks, and it's becoming critically important, and we're talking some of them are in this room, and are in the FDA itself, and some of them are outside the FDA.

And this is a different world that we're going into; it's no secret to anybody sitting here. And then consequently, I do think that there's an audience internally, when I say internally, within this environment that needs to be reminded that this is an important project, that this is an investment in our future that will return significant dividends if supported properly, because there are a lot of things that are going to be competing on that, you know, for that support these days, and I think it's important if we really believe in it, that we do need the message to the right parties that this is – that we stand behind this. And how that's done, that's a question for another day, but I do think we can't ignore that.

DR. McCLELLAN: And just to push a little bit more on this topic, you know, you all pointed out that this fits with a number of other issues in areas where FDA is facing challenges in terms of communicating with the public, and that anything that's done related to Sentinel

communications has to be done within the realities of limited budget and resources available certainly on the agency side.

You all have had several specific suggestions, including more focus research on communication and how to get information accurately to patients and consumers, as effectively as possible, on a framework or plan that FDA and Sentinel could – and Sentinel participants could develop, so as information is developed, there's a prior process, a framework that that can fit into in terms of how communication might occur. Those seem like good starts. Anymore to add to that, again, given the practical realities here?

MS. WEINBERG: I just have one thing, and that is, I just wanted to reemphasize that there are a number of entities external to FDA who have done a great deal of research and message testing, et cetera. So it's not necessarily sort of starting from scratch as much as it is putting our heads together, working out a plan, understanding from FDA the messages that are important, and then allowing and working with external groups who already have some of this expertise to potentially move it on and research a message development, but also in really getting the information out and then having some kind of evaluation system of what's working, but moving forward I think more rapidly than maybe we were implying.

DR. ZUCKERMAN: This is perhaps an off the wall idea, but it would be really great if FDA and other folks in this room could be working with our educational system to help, as part of education, to educate our future consumers, kids in high school and college about how to understand the kind of information that's going to help them live a healthy life.

And if people can't understand, you know, what a ten percent risk of heart attack means, they can't make decisions. And this is the kind of information that every educated person should at least have some idea what that means. So I think we could do a better job in this very big way of, you know, for all the things that many of us do, including Sentinel project.

DR. McCLELLAN: And the FDA does have some existing mechanisms for collaborating with a lot of consumer groups. It sounds like maybe something that's a bit more focused on Sentinel and on the Sentinel partners could be worthwhile at this point, even thought we don't – there are not any definitive results yet, but now is the time to perhaps get out in front of

that.

MS. WEINBERG: It's really, you know, it's evaluating evidence and risk. And there are some basic concepts, which I think I alluded to before; we would get to really communicating specifically about this initiative.

DR. McCLELLAN: Thanks. Jonathan, a question?

MR. HARE: Jonathan Hare with Resilient Network Systems. First of all I want to say I just really enjoyed this panel; every one of your contributions is really good stuff. It kind of reminds me what you guys called for, sort of the aspirational goals of what Sentinel should be. It reminded me of the original Sentinel network, which was – I think it was created in the spring of 2007, maybe six months before the FDA Reauthorization Act that funded all the stuff.

And it's been a while, but I recall it's a network of networks connecting things like – and the research networks acknowledging – it's not just a safety thing, we need to connect all the other systems that have data and have motivated users into one holistic thing, and a really strong focus on communications and decision support at the point of care for both clinicians and patients, because until we get to that point of patient centricity and relevance, it's not really a valuable resource for most people, it really won't make that much of a difference, you know. It may satisfy the letter of the law, but it won't satisfy what's really necessary.

And again, you know, I think Mini-Sentinel is a necessary and very important foundational step, but I think we need to start talking about Maxi-Sentinel and getting a broader stakeholder group, because it's not a scientific thing, that's indespengable foundation of it, but what will be necessary in terms of communication and coordination, who needs to be involved, how do they get connected, and when it will be necessary to actually do that, because there's no amount of refinement of the statistical analytics, the sort of Mini-Sentinel taken, and it's agreed that we'll achieve what's necessary, it's not refinement of that, it's actually different types of capabilities.

So I don't know if you guys are the right audience, but is there a process to map that out and get a plan to get there, and how do people participate?

DR. McCLELLAN: And that's considerably broader than Sentinel itself, but it certainly relates to what Sentinel is trying to accomplish.

MS. WEINBERG: Rachel or someone from FDA can answer. To my knowledge, there's no –

DR. McCLELLAN: Who's conveniently at the microphone?

MS. WEINBERG: -- formal – there she is. I think it's what – we're saying that we would be willing and are encouraging, that we would love to see happen, and we would participate if there were the resources in time to have that happen.

SPEAKER: To think about how we're evolving, yes, that's a big part of our big picture and part of the meetings that Brookings convenes for us.

But I want to return to your previous conversation, because I'm a little confused. I think there were three or four things on the table, all of which are very important to us, but if we could parson that, it would be really helpful.

Okay, so Dan very reasonably raised the issue of other interested parties and whether there will be misunderstanding, so that's sort of one bucket, and that's the inside the beltway conversation which relates not only to misunderstanding, but whether or not anyone has ever invested any resources to actually pull this off. So there's – and that has to do with messaging and selling what we're building and sort of building the airplane while we're flying it and proving our worth. So that's one conversation, which it'll be interesting hearing how we might do that.

The other was, Myrl, you sort of – has to do with communicating with patients and the consumers, and that I think is a difference conversation. I almost feel like we're in our PMI meeting, our Patient Medication Information meeting, where we really are trying to learn how to communicate better medical information.

But we're sort of puzzled, and we have a number of our data partners, our health plans in the room, and maybe some of them could speak to this, about whether to or whether not to, and if so, how to communicate about Sentinel as an entity to patients and consumers, because, in fact, we're going to get to the data, or to the plans, or to our data partners, and I'd be curious what our data partners are doing about communicating how these data are being used and whether they're support and so forth. So I guess I see them as separable, and I'm not – I'm

certainly going to stay away from the word “advice”, but I’m not clear on the direction this panel is trying to urge us to head in. Are we having a PMI conversation, which we have to send you to a different Brookings meeting, or are we having a how to sell Sentinel conversation, which we’d love to have, or are we having – are we afraid the plans are going to lose support and enthusiasm from their members? So did I – is my question clear?

MS. WEINBERG: So if I could go first, which we seem to be doing. I think we’re not talking about that individual conversation, I wasn’t at this point. I agree with everything that was said about how that happens, and that’s when relevance really becomes evident. I was talking about Mini-Sentinel in a broader context, recognizing these issues of all of us that communicate with these audiences.

We have these issues of how do we communicate about evidence, about how to think about it, about how you understand these relative risks. Those are a broader, not individualized kind of communication and an education that needs to go on, and, to me, the place to start is with national organizations that can begin and lay the groundwork for those broader kinds of communications that then feed out through all of their many ways they communicate to their constituencies to create the base for when that individual conversation takes place, there is that awareness, and there’s some understanding of that broader picture, and hopefully of Mini-Sentinel and what we’re doing.

And that, you know, if it gets to the point of the Mini-Sentinel Initiative itself, then I still think there’s very important things to communicate, which you’re doing, with us, and that we should then, in turn, with you, communicate throughout our organization to some level that we would determine would be appropriate at this point in time.

DR. ZUCKERMAN: Yeah, I guess I would just add to the question of, you know, how much of this is the communicating about what is the Sentinel project to the public. Given the lack of resources, I’d hate to see much devoted to that, just because when I think about – I mean think of all the huge data sets that, you know, the National Center for Health Statistics has, you know, the public doesn’t know what those different surveys are and how they’re important and how they’re used, and they don’t care, even though it can effect decisions that are made that

effect their lives every day.

But we will need to communicate and sell the idea of Sentinel project if there's going to be opposition when results come out, and that, you know, I guess is likely, and I guess we have to prepare for it, but it just seems to me such a pity to be spending our resources that way, but, you know, maybe that's just naïve.

We have to – if, in fact, you know, results come out that say that a particular product is less safe than anther product, there's going to be people explaining why that's not true and perhaps undercutting the Sentinel project as part of that discussion.

DR. McCLELLAN: Glen.

GLEN: I think it's all of the things that you talked about, and I think they're all important, but in different ways, as you pointed out. If findings come out that need to be discussed with a patient as a result of the Sentinel research, then that – providers and patients need to know how to communicate about that. But if Sentinel is going to really be a tool for both providers and for patients, they need to know how to use it, and they need to know what it means, and there has to be communications about that. And one of the ways, as I suggested earlier, is to partner with, as some of the other speakers have said, partner with some national organizations about how we can get that information out to patients, and so it increases the band width of FDA with people that already have connections and interactions with their patients.

SPEAKER: And just to push on this a little bit more, I'm not sure this is where Rachel was going, but more of a process or structural version of this question, what vehicles or what mechanisms should be set up now as Sentinel is getting off the ground, and as FDA is undertaking more work in this area to help make this happen?

In place now are things like, as Rachel mentioned, sort of a regular series of meetings and opportunity for groups like yours to participate. FDA also has a number of other mechanisms like that in place at Cedar and elsewhere. Is it time to augment some of those activities, and how could that be done given the realities of very limited resources right now?

MS. WEINBERG: You know, I think that you – from what all you've been doing up until now, there are some groups you could start with to actually form sort of a communication

working group with specific audiences identified and some organizations, it won't be everybody, but a few organizations to begin that discussion in a more regular way, and it's just to sit down together, talk about the challenges, but not have a meeting every six months or a year, but really come with some charges for the group to come up with, what are the objectives we're trying to address, what's the scope, and then what's the plan of communication, you know, whether it's the pharmacist or physicians or patient groups in some focused, limited way, kind of like your Mini-Sentinel, this is a mini communication strategy working group, but I think they have to do more than just convene.

DR. McCLELLAN: Rachel, any further comments on this right now? Okay. Before we go to the next question, one of the issues that did come up was, look among all of the Sentinel partners, there are a lot of organizations that have members, beneficiaries who are, in effect, participating in Mini-Sentinel now. Any thoughts, ideas about how that – what kind of communication with them about this program is taking place now and what kind of communication may be optimal? I know we have a number of participants from health plans and other data sources here in the audience, and I can go back to my old classroom style of just calling on people, or if maybe one or more of you could come up to the microphone, I'd really appreciate hearing thoughts on that, too. But in the meantime, go ahead.

MR. WEITZMAN: Steve Weitzman, DataPharm Foundation, with a ph. I represent institutional memory going back to Doctor Edward's days, and my major concern in all the discussions that we've had today is the lack of funding for FDA. And I don't mean FDA at large, I mean the Center for Drugs and Biologics, which is a very serious problem that all stakeholder groups should be advocating on a non-partisan basis.

Mark lived through it, Dan lived through it, and I think it's remarkable, and congratulations should go to Doctor Woodcock for staying here despite her deputy going to Am Jam where I'm sure he's enjoying himself at the present time, leaving all the headaches at the FDA. But I think that's a very serious problem.

To go to Leonard's point, Leonard raised Vioxx. A very interesting situation with Vioxx. The data now is showing that since Vioxx is off the market, an increase in bleeding. And

there has been consideration of bringing Vioxx back onto the market. And Mark is sitting there wondering what to do. Obviously, he's scared. Dan raises the issue, product liability, what do we do. And all of us here know that despite how good we do clinical testing, there are going to be things that we're going to discover after a product goes out on the market. And how do you protect GSK and the other companies for a legitimate risk in terms of investment going forward and not to get penalized by the surprise, and that is part of the dilemma of your communications with the public. I don't have an answer –

DR. McCLELLAN: But do you have a question about the liability issues related to this evidence and –

MR. WEITZMAN: Yeah, and this is a fundamental issue, can we, on an individual patient basis, until it gets down to the doctor with the patient, really do anything in communications?

DR. McCLELLAN: I mean there are several questions in there, but I think this liability issue is an important one, it's come up in some of our previous discussion and certainly been an ongoing issue for the Sentinel Initiative, and this gets back to some of the individual communications issues, as well. Go ahead, Leonard.

DR. LICHTENFELD: I say this with some trepidation, but I will tell you I have been concerned about the liability issues for several years. In my past, when I used to live in Baltimore, I did a fair amount of malpractice related work, primarily defend some plaintiff, and so I have some insight, and I will tell you that when I look at what I call the big mega data base situations, for example, and I know there's some insurers present in this room, there's some insurers who participate in this project, but they have large data bases.

As part of that – managing those large data bases, they have practice patterns, and they have notifications, they have all sorts of things that they do with their physicians and with their patients, but with their physicians, and there is no fundamental protection for them trying to do the right thing to improve the quality of care through that process.

So here we have another situation where we're trying to improve the quality of care, and I think that one of the things that was never addressed by either party when either party

was in control of their respective House and Senate, so to speak, was in the issue of tort reform, to try to figure out how can we as a country do the right thing by our patients and protect the party's interest if, in fact, there is some legitimate public need to do it, and I think we need to get past that.

So I think the liability issue is real, it's been out there. Why it hasn't penetrated – pierced the veil, so to speak, at this point, I don't know, but having said that, I think it's important, if that's a concern of the Sentinel project, it's a concern elsewhere in quality of care, in administration of quality medical care, and I think we need to really address it and do it the right way.

MR. TROY: Well, it's not just the pharmaceutical sector that potentially faces liability associated with this as, you know, perhaps been explicit. I mean if the data partners have this information and they don't warn about it, right, are they then liable for failure to warn, never mind us?

MS. WEINBERG: That's right.

SPEAKER: And to play off that, too, some more, you know, it's going to potentially increase liability for physicians, too, because as a learned intermediary, do they have an obligation because this information is out there, to provide it to patients when it may be softer data than they would normally react to? So it may create increased concerns amongst patients because physicians feel like they have to share this information with the patient.

MS. WEINBERG: So I would say that better information, more information is better than what we have right now. And I absolutely think that we can only make things better if we get this information, which is better data, more data, more information than we've had, which is what patients want, and we communicate in a way that tries to mitigate against the potential downside, but it, in my mind, will be far better than what we have today.

DR. ZUCKERMAN: I would love to agree with that, and I do agree with that, and I would just add that I want to make sure that we don't end up with manipulating the system by manipulating informed consent processes to make them evermore protective, but not informative, because a lot of informed consent forms now, you know, basically warn about, you know, you

could die, and every person you've ever met could die if you take this product, and I've actually signed a couple of forms like that, so I have experience, and so we have to make sure that people are really being informed, not just to protect their doctors or somebody else from liability, but to inform them in a way that's useful.

DR. McCLELLAN: All right. So I heard a lot of agreement there about the value – the potential value of this information, of getting better, useable information out to consumers sooner rather than later. I'm not sure I heard any specific suggestions on how to address the liability concerns along with this. I think you agree that the question is a problem.

SPEAKER: Well, you know, I thought I did say something. I think it needs congressional action. I think there needs to be tort reform that protects people who do – who engage in realistic quality initiatives to improve the public health, and if this falls under that, then I think that needs to be part of it, and I think there are a whole lot of other things that some folks do that could be a part of it.

I'm not going to write the legislation sitting here, but I will tell you, I think it's time that we tackle this. And I could get in a long discussion about state versus federal and all that. I don't care how you get it done, but, you know, when somebody tries to do the right thing, and they're afraid to do the right thing because they're going to find themselves – you know, you all can sit around – I don't know how many of you are doctors in this room and I don't know how many have ever been sued and I don't know how many have sit in the courtroom, but you can talk theoretically about the power of the jury system, go sit in the courtroom for a week and have somebody call you a liar and a thief, and when you tried to do the right thing.

I'm not saying, you know, so it's not necessarily the doctor in this case, it may be the company, it may be the – I don't know whoever else it may be, the insurer, what have you, but it's about time we recognize that we have a huge gap in quality medical care, we don't have adequate information about how we deliver that care, we're sitting here talking about how we can find out what the real reactions are to medications, and all of us know when they go out into the community, there are potential reactions, and we need a system in place to get the job done, so figure out how to do it.

I can't do that here, but it's time, if there's some smart people, let's figure it out. And it has to be federal, make it federal, because they've ignored it for too long.

DR. McCLELLAN: Thanks, next question.

MR. FITALL: Simon Fitall from Galileo Analytics. We work with the analysis of electronic medical record data all be identified. A couple of points come to my mind; one is that the ability to surveil tens of millions of patients on a continuous basis already exists, but it's commercial, it's not federal, which opens up the opportunity for a commercial entity to find out stuff that a Sentinel project won't find out for another two or three years. How do we envisage that situation in terms of the way in which it potentially opens up two opportunities?

One is the opportunity for the commercial entities to influence the way in which the Sentinel program questions are asked, and the other is that you end up in a situation where one study demonstrates that five different patient groups each have totally different safety profiles, and as a result, all five people sitting on the panel are saying different things to their particular constituents.

DR. McCLELLAN: I think part of that question might be good to address to our next panel, which is going to include a number of private sector perspectives including some that have a commercial role here, too, but I would be interested in any of your responses. It was a good question. Any thoughts? Okay. We will come back to the topic. Sam.

DR. NUSSBAUM: Sam Nussbaum from Wellpoint. Mark, I'll take you up on your challenge to respond to health plans effectively communicate this information, and Rachel, to you, also. First, it's important to recognize that we do have lots of communication with our members, but we really believe fundamentally that the physician and the health professional should be at that very important point of sharing information in confidence, but they need to have the information to share.

So what we do today is, if people are involved in our care management or disease management programs, we actually reach out to them, by nurses, we've got 4,000 nurses, and those nurses will share basically best practices, gaps in care, when appropriate therapies are given or not being given in accord with clinical guidelines, and we try to do this as

much as we can with physicians.

When we have actually found through our own safety research, and we'll talk about that in the next panel, what we do is actually make that information known to our members. So, for example, when there was emerging information on the safety of Cox 2 drugs, we actually reached out to all of our members taking a number of these drugs, told them what our own findings were, and then said speak to your doctors about whether there are alternatives for you, so that's the second overarching theme.

But one more element that we do, and it's really been controversial initially when we got it underway, but it's working far better than many of us ever envisioned, and that is, we take claims data and we look at guidelines, best practices for clinical care, often advanced by specialty societies, and if there are gaps in care, and we get this from claims, we actually notify our members and their doctors where that gap is and where the evidence lies.

So initially we had, you know, a lot of controversy; are we practicing medicine, are we telling patients more than their doctors are telling them. But now it's become increasingly recognized that this of value, that often it's not the doctors or nurses or others are not giving the right care, it's that they just didn't have the information on which to base their decisions.

All that said, I think that out of Mini-Sentinel and Sentinel has to come a more concerted effort to message when we do find important issues, because it is not going to be reasonable in this very complex environment for physicians to give one set of information to patients, for health plans to give another, to the FDA to, you know, sort of give perhaps even a third overarching consideration, so I think that's one of the opportunities as Sentinel moves further, and certainly Mini-Sentinel, is how do we get this information out in an informed way, in a way that people can really understand and in a way that's meaningful to them and in a way that looks at what alternative treatments are.

DR. McCLELLAN: Comments on Sam's?

DR. LICHTENFELD: Yeah, if I may, and frankly, that was exactly the kind of thing I was talking about a couple minutes ago, when you mentioned about analyzing your data, notifying and so forth, because that's exactly the process. But let me share something with you

that I'm a little concerned about and I didn't get a chance to mention in my talk.

There is an assumption that I'm hearing, and I'm not, you know, criticizing, but I think it's an assumption that what comes out of Mini-Sentinel when this diabetes/AMI study is run that is going to give us the answer. I don't want to sound -- look at my FDA colleagues; we were talking about this at lunch. My understanding is, and correct me if I'm wrong here, in the interest – and I read this and that's what came up at lunch, I read it last night on the plane, in the interest of transparency, the objective of this program is to get the information into the hands of the public very quickly.

I know that is the data is run, the expert panel looks at it, I assume an expert panel or whatever, processes it, the FDA looks at it, and the FDA says, you know, is going to try to release that.

All of us sitting in this room can understand that what we're looking for are signals, thoughts, things that need to be confirmed, I would think, need to be looked at, and not absolute evidence of conclusion, and that's the risk, so that the Sentinel information may have to be further evaluated. I don't know what processes may be used, so I don't want to get ahead of myself, but it is not the final word.

So Sentinel can come out, and we can put into the public arena Sentinel showed X finding, but there will be a legitimate discussion, and I like to say this about all scientific findings, within the medical community and experts – among experts who will parch that data, talk about it. It's like when the major medical organizations had their meetings, and something gets blown around the press on an abstract, and you get a phone call from the reporters and you say, I'm not ready for prime time, you understand what I'm saying, you must run into that all the time.

So we have to be careful that the Sentinel data and Mini-Sentinel data not be held out as being the final answer, but merely the beginning of the answer to try to address the question.

DR. NUSSBAUM: And while that may be valid, I certainly appreciate that perspective, think about every scientific report that comes out, whether it's ASCO or other meetings, we all then, you know, we have wonderful hope, and then it's tempered by scientific

knowledge then how its drug or treatment is used in the real world.

What happens here, though, is, we have an observational base of tens of millions of individuals, and I think that it allows extraordinary acceleration of good information. So if you look at the controversies in treatment over the last decade, many of them still aren't answered. And it takes really a decade and many, many tens of millions of dollars to begin to answer them. Here, I think we're going to have some real world observation based on, you know, broad populations that can highly inform and help us make those decisions.

MR. TROY: But I heard FDA very clearly, I heard Rachel say this is a tool, it's not definitive, and there is going to be the reality of false positive, false negative results, right. And so let's – as powerful as this is going to be, it's observational data, and it needs to be viewed, as the FDA has said, and I think the only point I'm making is, we hope that FDA can be as clear to the public at large, whatever that means, as it has been in this room, to say that this is not – it's not the be all and the end all because it's just observational data, and there are, you know, lots of other pieces of data that need to be brought to bear in order to make a really informed judgment, that's what FDA does, that's what it has to do, and the concern that at least (inaudible) is that we not get so swept away by the power and elegance and beauty of Sentinel or Mini-Sentinel as to say that it is the be all and end all and it's going to provide all the answers.

DR. NUSSBAUM: And it seems to be a theme of this meeting that whenever Rachel's name is called, she is right there to respond to the question. But I think what – that was not my –- my statement is, this will rapidly advance knowledge in a very different way than going back and looking at the gold standard randomized perspective trial.

Plus, part of Sentinel and part of the work going on is to really enhance statistical methodology that I hope is going to be part of (inaudible) so we're going to start seeing integration of a lot of these activities so that we can get to a more fundamental understanding and knowledge much more quickly.

It will never be the sole answer, but then again, think of, in instances where certain therapies have proven to be ineffective or now not on the market anymore, that was, you know, sort of met analysis and population studies, so I think this is one accelerant for that

process.

DR. McCLELLAN: So Diana, I know Brian had a comment, too, and then Rachel gets to comment, and one last question, as well, but you all go ahead.

DR. ZUCKERMAN: Yeah, I just want to agree with what you just said. No one study can ever answer, you know, be the definitive study, but you put information from different parts, and this is potentially a huge, rich amount of information. Somebody earlier said something about how unfortunately the data set won't have too many people who are very young, like kids, and very old, but compared to clinical trials, it's going to have a lot of information about children and the elderly that you'll never find in clinical trials.

Compared to the data sets used to make the original approval decision, it's going to have a lot of information. And, no, claims data isn't, you know, lacks a lot of information, but one of the things that we heard about in the earlier panel is that data set, you know, data are being reviewed very carefully, they're not just saying, okay, the claims data says this, they're looking through medical records, they're gathering additional information to supplement the claims data.

So, you know, no, I'm not saying that Sentinel is the be all, end all data set, or data sets, but it's going to be a hugely important one, and I agree, it's going to accelerate our ability to make decisions as best we can. I mean really it's often impossible to know whether a person had a heart attack because they took a particular drug, it's virtually impossible to know for any one person, but you can, I say that with trepidation with all the lawyers in the room, but you can say, if 100 people take this drug, compared to 100 people or 1,000 people who take something else, they're more likely, and that's a very important source of information.

DR. McCLELLAN: Brian.

DR. GALLAGHER: To amplify a little bit what Dan said earlier, one of the things that I think we need to guard against is that Sentinel information doesn't become more important than pre-approval testing information, because you could have something that's a black box warning, and because of the risk benefit analysis, the patient is still allowed to take that, but then there's all this press about, you know, these new things were discovered, and the pre-approval stuff doesn't come out in a big press release like that, whereas the post marketing stuff, it always

does.

And so we need to make sure that patients understand, back to having providers be able to explain what this information means, that just because they found something post market and there was a big press release about it doesn't mean that it's a really, really horrible thing that's worse than other side effects or issues with the medication.

DR. McCLELLAN: Rachel.

DR. BEHRMAN: Just to answer Dan's point, yes, we agree, the Sentinel is a tool in a toolbox, and (inaudible) data has been posted quarterly for quite a while, the world hasn't ended. So I think we at FDA are pretty comfortable figuring out how to – it's our bread and butter, to try and reduce uncertainty, and this is a tool.

Whether we're good at communicating Sentinel's strengths and limitations, at the same time we're trying to sell it so we get resources, that's trickier. But I wanted to return to liability, because that's very much on our minds. Anything that can drive Health Corps or Glaxo or everyone else away from the table is on our minds and we're losing sleep over that.

So liability, short of congressional action, which one – we obviously don't control, whatever, how does one – and so we thought – we convened the privacy panel, the report, that was extremely important and very helpful, and we've been going back and forth about – we had one meeting at Brookings on liability, and we are considering how to move forward, how does one – how do we position message tackling liability, which we believe is crucial to keep the data partners, the industry at the table, and it's crucial that the Sentinel to protect patients, but we also use the patient protection effort, and not have it appear as if we are essentially, for one –- a better term, selling out the patients and the consumers.

DR. McCLELLAN: The last question. The only solution I've heard from the panel is the legislative one and that it's a challenging issue.

SPEAKER: It has to be, there is – Mark, the bottom line is, it has to be legislative, there is no other way. You can't have a public relations campaign; you have to have legislative action.

DR. McCLELLAN: All right. We'll be coming back to –

MS. WEINBERG: Can I just make one comment? I mean there are different kinds of liability, too, I mean and you're hearing what the physicians or other providers feel on their profession and their practice or what companies feel when they are in a situation where they're sued or have a liability concern, and so on it goes. So it's not all the same. Some may be addressed eventually congressionally. I still think that where we are now, and with the real concerns of the FDA that were just stated, that the answer is in communication, communication, communication. And listening to the other parties, figuring out what the concerns are and how to address them, and you don't do that in one fell swoop or in one particular way.

And I applaud FDA for being concerned about it with the different stakeholder groups, and I think that will help you as you move forward.

DR. McCLELLAN: Thanks. And we're running a little bit over, but I would like to get in this last question very quickly.

MR. BORTNICHAK: Thanks very much. Hi, I'm Ed Bortnichak from Merck. And just a simple question to try to put together an answer to a question to panel one, to combine that with a response that I think I was hearing from everyone on the panel this afternoon, and that was a key question that Dan Mines, Doctor Mines asked this morning when he asked the Saxagliptin protocol, the proposed Saxagliptin study, what is it, and the answer came back quite resoundingly from the scientific panel that, well, if they had to force a decision, there was signal refinement, but it's really a continuum and the borders are very fuzzy between these divisions in the process of data gathering within Sentinel. The point that you all seem to be making, each in your own way, is that the communication will be very much driven by, indeed, where we are in the data gathering process and the confidence that we have, in the position of the data gathering.

So my simple question is can we evolve in effective communication strategy a way forward with communications if those borders are still fuzzy, or is it waiting essentially a better division between these phases in the data gathering? Thank you.

DR. McCLELLAN: An important question, need a quick answer.

MS. WEINBERG: Well, I'll just say, I mean a lot of it is going to depend on what the data show. I mean if you have really persuasive, strong data, that's a whole different story

than if you have very small differences that are statistically significant because you've got three million people.

You know, I think that it's going to depend, you know, how persuasive, you know, where are we on this continuum of signal refinement and findings is really going to depend on the data.

DR. BEHRMAN: I just want to say, that is exactly what we're trying to address and we recommend that there be an objective framework developed now that can look at, if this were to leave the data or happen, this would – this is when we would go, and take into account individual circumstances, et cetera. But somebody has to sit down and really develop a framework for how and when these decisions get made.

DR. McCLELLAN: All right. I'd like to thank all of our panelists and all of you for a really interesting discussion on an important evolving process. I look forward to hearing next year's version of this discussion, too, clearing an evolving set of issues. We're now going to take a short ten minute break and then reconvene probably for our last panel. Thank you all.

THE BROOKINGS INSTITUTION

THIRD ANNUAL SENTINEL INITIATIVE PUBLIC WORKSHOP

Wednesday, January 12, 2011

PARTICIPANTS:

Session III: Sentinel as a National Resource for Evidence Development:

MARK McCLELLAN, Moderator
Director, Engelberg Center for Health Care Reform
The Brookings Institution

JANET WOODCOCK
Director, Center for Drug Evaluation and Research
U.S. Food and Drug Administration

SHERRY GLIED
Assistant Secretary for Planning and Evaluation
U.S. Department of Health and Human Services

DAVID BLUMENTHAL
National Coordinator for Health InformationTechnology
U.S. Department of Health and Human Services

REED TUCKSON
Executive Vice President and Chief of Medical Affairs
UnitedHealth Group

SAM NUSSBAUM
Executive Vice President, Clinical Health Policy
Chief Medical Officer, Wellpoint, Inc.

Closing Remarks:

MARK McCLELLAN
Director, Engelberg Center for Health Care Reform
The Brookings Institution

* * * * *

P R O C E E D I N G S

DR. McCLELLAN: All right, so, I'd like to ask everyone to take their seats. We're going to get started right away.

We have a lot to discuss. And I especially want to thank all of our panelists for this panel, and everyone has a busy schedule, but these people really do, and for our last session today on Sentinel as a Natural Resource and Sentinel fitting into a broader set of approaches to develop better evidence in the United States. We're going to look beyond medical product safety surveillance to think about ways to coordinate what Sentinel is doing and what FDA's post-market safety activities are undertaking with other ongoing evidence development initiatives.

And I know earlier in our previous discussions, we identified a number of significant issues and challenges: methodologic, resource related, infrastructure related, communication related, and so forth. So, certainly, there are some real challenges here, but I think something that's very important to recognize is that a lot of other issues and a lot of other areas where we are trying to develop better evidence, whether it's on quality of care or comparative effectiveness or other topics are facing some of the same challenges. So, thinking about all of these issues in a broader context is very important and we've got a number of people here on this panel that can provide a range of those perspectives.

We'll be hearing first from Janet Woodcock, the director for the Center for Drug Evaluation and Research at FDA.

And then Sherry Glied, the assistant secretary for Planning and Evaluation at the U.S. Department of Health and Human Services, and there, ASPE is very much involved in some of the strategic thinking at HHS on developing better evidence and the range of different data resources available and methodologic resources to bring to bear on that challenge.

And then my friend, David Blumenthal, the national coordinator for Health Information Technology at HHS. ONC has been very much involved in leading some of these major steps to support better information systems for evidence on safety and many of these other areas, as well.

And then we're going to hear from a couple of private sector leaders. Sam Nussbaum is the executive vice president for Clinical Health Policy and the chief medical officer at Wellpoint. You've heard from Sam briefly earlier, and, as you know, they are one of the major participants in the Sentinel Initiative.

And Reed Tuckson, the executive vice president and chief of Medical Affairs for United Health Group, oversees many of United's strategic leadership initiatives related to improving quality of care, improving evidence, and other related areas, as well.

So, it's a terrific panel, and, once again, I have the same format with some initial opening comments from each of our speakers, and then you all should be ready for comments and questions to continue that dialogue.

So, let me get started with turning to Janet.

DR. WOODCOCK: All right, so, I'm going to make a few brief remarks about where we are now and how this might fit into a broader scope of evidence development from electronic health records.

So, what we've been talking about in Sentinel is, of course, medical product safety surveillance through the Food and Drug Administration, through our coordinating center at Harvard Pilgrim, and there is a circle in the center of this diagram. And I think this circle is important because really the data partners have to be central to this whole enterprise because they are not only the folks who have the patients, they're the folks who need the information to deliver the best care.

And, so, while the Food and Drug Administration and other folks who might use these data are important, the real key should be driven by those who have the data and those who have the patients and those who represent patient and provider communities. So, they're in this center of this, and, of course, there are also payers who have data and other groups that have data, and there are registries out there, and within this circle, it shows that from the analytic perspective, we're trying to unite this in some way using a common data model. And I think that's been talked about this morning; that's how you can do queries.

Now, of course this isn't the only use of these data, and what we've heard and

we can maybe hear a little bit from some of the folks representing health care systems is that they are viewed as the repository by everyone of the data. So, this data might be used for medical product safety surveillance, it might be used for quality, it might be used for many other things, and, so, they have many people coming at them asking for the use of this data.

And another area related to medical product safety surveillance is that there are many sponsors and other researchers and private parties who are interested in medical product safety who are not going through the Sentinel, not through the Food and Drug Administration arrangement, but also want to do the same kind of queries and get the results for their purposes, but from the same data sources, the people in the center of this diagram. All right, so, one thought that we've had is can we have more a public-private partnership that would also enable this type of activity utilizing the same infrastructure because don't forget the people in the center of this diagram, do they want to have 7 common data models and 12 different infrastructures to offer these data for different sources?

So, that raises the question, if we move on, what's the potential future scope of using secondary electronic health information generally? All right, and it isn't just medical product safety. How about on the other side of the diagram, quality of care? The data that would be accessed from these data partners, registries, payers, is the same kind of data, and should they have another several sets of common data models for that use of the data?

And then public health surveillance, there are many, many issues that people want to look at this type of data for public health purposes that is separate from medical product safety, and, again, the same group of people may be asked to contribute data to that use.

And, finally, there's great interest in biomedical research, identifying and accessing patients with particular conditions or whatever based on this electronic health data, which is a lot more efficient probably than trying to recruit them in one or two medical centers in the United States to find these people to identify them and recruit them into studies or what have you. Again, it's really the same type of data that we're talking about, probably not just the claims data, but the extended health record data put into some type of query-able form that would be used here.

So, and then at the very bottom, a lot of people are initiating comparative effectiveness research on electronic data that, again, the source of those data would be to providers, the registries, the payers, and so forth. And, so, we are hoping that we're building Sentinel, but if you see the larger circle around this, which it says "distributed network governance," we're hoping that whoever comes together for whatever purposes of use of electronic data, we could build a common infrastructure. I think the Office of the National Coordinator is building the existence of that electronic data, which doesn't exist to the extent that it needs to exist now. They're also building some of the interfaces and interchanges so that the data is easily exchangeable, but these uses of data are analytic uses, secondary uses where you have to do analyses.

So, they're extremely common, and I would be very interested to hear from the folks on the panel who, in fact, represent a health care systems or payers and so forth about how all this could come together. I think this is one way that it could come together that those who have the data, the data partners, could actually represent a distributed network that could have governance, could have common data standards, and would kind of be the interface between all this data that's out there and all these different analytical needs that exist for secondary electronic health information and the use of it.

And we feel that in Sentinel, we're moving ahead on our part of this, which is simply the medical product safety, but we're certainly more than willing to only be a node on this larger network that we would foresee existing in the future for analysis and advancing public health in general.

Thank you. (Applause)

DR. GLIED: I can stand because I don't have any slides. So, what I want to talk about today is an initiative at ASPE in my office that is kind of complimentary to the Sentinel Initiative, which is ASPE's Multi Payer Claims Database, MPCD. And also to talk about how Sentinel and the Multi Payer Claims Database fit into the overall HHS data strategy, which we're continuing to develop.

I want to start off by talking a little bit about this ASPE project, the Multi Payer

Claims Database, and to talk about some technical aspects of that database, which I think complement a lot of the discussion around Sentinel, and then conclude by talking more broadly.

So, our Multi Payer Claims Database was established as part of the Recovery Act, and was intended as part of its investment in the infrastructure around comparative effectiveness research. That kind of research is going to require the development and expansion and use of many different kinds of data sources and methods, and this Multi Payer Claims Database is intended really as a pilot project to think about where we can go with that kind of infrastructure development.

The project began just now in January. It's supposed to run for 33 months. And we're working to build the database that incorporates data from many different types of health insurance plans, and includes as many people as possible so we can conduct comparative effectiveness style research on multiple priority populations, on multiple interventions, and many kinds of conditions.

The MPCD is going to be implemented as a hybrid architecture, so, it's going to incorporate both a central warehouse and the kind of distributed data network that you see in Sentinel. There will be like in Sentinel a central coordinating center that will perform the function of taking requests from researchers, querying different data partners, consolidating results, and delivering them back to researchers. The central warehouse is going to include from CMS. We are still working out exactly what data that will be, and private plan data, which are contractors, are going to de-identify so that they can be put into the central warehouse. That warehouse is going to be supplemented with a distributed data network. The network will include several private sector health insurance plans and possibly also some providers who voluntarily choose to participate, and as in the Sentinel Project, they would allow their data to be accessed from behind firewalls so that they can retain control of their data and privacy concerns can be addressed.

We're also collaborating very closely with ongoing state efforts to maintain and develop state all payer claims databases and the distributing network is intended to also include data from those systems.

As in Sentinel, the coordinating center is going to query the distributed network

with one set of programming code, get the results from multiple partners, pull them together, and send them to requesting researchers.

There are a couple of innovative features in this design that I think I want to emphasize. I think one important feature is that it's going to incorporate analytic tools that allows researchers to perform preliminary analyses before they actually have to make full data requests, and the hope is that that will allow us to really tailor the data that people need and make the request happen quicker, so, on a faster timeline.

Another key feature is that we intend to lay the foundation to incorporate clinical data in the database into the future. That should make the database much more useful for doing clinical types of comparative effectiveness research.

Very clearly, there are some important design and methodological overlaps between the Sentinel Project and this project. But their missions are different in intention. So, the Sentinel Project's mission will concede for the primary application of drug and device safety surveillance, really resonates with the comparative effectiveness theme, and we can imagine that there are comparative effectiveness research questions especially around drug and device choices, but which the Sentinel Network would be ideally suited.

In parallel, the Multi Payer Claims Database, which was built to contribute to data infrastructure development for comparative effectiveness research, will also likely be valuable for additional applications, including safety surveillance, delivery system research, and so forth.

So, we're actively exploring synergies between the two projects, particularly by way of the Mini Sentinel Pilot Project. We're looking into ways that we could utilize the same data network infrastructure, including overall design, design platform, the way communication occurs, the format for data so that requests will be coordinated and we don't have to bother our data partners unnecessarily.

We also hope to coordinate outreach to new data partners to minimize the cost they face in participating. Based on feedback, we are really designing this network to be very cognizant of what our partners need in order to participate.

Going forward, we also see that future investments would be made in the context

of both initiatives. For example, both initiatives are aiming to capture clinical data as they evolve, and, so, we are going to be working together to make sure that we can facilitate the process for doing that.

One idea that we've been developing is at the Multi Payer Claims Database, and Mini Sentinel could each be a node on each other's distributed network. That would mean that they would overlap, we'd get the full richness of both efforts, and they could serve as a portal to access of complementary set of data sources.

In collaboration with the Sentinel Project, we're working closely with other divisions, particularly with CMS, but not exclusively so, to determine how the Multi Payer Claims Database can potentially support other comparative effectiveness work and other affordable Care Act initiatives and other data strategy initiatives across HHS. In particular, HHS is really committed to a new initiative that's focused on data transparency, on getting data out to researchers in a variety of ways, and we're charged in the Affordable Care Act with releasing a great deal more data that we have in the past. We're trying to see whether this Multi Payer Claims Database and other similar initiatives are a way to meet those needs.

For example, we're working to create virtual research data centers that will allow use of data without possession of the data so the privacy is protected and to disseminate additional public use files, which are files that are stripped of identifiers so that they can be used with virtually no privacy risk. We're exploring how the Multi Payer Claims Database and other initiatives like Sentinel can help support CMS initiatives around performance measurement, reducing readmission rates, and other delivery system reforms. We're also developing an HHS-wide data strategy that will think about how to incorporate ideas like the Multi Payer Claims Database and Sentinel and the new electronic health records that we hope will be coming online soon within a coherent framework in conjunction with existing HHS data surveys.

So, HHS has a long history of doing utilization surveys, provider surveys, and so on, and in this new era of a lot of claims data and electronic data coming online, it's really important for us to explore what is the place of surveys, what is the place of claims data, what is the place of clinical data in constructing a picture of the health care system and enabling policy

reforms going forward, and that's one of the big efforts that we're doing within the department.

Overall, a key departmental strategy which I think is evident in both the Multi Payer Claims Data and in Sentinel and so on is to think about how to best use new methods, advances in data storage and computation, in protecting privacy, and increasing availability of data just as more of this goes online to learn more from the health system all around us and to put that learning to work in the service of our programs. Together, these initiatives form an important part of the new research data infrastructure at HHS. (Applause)

DR. BLUMENTHAL: Well, good afternoon. It's great to be here. I want to thank Mark for his continuing efforts to explore opportunities to use information better to serve the health care system and Brookings and the Engelberg Center, and FDA for the leadership it's showing in this Mini Sentinel Network, which is an example of exactly the kind of use of electronic information that the Office of the National Coordinator, my office, is charged ultimately with promoting, and, of course, they are way out ahead taking advantage of existing electronic sources of information.

This conference focuses primarily on what are called in the lingo secondary uses of electronic health care information, and that may lead you to ask the question: So, what are the primary uses? And the primary uses are one of the Office of the National Coordinator's primary charges. We are not without responsibility for encouraging the secondary uses. In fact, that's very much on our radar screen, and we're very committed to it. But when the Congress created the Health Information Technology for Economic and Clinical Health, or HITECH Act, in 2009, they charged the Office of the National Coordinator with creating a nationwide, interoperable, private and secure electronic health information system. And just a modest charge. (Laughter) And first and foremost, working with CMS, they charged us with getting the nation's doctors, hospitals, and other health professionals to be meaningful users of electronic health records.

In a very basic way, our job is to make your health care better by giving you access to the benefits of the most modern information technologies in a private and secure manner when you go and see your health care professionals every day and when your families do the same thing. So, we are very focused on quality of care, improving the efficiency of care in

the personal health care system, but we want to do that in a way that enables any information harvested for those purposes, collected for those purposes, to be used for the kinds of initiatives that the Mini Sentinel and the Multi Claims Database make possible.

We have a huge number of programs -- not huge, but a substantial number of programs that are aimed at helping solo practice physicians, for example, in rural areas get to meaningful use of electronic health records. Ten and twenty-bed hospitals in rural areas get to the meaningful use of electronic health records. And, also, of course, larger practices and larger organizations. But we are also very much focused as part of that on making it possible for the information that enters their records to become electronic to be available for exchange across practices, across institutions, and ultimately in the process of exchange to become accessible for these other very important uses, the so-called secondary uses.

So, we actually are also spending a great deal of effort, increasing amount of effort on what's called exchange and also which requires something called interoperability, meaning that when data moves, it can be received and interpreted and incorporated into the next electronic modality so that when your cardiologist needs to communicate with your primary care physician, that can all take place electronically without any paper being involved. Or when the hospital, when your primary care physician wants to get access to the results of the test that you received at your hospital when you were hospitalized, that that can all happen electronically.

Once you begin to mobilize data in that way, you can technically if the standards are clear enough and the definitions are clear enough, the vocabularies are clear enough, you can begin to tap that data for so-called "secondary uses."

Now, we are involving lots of groups in that process. For example, we have given grants to all the states and territories to enlist their support in creating the infrastructure for health information exchange. We have set standards for electronic health records to encourage interoperability so that they use the same words for the same things that you can identify data in their records to pull it out, and we have also developed a process for certifying electronic health records to make sure they actually incorporate those standards before they are marketed. And

we've already certified over 230 electronic health records and modules to see that they can form to the standards that we've adopted by regulation.

The other thing that we've paid a lot of attention to is the privacy and security of information, and we have several federal advisory committees that has given us enormous assistance, and they are helping us right now with defining how do we protect, what policies are necessary with respect to patient information, with respect to security so that when information starts to flow in the health care system in the primary use, it can also be made available in a private and secure way for secondary uses.

Recently, the President's Council Advisors on Science and Technology, so-called PCAST, made a series of recommendations to us on this subject which we are actively pursuing and could play an important role in making this exchange of information more widely prevalent.

One of the things that we have to manage in this process, and I think it's an underlying theme for all of the work today, is the question of whose interest is it to create these data sources and to then use them. The fact of the matter is that for the local doctor and the local hospital, the local nurse, there often is no reward at all and considerable costs for putting data into electronic form and them exchanging it. That is a fundamental obstacle to everything that we are talking about today, and an obstacle that we have to solve as a society before we can realize the lofty ambitions that we're talking about.

What I like to say is that information exchange is a team sport, and you can be the best exchanger, you can be the Peyton Manning or the Tom Brady of information exchange, but if there's no one down the field to catch the information when you're passing it, you might as well hang up your cleats. We need teams, and those teams have to be nit together by business cases, by collaborative cases, by policy as communities to become nodes on this network that we're talking about. We do have responsibility speaking to the slide that Janet showed; we do have responsibility for creating the governance of the something called the Nationwide Health Information Network. We are responsible for creating a network and for creating a governance mechanism for it, and we are working right now on that process. So, I hope that we'll be able to work with Janet and other colleagues both in the private sector and the public sector to work

through that governance mechanism. The idea of distributed databases is very much on our mind, and it's good to hear that these are actually being made to work in real experiments.

There are huge technical and policy problems to overcome, but I have no doubt that we will get there, but it will require the collective activity of both public and private actors and it will require motivation to overcome those problems. And one of the things that I think we are going to have to work on very conscientiously is defining the business case that will result in the liquid information, the available information that the Mini Sentinel Network is taking advantage of and that all of us wish to have available so that our health care system can be improved.

Thanks very much for your attention. (Applause)

DR. NUSSBAUM: And it's really wonderful and energizing to be here and see all of us working together to begin to improve the quality of health care and what clearly needs to be a transformation of our health care system and the early and what we envision will be highly successful use of data models.

Wellpoint and its subsidiary health corps are really proud to be a key partner in the Mini Safety Sentinel Initiative. We're deeply committed to working with federal agencies, particularly the FDA and CDC, with whom we're working, to improve health care for the American people. Why? If we look at our own footprint, we have 14 Blue Cross Blue Shield plans, we cover more than 33 million Americans, that's 1 in 9, we work closely with the Blue's Association that has about 100 million Americans, so, that's 1 in 3, and it's that scope and breadth of the data, some of which has been talked about today, that gives us both the capability of working with partners and the responsibility to improve the quality and safety of health care for our nation.

And health plans today have critical needs that are not being met with knowledge. We have need for evidence, need for real world information to make decisions regarding medical and drug therapies, but also what are the best approaches to care for clinical conditions? We also need to extend the observations that you heard about today in drug safety to comparative effectiveness research. Janet, you've mentioned that, and Sherry and David. That's really essential to go beyond where we are.

So, I'd like to briefly mention three themes. The first theme, which has been the

focus of today, is the data environment; the second is a commitment of health plans to advance knowledge of what works in health care. Health plans haven't always taken that as a very meaningful commitment, but it is, and it needs to be. And it's also to collaborate with government, with industry, and with academic partners to achieve those goals.

So, let's first talk about the environment. We've advocated for not only collaboration, but a federal data environment model for Sentinel, and we strongly supported that type of model to advance comparative effectiveness research.

There's another great example that I know people alluded to today, and that's been the Vaccine Safety Data Link Project managed by Centers for Disease Control and Prevention, and that is giving our nation very important information on vaccine safety. So, why this federated model? Why have we moved there first? And it's really because each research environment and each research organization knows its source, knows how to manage that data and its complex systems, knows the apparent and then often the not apparent confounding factors, and has the ability not only to know how that data environment is managed, but if we need additional information, how to go to it, whether it's chart review, whether it's physician and hospital partners. So, it's really improving the utility and reliability of data.

The other issues that I think particularly in our political environment is that the federated data remaining local to the environment in which it's generated really allows a greater security than perhaps other models.

The third theme of this is, by its very nature, the collaboratives that have been described, and Mini Sentinel's a perfect example, is it maximizes the impact of a shared learning environment, and it's really as much the contributions of the data partners, the intellectual contributions, as it is the specific data that's going to advance foundational knowledge. So, it's the experience, it's the environment, it's the confidence in the data, and also the collaboration of federated partners. And we've been working in our company for over a decade to do a clinical outcomes and comparative effectiveness and safety outcomes.

And, so, what have we learned from that? First, we've learned that claims data is valuable for a number of initiatives, but not for all initiatives. So, we've been developing over the

last several years what we call an Integrated Research Network. We have about 4,000 hospitals and doctors now participating, and this enables us to perform much more robust research to use information, gather the point of care. David, to use the medical record infrastructure that is being built through your leadership. And, so, that's one way of actually taking this claims database and enhancing it.

So, we've got three projects underway in that area, we're working, again, with Harvard and Brigham and Women's Hospital and University of Pennsylvania, North Carolina, and a whole host of academic partners, including Indiana University and others.

The other theme of how can we make a difference in research is to collaborate with others. We're part of three; decide networks in the ARC sphere of accountability and influence. And that's the way we're going to get answers.

So, let me give you two specific examples of how we can get answers. I mentioned an earlier example of how we manage the COX-2 inhibitors, but when we looked at childhood asthma, we found that there were drugs that are least preferred or less preferred in any of the clinical guidelines, the clinical pathways for asthma, yet we found that the use of these drugs actually lead to reduced emergency room usage and reduced hospitalization when compared to the more generally appropriate beta agonist bronchodilators and inhaled steroids. So, what we did is what that information, which is published and which involved a lot of collaboration of asthma experts across the country, but we actually took this drug and moved it to a preferred tier, even though most health plans would not prefer it as therapy.

Back pain. It's ubiquitous. One in three of us experience it, we spend more money on back pain than other illnesses, but we look at over two hundred thousand of our members and saw how back pain was being managed. How within six weeks of non-neurologically sort of impaired back pain within six weeks. People were actually having thousands of surgeries, getting tens of thousands of MRIs, care that none of us would embrace, and we took that information and worked with the American Academy of Family Practice to develop some programs and also with Dartmouth Hitchcock in terms of evidence-based care.

Another initiative that is not only based on data, but on using this information a

far broader way is the work that we've done with the Indiana Health and Information Exchange, and Marc Overhage is in the audience, but with IHIE, Indiana Health and Information Exchange, we are part of what's called Quality Health First, and this is an initiative where all of the data from our health plan and others working with doctors and hospitals that generally are competitors in the environment drove a dramatic increases in quality. So, we took all of the information that we had, we measure a whole array of quality programs, we pay differentially for performance in these quality areas, and have made an impressive improvement in quality of care in Indiana. So, we were able to take and leverage the about $4 million investment that we made and improve quality to see scores dramatically improve on 10 clinical measures.

So, in closing, I believe that we have an opportunity based on the models that have been presented, collaboration that we can build, knowledge that we can gain together to significantly enhance and expand programs that drive quality and affordability of care. This is the power of the Sentinel System, this is the power of all of us working together, and we look forward to sort of harvesting the fruits of this work and working with all of you to continue to advance and improve health care.

Thank you. (Applause)

DR. TUCKSON: It's a great pleasure to be with you. I share my comments from the perspective of a Fortune 25 Health and Wellbeing Company that has a leadership position in the commercial Medicare and Medicaid and individual health benefits businesses, but also we are in GENEX, the largest data and analytics company. We offer our own electronic health record. We are engaged also extensively in the health information exchange business, and we look at this very broadly, and it is obviously exciting to us that this much progress is being made.

And what we also encourage as we experience this meeting is how thoughtful you are at being able to bring the necessary stakeholders together to think responsibility. We touch 650,000 physicians and other health professionals, 5,000 hospitals, so, we have a sense of scale, but we are really driven here and excited about is the importance of being able to meaningfully and responsibly improve the quality, the safety, the appropriateness and the cost effectiveness of the delivery system. I think you understand that we are at the tipping point, that

no way can we possibly afford the escalation in health care costs, especially given the drivers which are in the physician and hospital delivered care environment along with the fueling of technology and pharmaceutical innovation. This is where the issues are, this is where the problem is.

We have a gazillion people with preventable chronic illness who are being delivered into the hands of a delivery system that is more than prepared to continue to skyrocket costs out. So, if there's going to be something new, it had damn sure better work. (Laughter) It had better be cost effective, and we had doggone be sure that we can control how those things are distributed and disseminated through the delivery system.

We are interested in any ability to advance multi-payer data sources augmented by others to define and facilitate access to quality and/or the absence therein. We are very interested in having data and information to give feedback to the delivery system so it can ramp up its performance. We absolutely need to have data to be able to influence as we discussed in the previous panel patient choices and decisions. People have got to know what they should appropriately personally get access to and evenly what they stay away from, the good news and the bad news.

There are a gazillion people who are trying to these kinds of things. Good news and bad news. More than 100 requests on my desk right now. Please participate in data analytic, data aggregation activity for regional, statewide, or intrastate initiatives. Voluntary and mandatory. There's an HIE, there's a RHIO, there's Aligning Forces for Quality, there's the Beacon, there's the public surveillance and research, there's the regulatory activities, they're the primary care medical home and the accountable care organization demos. We love them all. (Laughter) They all cost money. Data is expensive. There are fees to participate and fees and costs to massage the data.

So, I love this meeting because you are saying we get it, we get it, we're not going to be crazy, we're not going to be irresponsible. We're actually going to all work together. Well, you better, because this has no chance to succeed whatsoever. None, if you don't. The data content elements, the data extraction formats, the data aggregation techniques, the files and

layouts and the formats, the structural measures for which you're going to evaluate quality and costs and whether or not it was a good outcome, all of these have to come together because, if you don't, it undermines the value proposition. Who in the world can develop a value proposition to scale this beyond the mini to the maxi if you don't do that? So, you have to line it up.

Because we have to be very serious about our responsibility to act on behalf of the people whose money we spend to access expensive health care assets, we have to think about these things from a couple of perspectives. Number one, the governance we talked about. Is it efficient? Please don't give us bureaucratic governances that make things tough. Are the people in the governance the right people? Do you have all those stakeholders at the table? And, above all, in that governance, is there accountability for the use of resources? You cannot imagine how many people get excited about ooh, ooh, let's do this. We're going to have a party. Mickey Rooney. Everybody's together. (Laughter) Are the responsibility of governance there?

Number two, the funding. What are the fees, what are the data management costs and are we keeping it to a minimum?

Number three, sustainability from a funding perspective over time or scalability, which you all obviously are, so, that's terrific.

Likelihood that it will get to the key quality and cost drivers. Everything isn't important. Knowing everything is not hey, did it decrease in emergency room visits? Did it decrease preventable hospitalizations? Did it decrease lengths of stay? Did it decrease readmissions back to the hospital? Now you're talking because that's what America needs. American citizens demand it. They can't pay for the rest of this stuff, so, it's got to zero in, it's got to be relevant. Everything isn't equally important.

And then you have to make sure things like new specialty drugs and new specialty pharma, and then there are the devices. So, if you contribute data, what do you get? If you don't contribute, what do you get? Data costs money. So, you got to level the playing field. You connect with registries, and what will the registries tell us? I want to know did that device by that company kill off my customer. Because I want to tell the rest of my customers please avoid that device. If it doesn't do this, what are we doing?

So, let's get specific. Can we get real? We have to be able to make it -- patients deserve real information to make real choices in real time about their health. We owe it to them, and I'm not going to be shy about asking for it.

And then we have to population specificity. Which people were supposed to get the thing? Did the bad outcomes occur? For what reason? So, I really want to know did the bad outcomes occur because the doc was no good. Technique was lousy? Bad patient choice? Didn't use it according to the prescribed mechanisms? Did the patient screw it up? Took it all kind of weird times in the day? Ate it with orange juice? (Laughter) I want to know whether or not it was -- and then I want to know about the outliers. I want to know whether or not the -- I want to know about early adopters. Hey, look, early adopters, now we know right at the point early on, hey, what happened? Is it just that you all were crazy over here, medical center number three, that we need to be able to drill in and understand? So, we want to be able to get at that.

And then, finally, I really want to emphasize this notion about getting to the patient-centered choices and decisions, and I'm glad that my colleague, Sam, talked about that because he's really, really right on. We get to have these conversations with people. Most people who think about health companies, most people do not take the time to understand what it is that we do. Somehow though you think we just pay claims in the back room and that's about the end of it. Now, thousands and thousands of people get talked to all day every day using every new technological device known to man to have a conversation about quality, about patient choice and decision-making. And, so, it is important for us to be able to take our capabilities and to describe that.

And, last, I'm really, really excited about preparative effectiveness research. We can't pay for crappy stuff. (Laughter) Doesn't work, not better than placebo, I could care less. That's the FDA, you all do that. (Laughter) Does it work better than the what we have now, from a total cost of care perspective, and then does it work better? Economically justify the economics of it.

Now, by the way, just so we make it clear, it makes me crazy. You're going to kill grandma if you know that it costs a lot of money. Like there's a business model that says hmm,

I'm going to really make sure that she gets sick and dies because the drug was expensive. (Laughter) You see, now, how is that supposed to work?

My point is that we give away expensive stuff. You got leukemia and you need the lead drug for Philadelphia Chromosome-Based Leukemia, hey, it's like fluoride, take it, please. It's expensive as hell, but total cost of care drives it all down. So, that's just dumb.

But what I really worry about is promising but unproven treatments because this is where the action really is going to be. There are so many new things coming down the road for which we cannot do traditional clinical trials. And you're going to have to have some other ways of assessing it. There are going to be a lot of patients who are not going to get access to promising things that the FDA says is cool but that is unproven ultimately in the way in which we would normally want. And, so, I think this process is going to be very important at giving us some opportunities to go after that.

So, I think this CER thing is hugely important to this. At the end of the day, ladies and gentlemen, we're excited about it; we think this is very important. I think you're doing all the right stuff, but above all, just don't screw it up. (Laughter and applause)

DR. McCLELLAN: Thanks. Now I'd like to open up the session for a discussion. So, again, as usual, if you have a question or comment, please go to the microphone, identify who you are.

While we're getting started on that, let me ask any, particularly the earlier panelists if they have any additional comments or reactions to what they're heard.

Go ahead, Janet.

DR. WOODCOCK: I'd like to say a couple more things about how I think we could move forward in constructing this.

Yesterday, we had a meeting of the OMAP, the Observational Medical Outcomes Pilot, where we presented a very large body of methodologic research on how to do these things, and I think going forward, the diagrams I showed, we need to have a very well-funded and vigorous research arm because I think we don't know how necessarily to do this yet and reach actionable conclusions which is what Reed is asking us to have, and I think we all agree --

DR. TUCKSON: Really? (Laughter)

DR. WOODCOCK: We want actionable findings, okay? Not more research is needed for the next 10 years. We want things, what we can make decisions on, decisions about care, decisions about patient safety and so forth.

And the second thing, I want to ask David about this. David, it seems to me that the Health Exchange Information Networks, of course, that's really needed because, for one patient, we lose all their data if the data is not linked to patient, we don't have good longitudinal data and we don't have data about say a patient has to go to the emergency room and then we lose that data somehow. But it seems to me that the network I was talking about is kind of like a metadata or whatever, it's on top of the primary. The primary is here, and the Health Information Exchanges are here with the primary data.

And then there's another different level for the secondary data, which is analytic type, and that's where I think we need a governance for that. You need a governance for Health Information Exchange and how that is done, but we also need a governance for how we're all going to access these secondary data. And I think the two are somewhat slightly different. There need to be, obviously, closely coordinated, but the idea of the secondary use is somewhat conceptually different, I think, than the primary information exchange. But maybe I'm wrong.

DR. BLUMENTHAL: Well, I don't think they're as far apart as you think if you have Distributed Data Network because you've described the Sentinel Network as a Distributed Data Network involving a fairly small number of data sources. I don't know what the exact number is. Richard can tell us. But let's say it's 20 or so. We're talking about the opportunity to create a Distributed Data Network with hundreds of sources, where the data resides in the local records of practices. The Marshfield Clinic or the 20-member group, or even a solo practice.

DR. WOODCOCK: Right.

DR. BLUMENTHAL: Because the patient populations are different and you want a representative information source. So, the rules that govern access to that information and the governance that creates those rules is going to be very, very closely linked and integral to what the uses of the data are. So, when the data request goes out to study a drug and a side effect

and you want to send queries out to hundreds of practices, thousands of practices, hundreds of hospitals, you are going to have to involve the folks who manage the exchange of information. So, I don't see the clear distinction. I mean, if there were a central database.

DR. WOODCOCK: Right.

DR. BLUMENTHAL: Then there might be a clear distinction, but we've already talked about the fact that we're dealing with distributed data, which I agree totally with because the critical underpinning for this enterprise is trust by the consumer and the patient in how the data is stewarded, and the closer you keep that to the people they trust, their physicians, their hospitals, the more trust you will have the in the secondary uses.

DR. WOODCOCK: Right. Well, I agree with that, but let me just say that you heard from both Reed, I think, and Sam that maybe sometime in the future what you envision will happen, but, right now, there's work involved in making these data available for analytic purposes, and we found that's one of the most important steps is that the custodians of the data are going to have to do additional work on the data to make it analyzable by the queries, and, right now at least, maybe they'll be cooperatives and so forth, but we couldn't reach into an individual health record or whatever because those data would not be -- and I know you're working on that. We'd be able to exchange the data, but I'm not sure we would know the data were usable. And some time in the future what you envision may happen, but I don't know when that would be.

DR. BLUMENTHAL: Well, I think there's going to be a transitional phase, and in the meantime, you clearly may need to have pockets pilots of the type that you're discussing. But I think to expand this to an industrial strength search and query capability will require a whole infrastructure that goes by the name of the Nationwide Health Information Infrastructure that under conditions of trust and interoperability enable the widespread search of information.

Now, there may be other interim solutions and also spin-off solutions. It doesn't have to be a uniform system. If there are networks of plans that have decided they can do this independently with their own resources and their own governance structure, there's nothing to prevent that from happening.

DR. McCLELLAN: So, I'll ask if any of the other panelists want to comment on this topic. It's a pretty important one. Any others?

SPEAKER: Mark, the only comment I want to make and I think there are schools of thought, but to emphasize what Reed said is today, we are being asked by many states that are developing their own state claims and databases, we're being asked by many different resources, the large employer and others, and while the good news is that we tend to follow common formats increasingly for data, we're tending to look at measures that are NQF and otherwise endorsed by professorial societies. All of that is positive, but the Herculean effort of trying to respond to every one of these initiatives, some of which were mentioned, really actually takes away from the capability and the investment to manage and analyze the data and make it meaningful.

So, I think, David, what my concern is that during this what you call transition interval is that how do we manage from these 1,000 points of light that are being created because they're not only light, but certainly costs and redeployment of investment and duplicate of function, and that's not going to really work at a time we're trying to get information more quickly and better managed cost.

DR. TUCKSON: So, let me just piggyback on my friend here. I think that what we're got to really understand as we listen to David, David is in an extraordinarily difficult position. Now, let's just be real clear. (Laughter)

DR. McCLELLAN: Congratulations.

DR. BLUMENTHAL: It's getting more difficult by the moment though. (Laughter)

SPEAKER: Reed, David had $40 billion. Most of us would love to be in that position. (Laughter)

DR. TUCKSON: Yes, by the immunizing effect of money does not protect you from the challenges of politics, and what David has to deal with is a physician and hospital community that is very anxious and concerned about every step that he takes. And he can't say it, so, I'll just say it and he'll look and pass it. (Laughter) And, so, when he tries to advance real movement in this space, he comes up against very strong folks, and I'm not saying that they're

concerns are not legitimate.

Let me be clear, I'm trying to be very neutral on that, but he comes against people who have concerns. So, the point being is that what at least is encouraging for us on this end of the table is the fact that we have the data there combined with we have a Don Berwick at CMS, and they actually happen to know each other. We actually are pleased that there is a Sherry who happens to apparently know both Don and David. (Laughter) What we have to do outside of government is to create an unassailable environment where they are facilitated, encouraged, and protected to come together. Right now, they aren't where they need to be, and what we have to be mature enough is to understand why they can't move in lockstep together and what it is that we can do to help immunize them so that they can't. And they are in a crappy position because they can't talk about it. (Laughter)

So, my last comment on this is that David is right; you have to got to get it right. Of course, everybody wants to have the protection so that the patient if you don't get the trust right, you are done. All that's right. But this interim period can't be but so long because the world is spinning and spinning, and there are consequences to those spins. So, what we have to do is help them to be able to give us the leadership that they're trying to do and overcome the hurdles that they're up against.

DR. McCLELLAN: All right, I have one follow-up, and let's assume that we get through the short-term issues to get to David's model. And I can see how this governance is going to take -- and this is in the PCAST Report and all, too, but take quality measurement for these individual providers and groups that are now going to be sharing interchangeable data, if we get there sooner rather than later because all these efforts are going to be successful. You can see a mechanism for making that sustainable, that because they're going to be paid and because they're going to be reporting on quality, they'll have some built in incentives, and hopefully to get to Reed's point, some real standards for what those secondary use quality performance measures would be.

And there's a foundation of NQF endorsement. I would say, as Sam and Reed know, that NFQ endorsement by itself doesn't necessarily solve anything like all your operational

problems for turning the data that you have electronically into comparable, meaningful measures. There's still a lot more work to do there, but let's say we get over that. There is a financing mechanism and presumably a governance that go along with it that look; these are the quality measures that are going to be reported. It's less clear, perhaps, or at least it's different, how it might be sustained with some of the safety uses and some of these other uses where there aren't going to be payers like Reed and Sam, I think, who are going to be paying directly based on some of these safety measures. I mean, this is much more of a public good. It's something that's going to provide some value for everyone.

And getting back to Reed's question, what do I get if I do provide a data, what do I get if I don't? Well, whatever comes out of these safety studies or comparative effective studies is going to be much more global. It's going to be information, evidence that's available and relevant to everyone. So, it does seem like even if there's one kind of governance that applies to all this or one kind of infrastructure that applies to all of this, someone else or someone is going to have to do some additional work on what the standards are for reporting that information and providing some kind of financial incentives or sustainability incentives for supporting it that's seems quite different from some of the other applications.

And I wonder if that sort of gets to the point that I think Sherry and Janet were making about different nodes, perhaps, on top of a core infrastructure. I just want to make sure that I'm thinking about this in a meaningful way, and, if so, what does that mean as we get towards this longer run? What's it going to look like and what does that mean for what we do now?

DR. WOODCOCK: Well, I think in some ways, this information for some of those nodes, if you would accept the diagram I put forth, is valuable enough that various stakeholders could band together to help support the generation cleaning, maintenance, standardization, movement to a common data model, and so forth that are required for those data elements so that say for research purposes, for perhaps pharmaceutical and device safety, and perhaps we don't have to set up independent registries. Perhaps once we have the longitudinal capability that David's talking about, we can follow these patients through their career of their implant or

whatever, but that's valuable and that should be supported by various stakeholders who have a stake in finding out that information.

So, I think that's one of the reasons I'm advocating for some commonality in the infrastructure so that there's an opportunity for everybody who's going to benefit from this to actually contribute to it, to make it happen, and that'll make it happen, I think, faster.

DR. GLIED: I think we're also thinking a little bit about how these kinds of data could be useful to participants in the various distributed data networks. Can we develop mechanisms for benchmarking your performance that allow people who participate to get something more out of it than those who don't? So, can we find a private goods piece to go along with public goods piece? And I think that still remains to be worked out, but it's a critical element in going forward, as long as we're asking you to participate voluntarily, we have to be giving something back.

DR. McCLELLAN: Good. I'd like to get comments. Go ahead, Jonathan.

MR. HARE: Jonathan Hare from Resilient Network Systems.

So, first of all, Reed, I just want to thank you because I'm all fired up. (Laughter) And I think what you hit on is let's identify the metrics that really matter, right? Can we get personalized decision point at the point of care so people can make decisions to improve their health and be rewarded for that? That means tapping into population scale data that doesn't scale; it doesn't matter if it's too expensive. It assumes ubiquitous consensus and trust among people who don't trust each other. It won't work. And I think the key is we need to figure out what are those metrics and then get a plan to get there and accept no substitutes.

I think what Janet Woodcock laid out is the right approach. That's the right philosophical approach. We're not going to get there with different networks, special purpose in each silo. It will never work. It's never worked in any other industry. It's not feasible socially or technically or financially. And the challenge is to get there; it's going to take some breakthrough innovation.

If there's one thing that's been demonstrated over the last 10 or 15 or 20 years of trying to exchange data is that what we're doing doesn't work, right? It's a miserable failure in

terms of ability to exchange clinical data for decision-making in a decentralized network just doesn't work, and I think one of the challenges in a government environment when the general model is with sort of grant-funded projects, the general approach since it's public money is well, let's convene a working group of the best experts that are typically drawn from the incumbents or consultants or other lobbyists or whoever that kind of been there, done that, and been on all the previous committees, right?

And then they're expected to come up consensus on what the RFP should look like. And that RFP makes sweeping assumptions about what the solution is or what it looks like, usually by some sort of standards. And the reality is these people, they have a framework they come from and assumptions and their own incentives, and what you come up with is something that is not a breakthrough. You never get sort of breakthrough innovation or really any kind of serious innovation through that type of process.

So, I have a suggestion or a different approach, which is rather than having RFPs and grant-funded things which sort of imply what the solution looks like, to say what are the goals, what does success look like? What are those metrics? Do like an X PRIZE, if you're familiar with X PRIZE. It was like eight years ago, somebody said if you can get a privately-built spaceship 100 miles in the air and down and then back up again within 2 weeks, right, you're going to win $10 million. I think there was probably quarter of a billion dollars that was spent on that. All sorts of crazy ideas. There was no consensus whatsoever, but they got the job done, right?

So, in health care that can look like if you can set these metrics, you need to be able to reach every patient, every clinician, every caregiver in the country, give them timely, convenient access of the data and the decision support they need, do population scale analytics or comparative effectives research for safety and so on, that's what we need. And then anybody who can actually do that, right, your reward is we'll use it. We'll create a marketplace. Payers will use it and pay for it to coordinate care and avoid bad outcomes. That will attract the people that would never even apply for a government grant. The people that have the resources and the capabilities to do this cost effectively, they're not going to get in line for a government grant. It's

just not meaningful to them, and they probably wouldn't be eligible anyways.

So, what I'm looking for from you guys is can you describe a process where you could all get together and say we're going to do with this little percentage of our time and attention and funding create an environment for innovation, attract people who think they can solve this problem to find that type of process and get it done in the next two years before the Republicans de-fund all this. (Laughter)

DR. WOODCOCK: A very small example, in OMOP, we did a OMOP competition, and we offered a monetary prize for those who could develop the best novel data mining against the database that we had made, and we got tremendous interest and novel ideas from folks from totally different fields than pharmacoepidemiology, and upon how to do data mining. So, it is possible to have competition drive some things.

DR. BLUMENTHAL: So, we have actually just launched an innovation prize award through the Office of the National Coordinator. It's not $250 million. (Laughter) But it's enough, I hope, to get some attention.

I'd also like to think that a part of what the Congress and the president did when they created the HITECH Act was to do some of what you discussed, and it's called the meaningful use framework. It's just evolving. We're only in stage one. They'll be several more stages. Each will set more ambitious goals for what the performance requirements are for electronic systems. And it's putting money, incentives on the table for the use of those systems or penalties for not using them. We're not prescribing the technology, we're prescribing the uses. And there is a lot of innovation going on, some of it will be good, some of it won't be good. But in effect the meaningful use framework has for the first time in the history of any health care system given the government -- and it is the government for those of you who are not happy with that, I'm sure that's disappointing to you, but it is the government. The Center for Medicare and Medicaid Services is saying we'll put $27 billion of taxpayer money on the table in extra payments for 4 or 5 years, and then we're going to start taking away money if you or unless you do the following kinds of things electronically.

Now, right now, the meaningful use stage one is about getting essential patient

information into electronic form. Because none of the things that Janet wants to do or that Sherry wants to do can happen until information is electronic. I mean, if it's still on paper, innovation is not going to be very helpful. So, we've got to get doctors and hospitals and patients to buy in to the idea of an electronic health information system. Then you can begin to build on increasingly demanding uses of that information.

And the meaningful use framework is simply a way of setting goals for electronic use. Now, it's going to have quality metrics in it, it's going to have I hope efficiency metrics, it's going to have exchange requirements, and I think down the line, it could also have a framework for secondary use. So, I don't think we're far apart. We are very, very hopeful and committed to permitting innovation technologically to blossom in that environment.

DR. TUCKSON: So, I just want to again come back and underscore David's key point, but when he says hopefully efficiency measures, and, again, this is where we all have to bond together behind David to give him some lift so he doesn't have to say hopefully. And I think that what you got, Jonathan, your question was provocative and more complex and it's beyond pay grade to try to understand it all, but I would say that Janet and Peggy and Don Berwick all together, they sat down in a room, and I'm sure they do, have a whole bunch of data that tells you where CMS cost curve is about to go as you overlay it against where are the next innovations in health care assets, both pharmacologic and technologic? They can show you how deep doo-doo they're in, and they're in deep doo-doo, and just as David is trying to find and give money for physicians to adopt meaningful use criteria, on the other end, they're getting ready every year after year trying to figure out how to pay physicians to take care of Medicare and Medicaid patients. So, whichever end of the balloon you want to squeeze, it's got problems.

And, so, CMS can't afford, and, so, what they absolutely, if you want to figure out where the focus is, focus on where the controllable costs are or where the early warning signs are. So, if there's anybody that wants to know right now what you have to look out for that causes you preventable ER visits, admissions, longer lengths of stay, and readmissions, they ought to know it.

And whether there are high-profile areas that you want to go after first or watch

as the new technology, which they know the new technology that's in the pipeline about to come down the track, they know what you have to look out for, and then, ultimately, they will be able to tell you what David just said, is secondarily, is to have a scalable solution that lets you query even the lesser important things, even though if you add them all up, everything becomes important. But, at the end of the day, okay, I want to ask this particular peculiar question that maybe wasn't on the original hit list, and eventually, you get to that scalable solution. But at least I think that the next time we sit here, I think we ought to have the product of the conversation between CMS and FDA that says let me tell you where we're in deep doo-doo.

DR. McCLELLAN: Another question.

MS. OZANIAN: I'm Rhonda Ozanian. I'm a Robert Wood Johnson Health Policy fellow.

So, my question is about the secondary use of this data, patient level data, and governance and the data partners. If you have to de-identify data beyond the firewall, patients don't stay in the same place, they move between health care systems, payers, providers. So, doesn't there have to be some relationship between the data partners to make sure that once you get beyond the firewall, you're not counting the same patients multiple times because you won't know?

DR. WOODCOCK: Some of those are technical problems, and we are looking at different ways we can identify patients say from registries and also from health care systems because, actually, we want to link those people.

MS. OZANIAN: Right.

DR. WOODCOCK: So that we have that longitudinal and outcomes data and so forth. However, I think what David is doing, those pieces are aimed at having the portability of the data so wherever a patient goes, they have their records with them. That's what aiming to fix that problem. Right now, those are paper records. Even if you're in the same health care system, you probably can't find out everything that happened to a patient.

MS. OZANIAN: And, so, those same solutions would apply to the Sentinel Project, as well?

DR. WOODCOCK: Well, as those data become available, which they are generally as long-term -- I think the dwell time right now in the data we had from OMAP was about 18 months or something like that in any given system except for CMS, where they have them forever. Once they've got them, they've got them. But so it's a big problem on not short-term outcomes, but longer outcomes. So, yes, that's part of I think what they're doing and for the primary data. The primary data has to be linked.

DR. BLUMENTHAL: Yes, you've pinpointed a very important problem, which is that without a kind of a common patient identifier that travels with the patient, there is going to always be uncertainty about who is who. There are companies that have built very successful businesses around algorithms for identifying patients. They're probabilistic, they never give you 100 percent certainty, but they can give a level of certainty that is tailored to your needs. They can give you 100 percent certainty if you're willing to give them the data, but if you don't have that data, they'll give you a probable match. And then so we're going to have to come to some consensus about what constitutes a match, what level of certainty we want for what uses.

For research uses, you may be able to tolerate rater uncertainty than for care purposes because mismatching a patient for treatment is a lot more consequential than mismatching a patient when that patient is 1 of 1 million who is being used for -- that just expands your uncertainty. Your standard error. So, I do think that we're going to find solutions for these problems. They won't be perfect, but they'll be, I hope, workable.

DR. McCLELLAN: Next question.

MS. JONES: Judith Jones, the Degge Group.

In addition being an epidemiologist, I've been a passionate follower of electronic medical records from the time they were introduced in the U.K. in the late 80s, and pretty wide use by the 90s, and I'm delighted to hear the plan now, but my question has to do a little bit with Janet's system diagram, which is really a crosssectional diagram, and it doesn't give you a longitudinal view. Obviously, one of the big, I think, deficits in all of our plans for electronic medical records has been the failure to incorporate thinking about those in our medical training and actually nursing and pharmacy training, as well. I teach in a couple of

medical institutions, and I consistently find that although everybody uses PDAs now, there is not any consistent training on either the health care system or on use of electronic medical records unless they rotate through the Veterans' Administration, which, fortunately, a lot of medical students do, but that's not until they get to their clinical years. I think if we look at the origins of how we're going to implement this, we need to pay attention to the medical education system and make a full-fledged effort to incorporate that. And I'd just be interested in your thought.

DR. BLUMENTHAL: So, it makes sense. The challenge is a little deeper even than I think you've laid it out because what we do not have in today's academic environment are the learning hubs that are taking not just the HIT, which is only an ends to itself, EHR is only a means to an end. It's more of being able to deliver the new reorganization of care delivery that allows you to take electronic and other information and then be able to interact with a patient so as to coordinate comprehensively their care in a way that delivers better quality, more appropriateness, more cost efficiency, and more coordination of care.

The place where that is occurring, the good news is that there is an entrepreneurial spirit in American medicine today which is going very unnoticed. We are seeing it popping up everywhere, especially as companies like Sam's, mine, and others and as the federal government sort of starts to intimate through responsible leadership like Don Berwick, you get the sense that the reimbursement is about to change. So, now you're starting to see physicians respond with new, you call it whatever you want to call it, accountable care organizations, whatever the alphabet soup is.

So, I guess the point would be is that what you're seeing are learning laboratories out in the land, but you're not seeing very much of them inside the academics environment, and here's the killer on it: The challenge is going to be strongly that the model of new reorganization and reimbursement is a model that saves resources and piles them back into physicians and patients' lowered premium because you are able to decrease the use of hospital services. It's going to be very hard for the academic center when the person that runs the hospital hears about what's going on.

DR. NUSSBAUM: Your important question raises though a much more

fundamental issue, and while it's directed at the use of health IT, think about what we're going through. The structure of care delivery is fundamentally changing, whether we use ACOs or integrated care organizations. Within the last few years, more than half of cardiologists are now employed by health systems. Most major markets' primary care capacity is entirely acquired by health systems.

The American Board of Internal Medicine Foundation at their meeting this summer basically asked the deans and others in medical schools are we prepared? Is our learning environment prepared for what we need to do in health reform? And you know what the answer to that clearly is.

So, whether it's all of these, it strikes me that we're operating with a lot of a green field of opportunity. So, comparative effectiveness research will give us very important information so we don't waste 30 to 40 percent of our resources on unproven therapies. Health IT, while today we may have -- and, David, you know I celebrate everything you've done because my concern about electronic medical records, until you got involved, was that we were creating bridges to nowhere. That now we're going to have bridges to somewhere.

So, the work of the FDA, I think we're at that critical point where all of these are going to begin to intersect. Today, they're appearing to be in their own path, but increasingly, thought leaders are beginning to find that common ground in their section. But, fundamentally, health care has to be reorganized and to get the efficiency, the capability, the performance that we need in our health system.

DR. McCLELLAN: I think we've got a couple more questions. We've just got a couple more minutes, so, if you could move on to the last. Thanks for that excellent discussion.

MS. PATRICK-LAKE: Hi, I'm Bray Patrick-Lake. I am a patient in the FDA Patient Representative Program, and I am the patient serving on the National Planning Board for Mini Sentinel at least for the next two minutes. I may be fired shortly. (Laughter)

So, when we talk about the primary mission of the Mini Sentinel Program, I think it's incredibly executing from the patient perspective because it is going to improve patient safety. I think we all get that. And then when we take it to the next level and we start looking at the

secondary uses and we think okay, we're going to improve patient care maybe through comparative effectiveness research, I think all of us from our different perspectives and interests can say that we're all here because we want to improve patient care.

When we take that to the next level, Dr. Tuckson, I think you're an incredibly impassioned speaker, but you made the hair on the back of my neck stand up when we start talking about comparative effectiveness research and then we say cost effectiveness, and then we say reimbursement and CMS all in the same sentence, and then somewhere in there, you say it's patient-centered choice.

Well, I have an HMO insurance, and I can tell you right now it doesn't feel very patient-centered. When I go in, I get a list of formularies. It might not be what's necessarily for my individual patient care, it might have a low side effect or a low profile for side effects, and it may be cheap, but it's not necessarily what's best for me as an individual patient.

And, so, I think the patients in America are very well aware that costs is huge and cost of health care is huge, but I'm just wondering how we are going to balance going forward if we start using this incredible framework for comparative effectiveness research. How do we balance that with the true patient experience? Patients are more than just a P value, so, where does quality of life come in?

Let's say we have two therapies, we have one that is an innovative medical device, maybe it's an implantable cardiac device and we know that it saves lives. But you can also put the patients on an anticoagulant for $10 a month. One's very expensive, and if you look at the P value, maybe everything is the same, but yet the patient that was on the drug for $10 a month is too fatigued to continue their job, to play any sports.

How are you guys going to, as you make decisions that do affect patients when you take costs into account, how do you balance that? And I'm not sure I'm getting that from where we are, so, maybe it's just where we go next and how the patient experiences preserve through all this.

DR. McCLELLAN: And I know this is a big question, but we need a short answer.

DR. BLUMENTHAL: Very quick. Very quick.

DR. WOODCOCK: You've got 60 seconds. Go ahead. (Laughter)

DR. TUCKSON: All right, well, first of all, don't let them do anything to you because you need that voice, and you're right on there.

I want to separate out the two ends. You've mixed two things together, and I want to separate them. Number one is I think we would all appreciate that you have to have responsibility in terms of making rational choices about scarce resources. The null hypothesis doesn't exist. If you don't get at the things I tried to get at, no one could afford anything.

So, I mean, at the end of the day, there's no other way out of it. You have to grapple with it. So, what you are really saying is how do you do it, and you're basically saying will the research on comparative effectiveness and other decisions that have to be made, will they be sensitive to including fundamental things like the patient experience with care, like the work productivity back to the workforce? All those kind of things. Can you get them back to work, people having a better quality of life? And absolutely that has to be a major part of the research protocol, the research questions, the health services research query, the comparative effectiveness research. So, I would just sort of endorse strongly your point of view.

I do not see them as incompatible. There is a necessary group of work that has to get done. How it gets done must incorporate everything you just said.

DR. McCLELLAN: Thanks. One more question.

MS. PATRICK-LAKE: Okay, so, just from this group, I --

DR. McCLELLAN: We are going to have to move on.

MS. PATRICK-LAKE: I'm sorry. I just encourage you to keep opening the door for patients and the patient advocacy groups.

Thank you.

DR. NUSSBAUM: Well, absolutely, and that's why, for example, Meryl Wineberg is key to everybody because every time we take a step, we don't anything without talking to Meryl. (Laughter) So, you got it.

DR. McCLELLAN: Thanks.

MS. ST. CLAIRE: Hi, I'm Chris St. Claire from Med Star Health. I was just wondering since you have several people have mentioned bringing in clinical data to expand the datasets, are the RHIOs going to have any interaction with these large datasets that you're collecting for all these other uses, like the D.C. regional health information?

DR. BLUMENTHAL: Well, the RHIOs, the so-called Regional Health Information Organizations, I think we change these names every two weeks, whether you want to or not, so, that name is already kind of moving out of fashion, so, we're now calling them Health Information Exchanges. (Laughter) But we have to stay employed. (Laughter) They are mechanisms for letting data move. They're the switching lines of the railroad, if you will, and you want data to go from institution A to institution B, doctor A to doctor B, and nurse A to nurse B. How do you get it from point A to point B?

Well, you need to have a kind of switching place, an operator who's putting in those plugs, if you remember those things. So, that's what RHIOs do. Now, they can do that as a purely mechanical activity, and it's not even clear that you need them, but, right now, they are one of the options for making that exchange happen. In the process of making that exchange move, they can reach in and take out the data and hand it to Janet under the right circumstances, and that's one model by which data will start to become available.

So, in a sense, because they are a hub where information flows through, they are one node in a distributed network which provides access.

Now, having said that, it means that they would have to in order to be trusted conform to all kinds of assurances; provide all kinds of assurances about the stewardship of the data if they were to have that responsibility. And we have not yet conferred as a society, and I'm not saying this is a public responsibility or a government responsibility; it can also happen to private sector. We have not yet conferred on them any kind of official role of that kind.

DR. McCLELLAN: Well, I'd like to thank all of our panelists and all of you for an excellent discussion. Thank you. (Applause)

We are coming to a conclusion this afternoon. It's been quite a day. It's clear to me that the Sentinel Initiative is making a lot of encouraging progress and has the potential to be

a model for how other collaborative efforts like this might go forward for effective secondary uses of data or an element in this broader system that we've just been discussing of providing much better evidence to guide our health care system in the right direction or that guidance is urgently needed.

But, clearly, there are a lot of issues that still remain, and one of the things that has impressed me throughout my involvement with the Sentinel process is how much of that progress comes from discussions like this, especially for a public-private initiative like this one. The ideas from stakeholders, the perspectives, the insights, the pilots, all of that has a huge impact. So, the fact that so much of this discussion was driven by you all, I can tell you is going to have an impact what we do in our future involvement in this and I would think where the Sentinel Initiative heads.

So, I want to thank all of our speakers today and panelists for their contributions. I want to thank Rachel Behrman and Julie Racuse and Melissa Robb at FDA for all of the work that they put in working with us to pull this meeting together. I want to give a special thanks to the staff at Brookings who helped with planning: Josh Pfeifer, Ben Martin, Erin Weireter, Lindsey Spindle, Lisbeth Rafferty, and Michelle Wong, Sally Cluchey, Josh Benner, and Larry Kocot. And most of all, again, I want to thank all of you for putting the time and the effort and the heart into helping to transform our health care system. Thank you very much, and safe travels. (Applause)

* * * * *

CERTIFICATE OF NOTARY PUBLIC

I, Carleton J. Anderson, III do hereby certify that the forgoing electronic file when originally transmitted was reduced to text at my direction; that said transcript is a true record of the proceedings therein referenced; that I am neither counsel for, related to, nor employed by any of the parties to the action in which these proceedings were taken; and, furthermore, that I am neither a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

/s/Carleton J. Anderson, III

Notary Public in and for the Commonwealth of Virginia

Commission No. 351998

Expires: November 30, 2012