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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

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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.