ADVISORY COMMISSION ON CHILDHOOD VACCINES

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Agenda Item: Welcome and Chair Report

MR. SCONYERS: Good afternoon, everyone. Thanks for joining us for the meeting. Welcome to steamy Washington, D.C.

Before we dive into our program, I want to call your attention to a few things that are in your binder and invite you to take a look at them. We have the agenda for today and for tomorrow. We will try to move this. I know that some of you have flights to make, and we will try to make sure that that works for us.

One of the things that we have included in the binder and that I encourage you to take a look at is the charter for this commission. It tells us what we are supposed to do. We are going to have some discussion tomorrow about the role of the commission in the development of the National Vaccine Plan.

I also want to call your attention to the meeting dates for our next meeting. You will note that we are meeting on November 18. This will be a meeting that starts in the morning. I don’t know whether we will start at 8:30 or 9:00, but we will start in the morning and run all day.

I hope that commission members can stay and attend the judicial conference which is taking place downtown the next day, the Judicial Conference of the Federal Circuit, which is the circuit that deals with our program and with the cases that are pending before it. There is a significant set of presentations that are going to be taking place there, and I hope that you will be able to attend.

Geoff, have they gotten formal invitations to that? I don't know whether they have or not. Everyone is invited. The information will be forthcoming to you. I hope you can plan your travel so that you can stay that day. You will be able to depart by mid-afternoon, right?

DR. EVANS: The last word we have from the court is that the workshop session will be from 10:00 to 12:00.

MR. SCONYERS: So you should be able to get out of here that day and get back home. But I think it will be very useful for you to stay and hear the discussions there. So I hope you will all be able to do that.

Before I move on to action items, I want to welcome our three new members to their first meeting. They spent yesterday being inundated with information about the

program, about the staff, about the organization, about everything to do with the Vaccine Injury Compensation Program.

I would like to welcome Sarah Hoiberg, from Jacksonville, Florida, who is a mother of a vaccine-injured patient and joins us in that capacity.

I would like to welcome Sherry Drew, who is an attorney from Chicago, who is joining us in the role of representing petitioners to the program.

I would like to welcome Dr. Tom Herr, who is a pediatrician in Moline, Illinois.

So we have a couple of Illinoisans joining us. I'm not sure what that bespeaks for us. Welcome, all of you, to the commission. I hope that you will join in and ask questions and participate just right out of the box, as you feel is appropriate for you.

With that set of introductions, our first order of business is review and approval of the minutes from our June 2008 meeting. I would be happy to entertain a motion for approval.

(A motion was made and seconded to approve the minutes.)

Is there any discussion?

DR. FISHER: There are just a couple of sentences that aren't exactly sentences. There is nothing substantive, but since it becomes the actual record --

MR. SCONYERS: Meg, could you give typographical corrections to Michelle, with the indulgence of the group?

Before I proceed, I want to acknowledge -- Tawny, do we have you on the phone?

MS. BUCK: (Via telephone) Yes, you do.

MR. SCONYERS: Great. Tawny Buck is unfortunately unable to be with us today in person, but is joining us by phone.

Tawny, we always miss you when you are not here and we always benefit from your participation, so I'm glad you are on the phone.

MS. BUCK: Thanks, Jeff. I miss seeing you all in person. I appreciate the opportunity to participate by phone.

MR. SCONYERS: So we will have a few typographical corrections.

Any other discussion of the minutes?

(No response)

All those in favor of approval?

(Chorus of “Ayes.”)

Any opposed?

(No response)

We will consider them approved.

We will ask Dr. Geoff Evans to give us the report from the division.

Agenda Item: Report from the Division of Vaccine Injury Compensation

DR. EVANS: Thank you, Jeff. Good afternoon, everyone.

This is the 70th quarterly meeting of the Advisory Commission on Childhood Vaccines that I’m welcoming you to. It’s also just before the 20th birthday of the program’s beginning operation, October 1, 1988. So we certainly have been around for quite some time -- 70 meetings and now 20 years worth of performing service for the country.

For those that are on the phone, I want to give some background in terms of numbers.

(Administrative announcements)

Today we will be starting with an update from the program that I will be giving. Then Vince Matanoski will

be giving a program update from the Department of Justice on litigation activities. Tom Powers will follow with a report on the autism proceedings. Then we will have a vaccine safety update, on departmental vaccine safety activities, by Dan Salmon, from the National Vaccine Program Office.

After that we will be hearing from Marion Gruber, who will be covering thimerosal in vaccines. She will be going into a little bit further detail from the talk that she gave the last time. We have given her a little bit more time this time, because it is a very important subject. We will conclude today's agenda with a presentation by Dr. Walter Koroshetz, who is from the National Institutes of Health, who will give us a summary of a meeting that took place in Indianapolis on mitochondrial encephalopathies.

Tomorrow when we gather, we will have a CDC Web site demonstration with Michelle Basket and Cathy Hogan from the Centers for Disease Control and Prevention. We will have a National Vaccine Plan update by Ray Strikas of the National Vaccine Program Office and continued discussion with our chair, Jeff Sconyers, on ACCV input

into this process. Then we will have our usual updates from the ACCV ex officio members.

In terms of personnel changes, I'm very pleased to announce that Kay Cook has joined our office. She is the newly appointed branch chief of policy. She brings a wealth of experience working within HRSA, many years with the National Health Service Corps, but more importantly, this past three years with the Office of Financial Management in HRSA, because if there's one thing any program needs, it's someone that actually knows how the process works in terms of the way the budget is done. So we are very, very pleased and delighted to have her onboard.

I thought I would also take a couple of minutes and talk a little bit about the new members that we have.

Starting with Sherry Drew, she is a petitioner's attorney from Chicago, as Jeff mentioned. She is a managing partner at McDowell & Drew, LTD, and has handled vaccine injury cases for many years in the U.S. Court of Federal Claims. She has also represented plaintiffs and defendants in the practice of civil law. Ms. Drew participated in the attorney assessment of the Vaccine

Injury compensation Program, in a focus-group gathering of Vaccine Act stakeholders several years ago. Her public service includes work as an arbitrator for the Cook County, Illinois mandatory arbitration system.

Welcome, Sherry.

Next is Dr. Thomas Herr, who is in private pediatric practice in Moline, Illinois. He has served on a number of ad hoc committees and on the board of directors for such groups as the Boston Area Health Education Center, the Visiting Nurse Association of Rock Island County, Illinois, and the Pediatric Physician Alliance. His recent activities include serving as a member of the section on practice management of the American Academy of Pediatrics and also testifying before the Illinois House of Representatives about childhood immunizations.

I'm also pleased to say that he is a former member of HRSA's National Health Service Corps.

Welcome, Dr. Herr.

Finally, we have Sarah Hoiberg, whose daughter Caitlyn received a DTaP shot and subsequently experienced encephalopathy. In 2006, she filed a claim with the compensation program and was awarded compensation for her

daughter's vaccine-related injuries in 2007.

So we are very pleased to have Sarah also with us.

Welcome to you all.

Starting with the statistics for the program, as you can tell, for the non-autism cases there was a surge of filings in fiscal year 2007. That was due to the deadline for filing influenza vaccine claims. Influenza vaccine was added to the program in July of 2005. By statute, there is a two-year deadline for filing claims that go back eight years from the effective date of coverage of any newly added vaccine. That deadline was July of 2007, and the program received nearly 200 influenza claim filings as a result.

As you can see, now, with no more deadlines around for filing in terms of newly added vaccines, the rate of filing is around 12 per month for the non-autism part.

You can also see in the autism column that there was a trend downward, fiscal year 2005 going into 2006. Then, we believe, publicity surrounding the autism proceeding has once again brought attention to this part of

the program to the public, and there has been a trend upward in the number of filings. You can see so far this year we have received 221.

I should mention that, in contrast to the thousands of autism claims that were filed in the earlier years, those that are coming in since June of 2007 that have medical records or medical records are filed subsequently -- we are responsible for reviewing those claims and performing medical reviews, even though there is nothing further that is done with them, in contrast to the older claims, that those are all on hold in terms of needing medical review. So these newly filed claims -- a significant percentage do represent workload for the program.

The next slide talks about award amounts paid as of the beginning of August. The average has been, over the past eight years, $65 million, and $4 million annually for attorney fees and costs.

Key points here: Fiscal year 2007 marked the highest amount of payments, of outlays, for the program, of $97 million. This year the trend has still been up, but it will probably fall within $10 million of that. The corps

was very busy during 2007. It was fully staffed and it was catching up on a lot of these cases.

If you look at the data sheet, you will see that there is a total payout for the program, for what we call the current program, the post-1988 program, of $901,000. There is another bit of activity that is not so apparent, and that is what is called the pre-1988 program. Those were a series of cases that were adjudicated over a 14-year period for vaccines administered prior to the program beginning operation. Those were handled in parallel with the currently filed vaccines, but had different filing deadlines and guidelines for payment and so on. Those claims were finally all adjudicated in 2005. The payout for that was $902,500.

So all together, the program has paid out over $1.8 billion in compensation to date.

You can see data from both the pre-19800 and post-1988 program if you go to the Web site. You will see that the post-1988 data come on as you open it up, but then you can click and see the filings and the adjudication by year and what the total payouts were for the pre-1988 program.

This is always an area of interest for the program. The trust fund, three-quarters of the way through the fiscal year, stands at receiving all togther $246 million in receipts, which, if you project it out to a full year, probably is going to come in the order of about $320 million of net receipts for the year. So you can see that the trust fund is growing quite substantially.

Currently, it stands at over $2.8 billion. If in 2007, for example, we spent $100 million, then having receipts in the $300 million range means that we are netting over $200 million annually.

MS. BUCK: Geoff, I'm sorry to interrupt. I can't hear you. Can you guys talk into the mike, please?

DR. EVANS: Did you hear this last part about the trust fund, Tawny?

MS. BUCK: No, because the operator actually cut you out to check and see if I could hear. I'm sorry, I missed that.

DR. EVANS: The trust fund stands at $2.8 billion all together. If you figure in the amounts that we are paying out, it's still netting over $200 million annually. This substantial increase over the past couple of years has

been clearly the addition of influenza vaccines to the program. With the 75-cent excise tax on each dose, and distribution in the order of 120 million to 130 million doses annually, you can see that that is quite a bit of revenue coming in for that one vaccine alone.

In terms of significant activities, you will be hearing from Mr. Powers shortly. The final test case for the second period was heard the week of July 21. Each side called one witness to the stand. Parties will be filing briefs with the court over the next several months.

In terms of legislative activities, there was legislation introduced in June by Representative Dan Burton, once again. It turns out that the bill he introduced -- it's known as the National Vaccine Injury Compensation Program Improvement Act of 2008 -- is identical to the bill that he introduced in 2005. It looks to amend the Public Health Service Act with respect to the National Vaccine Injury Compensation Program.

If you look in your workbooks, under 5.1 is the usual table summarizing vaccine-related legislation currently pending in Congress. Under 5.2 is a list of amendments that are contained in the Burton bill.

In the blue folders, Michelle put together a very nice summary -- a one-page summary so it's easy to look at -- that contrasts what's in the 2008 Burton bill with the proposals that the ACCV sent to the secretary in March of 2007. The way it's broken down, those that are in the Burton bill are listed at the top part and then those that were not included in the Burton bill are shown below that.

So it gives you a clear sense that the commission's work does matter and it is noted by lawmakers and so on. There have been several bills over the past five, six years that have been introduced in both the House and the Senate. Hopefully, there will be some passage of these bills in the next administration.

MS. BUCK: Just to clarify for anybody who might be tracking these, Dan Burton is not from Alaska. I think you got that confused with Senator Murkowski's legislation, the Infant Immunization Act.

I think he is a congressman from Indiana. Is that correct?

MR. SCONYERS: I think that's right.

MS. BUCK: Just in case anybody wants to track him.

MR. SCONYERS: You don't want to take responsibility for him?

MS. BUCK: I'll claim it. It's okay. It might be hard for somebody to go on there and track if they are looking for a senator from Alaska named Burton.

MR. SCONYERS: Thanks, Tawny.

The bill itself says "Mr. Burton of Indiana."

DR. EVANS: For those of you who are wondering why our esteemed Alaska parent representative pointed that out, it's because our slide erroneously shows that Senator Dan Burton -- it's Representative Burton -- is a Republican from Alaska. Actually, he is a Republican from Indiana. Sorry for that.

MS. BUCK: Lisa Murkowski has -- do you have an update on her legislation as well, Geoff?

DR. EVANS: Are you asking about legislation introduced by Senator Murkowski?

MS. BUCK: Yes. I just didn't know if there were any updates or if anything had happened with that.

DR. EVANS: We are not aware of any updates.

Again, for the people on the phone, points of contact: You can write the National Vaccine Injury

Compensation Program at 5600 Fishers Lane, Parklawn Building, Room 11C-26, Rockville, Maryland 20857. The toll-free number for requesting information is 1-800-338-2382. You can also access the Web site, which is www.hrsa.gov/vaccinecompensation.

DR. FISHER: Geoff and Tawny, actually, you do have Murkowski's bill listed in that first sheet. It looks like it went to committee in April.

DR. EVANS: Right, and we had that summary in the June books. We have not heard of any further activity in relation to that bill.

Finally, in terms of public comment and participation in commission meetings, those that wish to should contact Michelle Herzog at the Parklawn Building, the same address that I just read, or you can email her at mherzog@hrsa.gov.

That concludes my presentation.

MR. SCONYERS: Thanks, Geoff.

Are there questions for Dr. Evans?

(No response)

Thanks for that. At this time, we look forward to hearing from Vince Matanoski, the acting director of the

Torts Branch of the Civil Division, the Department of Justice, to talk about litigation involving the program.

Agenda Item: Report from the Department of Justice

MR. MATANOSKI: Thank you. Again, it's my pleasure to be here, as it was in June and back in February, I believe, which was the last time I spoke.

Mark Rogers, the deputy director, who I'm acting for, remains in Iraq. We hope that he comes back soon. I certainly do, and I'm sure he does and so does his family.

Usually I start off by talking about personnel. We haven't made any new hirings. The last time I spoke to you, we had one attorney we were waiting to hire. We did hire her. We don't anticipate making any other attorney hirings in the near future. We are pretty well staffed right now to keep pace with what the court can handle. Certainly there is still a big backlog of cases to work through, but obviously the special masters themselves -- there are a limited number of them, and I think we can keep pace right now with where we are staffed.

I typically now turn to giving you some ideas of what has happened with the cases that have been filed in the last quarter. This time I also took a look back at

what I reported to you back in June, to see where we were then with the various filings and see how they compare.

At this point, from June 5 through a couple of days ago, when we compiled these statistics, we had 90 cases filed. Of course, 60 were autism petitions and 30 were non-autism petitions. So that's pretty easy math there -- two-thirds autism, one-third non-autism.

When I talked to last in June, we had at that point had 177 cases filed. At that time, that was a four-month period rather than the three-month period we are looking at now. I was trying to do a little math to try to get rough equivalents. If you figure that about three-quarters of that reflect a three-month period, that would have been 133 cases, so still far above what we saw in this last quarter, 90 cases. We had 125 autism cases filed the last time and 52 non-autism cases, out of that number.

The figure that always interests me and that I keep a close eye on is the number of cases resolved. Ideally, with a backlog of cases, we want to be resolving more than are coming in. We have not been able to do that very often, unfortunately, especially once we got all the autism cases filed, and since, obviously, you still see

that we have a great number of autism cases continuing to be filed.

In this last period, the total number of cases resolved at the court was 33 cases. In the same period we had 90 come in. You can see the simple math there is that we are still going to have cases building up, unless we can get that difference, so that we have more resolved than coming in.

In the same period in June, we had 101 cases resolved. Again, I said 177 had come in in that four-month period. One hundred and one were resolved. Again, we have more coming in than we are getting out the door.

Of the 33 that were resolved -- when I say “we,” I’m here as the Department of Justice. There are three different groups involved in that, obviously. It’s the Department of Justice representing the secretary; the petitioner’s counsel, representing the petitioners; and, of course, the court to decide the cases. All of us have to be working on that. We all have to be, obviously, working together on that.

Of the 33 cases that we had resolved, 20 were compensated. Thirteen were dismissed. Of the compensated

cases, 16 were settled and four were entitlement decisions by the court. Of the dismissed cases, 11 were decisions by the court, finding no entitlement to compensation, and two were voluntary dismissals on the part of the petitioners. None of the cases during that period were withdrawn pursuant to Section 21. I spoke about that last time. It essentially allows people to withdraw before the court has done anything with their case, because they don't want to wait anymore. We had no cases withdrawn pursuant to that. Historically, there have been very few withdrawn pursuant to that section.

To compare with the time I came before you last in June, there were 60 cases compensated. Fifty-three were resolved by settlement and seven of the compensated cases were resolved by court decision in favor of the petitioner. There were 41 dismissed at that point in time, 28 by decisions against petitioner, 12 by a voluntary dismissal, and one pursuant to that Section 21 that I talked about.

Figuring the percentages -- how this breaks out, what's happening -- they actually stayed roughly the same. Roughly the same number is being compensated versus dismissed. It's a rough equivalency. Just the raw numbers

are lower.

Again, that was a three-month period. One thing that I have noticed in the many years I have practiced before the court is that August tends to be a time when there is less adjudication of cases. It tends to be the time when most of the special masters end up taking some leave and some vacation. The decisions tend to come out -- we will see a bump-up in September and the months thereafter, as the decisions start coming out again.

I invite questions at any time about any of these figures or anything that I'm covering.

One thing that came up last time -- Ms. Buck had asked, can we look at the numbers of cases to determine how many are being settled versus how many are being conceded, and whether there are a lot more litigative risks, settlements versus settlements that are conceded cases but are also then settled, in terms of the amount of damages. Unfortunately, the latter point we couldn't break out without going back through each case. But we can get an idea historically, looking back the last five years, about whether the trend is up in the number of cases that are settled versus the number of cases that are conceded, or

whether it's stayed the same or whether it's reversed. My impression was that it was going up quite a bit. Certainly the overall numbers of settlements have gone way up.

Going back to 2004, on up through --

DR. FISHER: Can I stop you for a minute?

MR. MATANOSKI: Sure.

DR. FISHER: Can you just remind us of the way a case can be settled?

MR. MATANOSKI: There are a couple of different ways that a petitioner could get compensated out of the program. A case comes in, and the secretary could say, we think this case ought to be compensated. It meets the act's requirements for compensation, whether it meets the table or whether it meets actual causation.

The other method is that a petitioner could receive compensation through settlement. There are a couple of different kinds of settlements, as it were. That's really where your question was going.

One could be a case where it's determined that the petitioners meet the requirements for compensation under the act. Rather than have the court go through the damages portion and issue a damages decision and

compensating the case, the parties work together and figure out jointly what is acceptable compensation, and a settlement is entered, a stipulation setting out what the terms of the compensation are. It's not a court decision in terms of the compensation.

Far more of the cases that are settled are what we call litigative risk settlements. That is where the petitioners maintain they are entitled to compensation and the government maintains that they are not. But the parties agree that there should be a settlement of the case before a court has to decide that black or white decision, as it were, about whether they are entitled to compensation.

If it goes to the court, if the court finds, as they did in 11 of the cases that were resolved last time, that they should not get compensation, then they get nothing. Attorneys' fees will probably get covered, but petitioners won't get any compensation. If the court decides, as they did in four of the 33 cases in this past period, that the petitioner should get compensation, then it will go on to damages and determine what that compensation should be, or perhaps it will be settled as to

the amount of damages.

But it won't be that litigative risk settlement, which resolves the case without a resolution of whether or not under the act the person is entitled to compensation.

The amount of compensation in those instances isn't necessarily tied to what the petitioner needs, obviously, because this is an agreement between the parties that before we go for that all-or-nothing before the special master deciding the case, we are going to have a resolution short of that for some amount of money.

If there are any other questions on that, I would be happy to entertain them.

The interesting thing, in going back through these last five years, is, yes, settlements are up in the last year, but they are roughly the same. The percentage of settlements across the years has varied from a low point of 67 percent of the compensated -- this is of compensated cases -- 67 percent settled, versus 33 percent conceded by the secretary. That was the low mark. The high mark was so far in 2008, which is 82 percent of the cases were being resolved -- the compensated cases, this is, just to be clear, the compensated cases, not the overall resolutions

of cases -- 82 percent are being resolved by settlement, with a lesser figure -- obviously, roughly 18 percent at this point -- by concession. In between they have run in the 70s, 70, 75 percent versus 30, 25 percent.

My impression was that there would be more of them settled, a greater percentage settled in this past year. Certainly it is running about 10 percent more than we have seen in the past, but it hasn't been significantly higher in terms of the breakdown of how many are conceded versus how many are settled.

The more striking pattern that emerged when we looked at this is, in the last five years, the number of cases, total -- the percentage of cases, I should say, out of the total adjudications that are actually compensated. That has gone up quite a bit. In 2004, there were 296 cases adjudicated. Twenty-one percent received compensation. That was a high mark for adjudications, and I'm sure that some of those cases were dismissed because they were autism cases that were clearly time-barred. That probably bumped up the number of cases that were not compensated in that year and bumped up the total number of cases adjudicated. But, still, it was 21 percent at that

point in time.

So far in fiscal year 2008, we have 253 cases adjudicated. Forty-nine percent were compensated in some fashion. A fair number of those are probably by litigative risk settlement rather than compensation either through a concession or through a settlement that goes to all the damages necessary in a case.

But there has been a big jump over the years. That's just going back for a five-year period.

The interesting thing that comes out of that is, what happened in that five-year period? Were vaccines made differently? They haven't been. Yes, we added a couple of vaccines. I really think that probably most of this can be attributed to changes in court decisions, the court decision to law that has come out as far as what is required -- or believed to be required for showing for compensation, largely going back, probably, to the Althen case and the change that that made in terms of how the court viewed what is required to make a showing for compensation.

One takeaway from that is, if that is true, don't look at the resolution of these cases, the court cases, as

to whether vaccines are safe or not. It may not be a reflection of that. It may be a reflection of the changing patterns of what the law requires to prove compensation rather than what the evidence is on whether vaccines are really at the heart of whether injuries occur.

MS. BUCK: May I interrupt for just a second, Vince?

MR. MATANOSKI: Sure.

MS. BUCK: In June when we talked and I had the request that you provide a history of the conceded settlements, litigative risk settlements, and entitlement decisions -- I kind of missed your comment there right at the start -- was it that that information isn’t available for us in terms of a historical perspective?

MR. MATANOSKI: What we were able to divine, without pulling each of the case files and going back through them, were the cases that were conceded versus the cases that were settled. To find out what kind of settlement it was, whether it was litigative risk or it was a settlement because essentially the case was found to be entitled for compensation by the court or conceded by the respondent and then went to settlement, would have required

going back into each of the case files for those cases. We could at least get -- with going back through the statistics that we had, without pulling each of the cases and going through them case by case, we could get these general ideas.

As I said, the interesting thing that came out of that, to me, was -- I had expected a bigger jump in terms of the split between conceded and settled cases than I saw. I expected that the jump to the number of settled cases versus the number of conceded would have been more stark in the last two years, let's say, than it seems to me, though it is up.

MS. BUCK: When you are using the term "settled" -- you may have more paperwork there than I have in front of me -- I'm looking at the information you gave us today, which says the compensated number of cases is 20, and then you have 16 settled. That figure represents cases where there was no dispute in terms of the injury.

Is it possible in the future, then, to break that out and show us if any of those -- in that number 16 that I assume are conceded cases -- am I correct or am I missing something?

MR. MATANOSKI: Actually, they are not necessarily conceded cases, no. They are cases that received compensation, and they received compensation through settlement. The other four were compensated over -- the government did not settle the case and maintained that the petitioner was not entitled to compensation. In those four, the special masters found, nevertheless, that the petitioner was entitled to compensation.

MS. BUCK: There are no conceded cases, then, in that number 20 on this particular report?

MR. MATANOSKI: As far as I know, there isn't.

MS. BUCK: In the future, when you provide reports like this, if there are, is it possible to have that included in there?

MR. MATANOSKI: I believe that would be possible. I would be happy to do that.

MS. BUCK: I'm trying to write down all these numbers you are doing. I don't know if you are using slides that I don't have or something. If you do have some statistical information that everybody else is reading from, can I make sure that I get that?

DR. FISHER: We don't.

MS. BUCK: I'm not keeping up with all your numbers.

DR. FISHER: We don't. There is nothing more. You are not missing any stuff.

MR. SCONYERS: I know you are looking at it. Is it possible for us to distribute that?

MR. MATANOSKI: Yes. What I can do is do my -- I do my own math, and that's probably a very dangerous thing. I should have somebody check my numbers. Lawyers doing math is very dangerous.

But I can reduce these statistics that I have pulled together and put that -- Dr. Evans said we can put it together into a document and send it out.

MS. BUCK: Thank you. That would be very helpful. I appreciate it.

MR. MATANOSKI: Sure.

DR. HERR: This is kind of a new question. It goes back to your idea of incidence over the past quarter or the quarters before and why more cases are coming up. Are we assuming that every instance of injury is coming to court or coming to this active agency? Could there be

something that is happening, let's say, through the media, through some of the discussion, that is actually bringing out more cases to us? People are recognizing that they should come to this program for compensation, and that may reflect why there are more cases.

MR. MATANOSKI: I definitely believe that the publicity that surrounds vaccines does influence the number of cases we have filed. Whether those cases represent actual vaccine injuries is, of course, something else that the court determines.

DR. HERR: I understand. But it doesn't necessarily mean there are more injuries. It may just mean that there are more people coming to the program.

MR. MATANOSKI: Right. And what I was focusing on in my comment was the percentage of cases that are compensated out of the program going up. What I was suggesting was that a change in the law has influenced how many cases get compensated out of the program. So one shouldn't necessarily equate compensation with this program as an indication that vaccine has actually caused -- that there is a change in either the way vaccines are influencing injury patterns or that there has been a change

in how vaccines are made and they are more or less given to adverse events.

If you look at that number and see the trend upwards, we do know that there was a very significant change in the way the court viewed how causation could be proven, which certainly has influenced how many cases are being compensated. That's what I was trying to take away from that, seeing that fairly big jump in the percentage of cases that are compensated.

DR. FISHER: I just need a little more vocabulary lesson here. If you say a case is conceded, that means that somebody looked at that and said, yes, this meets the criteria and you should get compensated.

MR. MATANOSKI: That's correct. It actually means that the secretary looked at it --

DR. FISHER: So is that the same as "settled" a case that meets the criteria?

MR. MATANOSKI: No, it is not.

DR. FISHER: How is it different?

MR. MATANOSKI: It is a case that has come in and the secretary has looked at it and says that the petitioner has met the criteria under the act for compensation. That

case could end up being settled in the sense that the damages are settled. But it would not be what we call a litigative risk settlement, where the parties have not --

DR. FISHER: So would it show up as one of the 16 settled or would it --

MR. MATANOSKI: I believe in this last period there were not conceded cases. Of the ones that were adjudicated, they were all cases --

DR. FISHER: Okay. So I guess I'm with Tawny. Can you give us a better idea? To me, there is a big difference in something that is conceded and something that's settled.

MR. MATANOSKI: Right. I understand.

MR. SCONYERS: I think it would be useful to include just a glossary of what the terms mean. I think we are all somewhat confused by what they mean.

MR. MATANOSKI: I'm doing a good job as a lawyer. I have you all confused now.

MS. GALLAGHER: I'm wondering if you have a category of conceded and then damages settled. If it's conceded but you settle damages later, which column does that one go into?

MR. MATANOSKI: In terms of the way the HHS figures out and keeps statistics, that would be in the concessions.

MS. GALLAGHER: It would be. So it wouldn't be considered settled just because you settled the damages.

DR. EVANS: [Off-mic]

MS. GALLAGHER: I just wanted to know, when I look at this document, what column a case like that would go into.

MR. MATANOSKI: We will make sure that we make it clear on the document that is provided. When you have broken out the concession cases, it doesn't matter how they are resolved -- the damages -- whether it's resolved by settlement or resolved by court decision. It's still reflected as a conceded case.

MS. HOIBERG: We are really going to beat a dead horse here. But on the conceded and the settled cases, are you saying that there were 16 cases that were completely finished in three months?

MR. MATANOSKI: No.

MS. HOIBERG: You said, yes, the vaccine did cause this injury; now let's go into damages.

MR. MATANOSKI: What that snapshot is, is just the number of cases that were adjudicated in this last period.

MS. HOIBERG: And that means?

MR. MATANOSKI: Went to a decision in this last period. Those cases were likely filed before this period. There are only a couple of cases that are resolved that rapidly that I can think of. So likely, of those 33 cases that were resolved -- of those 20 that were compensated, they were probably filed prior to this three-month period, but they got adjudicated by the court -- that is, decided by the court -- whether that decision be that we adopt a stipulation settling the case or whether that decision be that they found entitlement or found against entitlement, during this period.

MS. BUCK: Is there any kind of formula or something that is used to determine if a case is conceded? How does that decision come about? Can you talk about that?

MR. MATANOSKI: To determine whether a case is conceded or not really would depend on the act itself and on the evidence that was submitted in a particular case. I

would say you can't really reduce it to a formula. One of the things that would be reviewed would be whether it met the parameters of the vaccine injury table. To the extent that one considers that a -- I wouldn't call it a formula, by any stretch -- and I have to say that in each case you are going to have to look at the evidence that is submitted or developed in that case to determine whether or not they either meet the actual causation burden under the act or they meet the parameter for the presumptive injury under the table.

MS. BUCK: Am I correct that they are a little bit gray, those conceded case? If it was real cut-and-dried clear, there would have just been an initial settlement? Or am I confused?

MR. MATANOSKI: Dr. Evans is grabbing a microphone.

DR. EVANS: I might be able to clarify things -- hopefully, not make them more confusing.

Our task in the Division of Vaccine Injury Compensation -- when the medical staff perform the reviews of the medical records, the first question is, is there evidence of a table condition? If there is does satisfy

the table condition, based on the records, is there evidence of another cause that there is greater evidence of? If that's not the case, then that is a straightforward table injury, and that would be a table concession.

Much less frequently would be the circumstance in which there is actually proof of causation, if it's not a table injury or if it's off the table parameters in terms of integrals. That would be another basis for a concession.

Much less frequently would be if there was evidence of aggravation, that the vaccine aggravated a child's preexisting condition.

When we perform our reviews, those are the three ways in which we would determine and make a recommendation for a concession to entitlement.

DR. SALMON: Just for clarification -- correct me if I'm wrong -- at no point does the program or the secretary, even in a concession, determine that a vaccine caused an adverse event, but rather the concession would be that the statutory requirements of the program have been met. When the word "causation" is used, it's used in a legal context, and not a medical context. Is that correct?

MS. BUCK: I know that's Dan. I can't hear him. I'm sorry. It's a good question.

DR. SALMON: I'm sorry, Tawny, it is Dan. Do you want me to repeat the question?

MS. BUCK: If you don't mind, because I know it's a good one.

DR. SALMON: You're too kind, Tawny.

MS. BUCK: They are always good ones from you. I need to hear it.

DR. SALMON: The question I asked was a clarification -- there was a comment made that the program determined that the vaccine caused the adverse event. I was asking for clarification, as I understand it, that a concession refers to the statutory requirements being met and that at no point does the program or the secretary determine whether or not an adverse event was caused, in a biomedical sense, by the vaccine. I was just asking for clarification.

DR. EVANS: To answer your question, Dan, nothing's 100 percent. I think there might be some instances in which, based on the available evidence, the scientific evidence, it might be that there is proof of

causation in a scientific, medical sense, particularly if there was a lab marker that was available. Clearly, with polio vaccine, the isolation of poliovirus was proof of caution. If there is a challenge-rechallenge -- in other words, if an individual received the same vaccine twice and the same condition happened in a reasonable time interval -- I think that's pretty strong evidence of proof of causation.

Beyond that, it depends on the particular circumstance and the type of vaccine, the type of injury, and so on.

So I think it's to variable degrees.

DR. SALMON: I'm not suggesting that it wasn't perhaps caused by it. You have given examples where there is quite compelling evidence that it is. But that's not what the concession is saying, correct? It may or may not have been biomedically caused by -- and you used an example of the vaccine-associated paralytic polio, a pretty clear biological marker. I just think this is important, because there is a lot of misunderstanding around this.

When there is a concession from the secretary that something should be compensated, as I understand it --

and please correct me if I'm wrong -- what that concession says is that this petitioner met the statutory requirements of the program. Whether or not there is actually a biomedical cause and effect -- maybe there is or maybe there isn't -- that's not what a concession means.

MR. SCONYERS: Can I interrupt just for a second? Dan, you can't be heard.

Can you try to summarize Dan's comments?

DR. EVANS: Before I summarize, I just want to point out, the example I gave, of course, was for poliovirus vaccine, the oral poliovirus vaccine, which is no longer being given in the U.S.

The question is, when we say that we are conceding based on proof of causation, is that a strictly medical determination, a scientific determination, or are there legal ramifications? The answer is the latter. This is both a medical and legal determination. Depending on the particular vaccine and the particular injury, it might be toward one or the other. But I think it's very clear that both are involved.

MR. SCONYERS: If I could just comment, this is an issue that came up yesterday at our orientation for new

members. It's a recurring issue in this program. When people say "cause," they mean different things by it.

Dan, your use of the word "cause" in a biomedical sense and Vince's use of the word "cause" in connection with the resolution of cases that are filed under the act -- they are the same word, but they don't have the same meaning. There is a lot of gloss, depending on the profession involved or what the particular reason for using that word may be. I think we confuse ourselves when we think that that same word means the same thing in every context.

DR. SALMON: Jeff, that's exactly the point that I was trying to highlight. There are different uses of the word. Thank you for your clarification. That's the point I was trying to make. The use of the word "cause" can be interpreted very, very differently.

MR. MATANOSKI: As this is a program that operates under a law, it's a legal standard. Even on actual causation, that's really a legal determination, though certainly the evidence will influence that.

It's interesting. We started with the notion, is there a formula? In some ways, you could say there is.

There is a legal formula. But there isn't a formulaic outcome. It's going to be dependent on the evidence that goes in. But the law influences, in actual causation cases, where there will be a finding of actual causation or not, a concession of actual causation. It has to, because this is a program operating under that law.

Thanks. That was a really good question.

I'm going to turn now to autism. I know that Tom Powers is going to talk about this, so I'm going to go quickly through part of that. I'm sure he is going to be covering it in more detail.

As Dr. Evans already said, we have tried the last of the second theory that was involved in these cases. There will be no trial of a third theory. The same evidence or same mechanism was going to be alleged for the third theory -- that was MMR alone -- as was alleged in the first theory, MMR and thimerosal working together. So the Petitioners' Steering Committee determined that no general causation trial would be necessary on the third theory.

Transcripts have been reviewed by the DOJ as to the second theory, the general causation part, and have gone out to the PSC for their review. When the PSC, the

Petitioners' Steering Committee, reviews those transcripts and is done with the review, then the court will likely set a post-hearing briefing schedule, where each side will put together their written submission regarding the evidence that has already been heard by the court.

DR. FISHER: For the second theory, did they find the third case?

MR. MATANOSKI: Oh, yes.

DR. FISHER: So there were three.

MR. MATANOSKI: Yes. That was tried beginning 21 July. They will all be ready for decision about the same time. The briefing schedule and everything will probably all mesh at this point. The transcript from the general causation in the first two cases was fairly long. It took a while to prepare. It took a while to go through. Now the schedules on the two -- they will probably mesh up, and all three will be moving together through the process at this point.

One of the things I mentioned last time -- the Petitioners' Steering Committee was interested in getting evidence from the United Kingdom trial on MMR, and they decided that they were not going to pursue that any longer.

The thing that I would like to talk about, about autism, that I mentioned last time that probably Mr. Powers won't be discussing is about the activated cases. At least he won't be discussing it from the standpoint of what this means for DOJ.

When I spoke to you last, the activated cases -- there were 5,000 that had been activated. We are out to 1,400 now. The review of those cases was essentially -- when the court activates them, the petitioners are required to put together some evidence going to whether their case meets jurisdictional requirements. Once they get that evidence in, DOJ takes a look at it. They have 45 days to review it and get a response in. The response essentially says that the case meets the jurisdictional prerequisites, and therefore is ready for further development; or it does not meet the jurisdictional prerequisites, and therefore should be dismissed; or it's impossible for us to determine at this point, based on the evidence, whether it does or it doesn't, so more development needs to be had on that jurisdictional question.

Some of those cases where we have said they haven't met the jurisdictional requirements have been

dismissed.

MS. TEMPFER: I just have a question about activation. Vince, will all of these cases eventually be activated? Is there a pace set for it? Or are just certain cases picked to be activated?

MR. MATANOSKI: All of them will eventually be activated. This is a process the special master has put together, the special master's office, in consultation with the petitioners' representatives and with DOJ. They choose essentially 200 cases a month. They get a lot of input from the petitioners as to which cases are much further along in terms of records being developed. They are probably more likely to be put on that slate for activation -- that is, get your records in.

So the court has had some communications or dealings with the petitioners as far as which cases are going to be activated. But the court essentially decides which cases out of the pending 5,000 are activated.

The idea was to get them all through this process, where there is at least an initial look at whether there is jurisdiction for the case, in a two-year period. It's 5,000 cases, 200 a month, 24 months, 4,800 -- we are

going to be one month over.

What's happening is that it is getting a little bit more difficult, I believe, for petitioners to keep pace with the number of cases that are being activated, since some petitioners' law firms have a great number of cases. They are feeling the burden of getting those cases activated.

It's hard for me to have a lot of sympathy, since all those cases come through our office and we have to handle all of them. We don't have 50 a month or 10 a month; we have 200 a month to deal with. Actually, I'm very proud of the way our office has been able to respond and meet the court deadline so far each time in those cases.

It has turned out to be a very difficult job -- we expected it to be -- in terms not only of responding to them, but managing those responses. Though it sounds very systematic when you say 200 are going to be activated each month, that means that petitioners have a certain amount of time to get their records in, but often they need more time. So then you start seeing deadlines move and switch. One case is not necessarily going to be done because they

are going to ask for more time, and then they are going to ask for more time again. So you are getting a lot of different deadlines coming up.

So it has been a big management challenge to keep up with that. But so far we have been up to that challenge. So far the petitioners have gotten a lot of cases with the records in. Petitioners' counsel have managed to get a lot of cases in so that there can be that review.

What is going to happen next is, the cases where there is either insufficient evidence to determine whether there is jurisdiction or where we believe at the Department of Justice that they have not established jurisdiction, yet the petitioners believe that they have, the court is scheduling conferences, status conferences, in most cases to talk about them and is actually scheduling hearings to determine whether the jurisdictional prerequisites are met.

Usually, if there is a jurisdictional prerequisite that is not met, it's because the case appears to be not timely filed. That is, they didn't get the case filed within 36 months of the first symptom or manifestation of the onset of the claimed injury -- here,

autism. What will likely happen in those cases -- some of them are already going to trial -- is that there will be not only factual evidence from the petitioners or treating physicians, perhaps, but also expert evidence as to what constitutes the first symptom or manifestation of the onset of autism. Obviously, if it's over three years, then there is a question of whether the case is timely.

MS. HOIBERG: I just have a question. With these autism cases -- I live it every day. My child is not autistic, but she goes to a school that has children with autism. What we have seen and the stories that I hear every single day are, my child developed completely normally for 18 to 24 months. They got their shots, and they stopped talking. How do you argue that? How do you sit there and go, it wasn't the shot?

MR. MATANOSKI: The scientific evidence that has come in is what will decide whether or not autism is caused by that. Certainly there is a lot of information for people who hold the belief that the shots are responsible, and they do it based on timing. They say the timing is right.

But if you look at how autism develops, it

generally develops in that fashion. If you think about what it is that determines whether somebody meets the requirements for autism, it's things like language. Obviously, a 1-month-old we don't expect to be talking. So they couldn't have that symptom of autism at that point in time.

Generally, when the symptoms of autism occur, regardless of immunization status, is at the 12-month to 18-month period. We also happen to be vaccinating at that time, between 12 months and 18 months.

MS. HOIBERG: There are a lot of vaccines in that time period. For me, the schedule needs to be looked at as far as -- I think that a lot of this could be alleviated and we could save a lot of children's lives and their parents' lives by changing what is in the vaccines and the schedule. When I was a child, I got maybe 10, and now they are getting 36. It's a lot.

MR. MATANOSKI: Obviously, this is arguing a point that is in front of the court. In the view -- though not only the view -- of the Department of Justice, who would be doing these cases, I think you have to decide these cases based on evidence, not necessarily on personal

feelings or beliefs. Right now the evidence -- at least the evidence that we have put on in our view -- this is the Department of Justice view -- has not supported that there is any link.

I wasn't going to talk about it, and I haven't seen anybody else talk about it, but, obviously, many of you probably saw in the paper today, on the second page of *The Washington Post* -- it was on the radio this morning, and it was on ABC News last time -- a new study just came out that said that it could not find a link between MMR vaccine and autism. Yet for 10 years that has been out there and argued that there is such a link.

The interesting thing about that study that came out is that some of the scientists that were on that study were proponents of that very link between MMR and autism. They have gone back in the 10 years and they have looked at it, and now they say there is no evidence to link MMR and autism.

This is obviously something that is going to be decided -- people are making personal choices about whether to vaccinate or not. Some may be making unfortunate choices. There has been a rise in the incidence of measles

in this country recently. That is a vaccine-preventable disease.

The evidence so far that we are collecting and putting on in front of the court doesn't establish any link.

MS. HOIBERG: Mercury poisoning mimics autism.

MR. MATANOSKI: Actually, there is quite a bit of information that refutes that, that has been out there. That was proposed, actually, by individuals who were not toxicologists. They did not have experience with mercury. They first proposed that in a publication that says that they publish things that will not be accepted by peer-reviewed publications. In fact, you have to provide money to get the article published in that journal.

I have been so immersed in the evidence in this over the last couple of years, I could go on. This is obviously not the forum of for it. I know that there have been other studies out that have looked at whether or not the trend of autism has gone down after mercury wasn't used in vaccines, and have shown that the trend of autism remains on the same path, regardless of mercury being in vaccines or not.

MS. HOIBERG: It is still in there. It's just in a smaller amount. But it is still present. That's on the CDC Web site, if you go and look. It's in there.

I don't understand -- it's epidemic. One in 150 children is suffering from this horrible, horrible, debilitating disease that they are not going to die from. They are just going to cost taxpayers and everybody millions of dollars.

MR. MATANOSKI: There's no question that it's a horrible disease. There is also no question that vaccines can prevent other horrible diseases. Right now the scientific evidence, in our view, doesn't support a link between vaccines and autism. Yet it's known that these other diseases that are vaccine-preventable will cause injuries themselves. In the time that you and I have been talking, there were probably -- I have done this math before -- seven kids across the globe who died of measles, which is a vaccine-preventable disease.

So there are lots of reasons to continue to vaccinate.

MR. SCONYERS: I would like to intervene at this point. Sarah, I think your questions are important ones,

and they are issues of concern. I would like to let Vince get through his report about the litigation that the department is handling on behalf of the program.

MR. MATANOSKI: Thanks.

I will run through this very quickly now. I only have five minutes left. I can go through this pretty fast.

MR. SCONYERS: We can expand your time, Vince.

MR. MATANOSKI: Thanks.

On attorneys' fees, I mentioned the last time that interim fees had come up because of a court case. We are keeping an eye on what happens with it. At that time, there was only one interim-fee case that had been filed. Since that time, 15 more have been filed.

Interim fees are attorneys' fees where they can essentially seek fees in the middle of a case.

We only had 15 regular attorney-fee applications during that period of time. So they matched the number of attorney-fee applications we had.

I thought this might mean that a lot more resources needed to be tied up in the resolution of attorneys' fees. It looks like it will. Hopefully, by the end of the case in some of these interim-fee cases, it

won't be as extensive. But it looks like it probably is going to involve more time. Unfortunately, that could mean that -- there are only a limited number of special masters that are called on to decide these cases, so it could take away their ability to move forward on resolving cases themselves.

It's something that we are keeping a close eye on. It looks like it has now received a lot of attention by the petitioners' bar and that we are going to be seeing a lot more of those in the future.

MS. BUCK: You have gotten some requests, is that what you said?

MR. MATANOSKI: Yes. We had 15 in the last three months.

MS. BUCK: You mentioned in June that when this issue came forth you were working with a group of petitioners' attorneys to sort of set your break points and all that. Are they continuing to be involved in that process?

MR. MATANOSKI: Yes, they are. Fortunately, of the cases that came in, most were meeting those break points that we were talking about, to keep a handle on the

number of interim-free cases that we see. These were limits on numbers of times you would actually seek interim fees, total amount involved, and when you would seek them.

Some of them that came in didn't meet those break points. Interestingly, Ms. Buck, yesterday the one of the counsel I was working with -- his firm has more cases filed in the vaccine program than any other firm -- he and I were on the phone yesterday talking about this very issue and decided that we ought to get together and speak with the chief special master to discuss further whether there can be some ways of streamlining the process to make sure that the purpose of interim fees is met, but at the same time it is not dragging down the processing of the cases themselves.

MS. BUCK: Vince, do you think it will be manageable, that you will be able to hit some sort of a combination where it works for everyone?

MR. MATANOSKI: I'm an optimist. I'm a little concerned right now. Maybe it's just that we are seeing a lot of it come through the door all at once, because it's new. Once we get through the cases that are out there, we won't see it taking as much of our time and attention.

I do have to say, the reason for my optimism is that my experience has been that the petitioners' bar has worked cooperatively in many aspects. They have approached this with a cooperative spirit. The court is always -- they are very practically-minded. They are very solution-minded. That is good reason to be optimistic about this.

But there are 6,000 cases pending. If we are going to be doing attorneys' fees two times or three times in a case, it obviously would mean that a lot more resources would be diverted to that.

MS. BUCK: This has been a really important issue for the ACCV, so it's good to hear that you guys are continuing this conversation and the effort to do this. Although I understand your concerns about it, I think for the families and for their counsel, it will be a good thing. I know I have said this before, but I really appreciate the effort that you are putting in to trying to make this manageable.

MR. MATANOSKI: Thanks.

I touched on appeals last time. You will be grateful to hear this: That's usually where I end. There are three appeals that are pending at the Federal Circuit

right now.

One of them actually involves fees, but an interesting little twist on it. It was a case where fees were not given to the petitioner's counsel because the underlying case was time-barred. That means there is no jurisdiction. The court has taken the view, as have we, that there is no jurisdiction to give compensation for attorneys' fees either. That case is up on appeal now in front of the Federal Circuit. It involves a question about time bar.

It leads to my next case that is in front of the Court of Appeals that I spoke to you about last time. That case was Mojica. The case was filed one day late, through no fault of the petitioners. The court has a very bright line as far as when the filing deadline must be met. It has to be met within 36 months of the first symptom or manifestation of injury. Both parties -- the petitioners agreed -- that this was one day late. The Court of Appeals for the Federal Circuit said that's too late, one day. We don't look at the other circumstances that involve why. You might have a suit against the carrier who delivered it untimely, the delivery service. But that's not -- we can't

give you relief here.

They didn't take much time to decide it. They decided it what we call *per curiam*, which means that it's a unanimous decision; it's generally taken to mean that the panel really didn't find this a very difficult legal question in front of it. It was decided only about one week after the case was argued. So they disposed of it fairly quickly.

The petitioners have moved for rehearing *en banc*, which means that the entire Federal Circuit would hear the case if they grant a rehearing *en banc*. The court is still considering whether it's going to grant a rehearing *en banc* in that case.

The other case that I spoke to you last time about -- a very important case. It was being argued the day that I was speaking to you, DeBazan. You have heard about the injury arising too long after the vaccine and there being a finding that there is not good evidence because the temporal association is not there. It's many months afterwards. DeBazan represented an instance where the injury occurred too soon. The type of injury that was involved was a demyelinating condition. That takes a

certain amount of time before the body could manifest itself after whatever agent it is triggers the demyelination. In the instance of the DeBazan case, the demyelinating disorder first arose 11 hours after the vaccination. There was medical evidence that the special master credited that said that's too soon; it has to be at least a couple of days -- generally, it's going to be a couple of days before you would see a demyelinating condition after the agent that would incite it.

That was the finding of the special master. The Federal Claims Court decided -- and that's a single judge sitting, listening on appeal -- decided, if you are saying that it couldn't be the vaccine, then it must have been something else that caused this demyelinating condition. And isn't that the government's burden, to prove something else?

It was a very disturbing decision, because that essentially would mean that you never had a burden as the petitioner to show the vaccine caused it. In fact, it's always going to be the government's burden to show that the vaccine didn't cause it. It's almost a presumption that vaccines cause everything that is before the court, unless

the government can prove otherwise.

The Federal Circuit looked at that case and said, indeed, the petitioners failed to meet their burden. It's their burden to show that the vaccine caused it. Eleven hours was too soon, according to this evidence. Yes, although that may suggest that there is something else out there that caused this, it does not change the burden in that instance. It's still the petitioner's burden to show vaccine causation. Since they couldn't show that the timing was right, which was one of the parts of their burden, then they hadn't prevailed in this case.

That case came out, I think, just a week ago. A very important case, decided by the circuit.

DR. FISHER: I'm sorry, let me get it right again. So the special master said, too soon. The Federal --

MR. MATANOSKI: I'm sorry, the Federal Claims court, which is an intermediate appellate court, as far as the vaccine cases. It's a single judge sitting. He or she hears the case and decides whether or not they agree with the special master. Not all cases are appealed, obviously.

DR. FISHER: Then that decision was appealed to

the --

MR. MATANOSKI: The Court of Appeals for the Federal Circuit. Decisions from the Court of Appeals for the Federal Circuit are binding on all the special masters and on all the judges.

It's like those old commercials for E.F. Hutton: When the Federal Circuit speaks, people listen. Here they said, yes, something can be too soon, and that is part of the petitioner's burden. It's not the government's burden, the secretary's burden, to prove what the other factor was in those instances.

MS. HOIBERG: I have a question about that case. Was that the first vaccine that he received or had he had previous vaccines?

MR. MATANOSKI: I don't recall whether that -- it was a she, an adult. I don't recall whether that was the first time she had received the vaccine. I assume that the instance of -- or the notion of rechallenge, which is one that we have seen in many cases brought up, was explored in that case, because it's one very well known to the court, to respondent and petitioners' bar, and obviously to the experts that testify. So if rechallenge was a potential

issue, I'm sure it was explored in that case.

MS. HOIBERG: It could have been just something that built on it. When she had the vaccine, it began the process, and then when she had the other vaccine, it just pushed her over the edge, like we are talking about. They can aggravate a preexisting condition.

MR. MATANOSKI: Right. That wasn't a preexisting condition in this instance. I'm not sure of the person's vaccine status, but I know that parties and the court are well aware of the notion of a second vaccination perhaps shortening the time period. They routinely hear evidence one way or the other on that particular issue.

MS. HOIBERG: Is there any way that I could get copies of those cases?

MR. MATANOSKI: I'm sure that the DeBazan will be published. The *per curiam* decisions are usually not published. They are just on a list of tables. But I don't think they are -- although it wouldn't be a published decision, it's not -- it wouldn't be that it couldn't be disseminated for the public. It's just that it wouldn't be what we call a published decision.

MR. SCONYERS: We will look into getting that.

Are there other questions for Vince?

MS. TEMPFER: How many special masters are assigned to the autism cases?

MR. MATANOSKI: There are three that are assigned to the big group, the Omnibus Autism Proceeding. But with respect to the activated cases, what the court is doing is, it seems to be making sure that those three that have the omnibus cases aren't having to work up these case-specific issues about jurisdiction. So the court -- the special masters seem to be assigning those cases that require hearings on the jurisdiction to the remaining special masters. So they are hearing the jurisdiction on the activated. The other special masters, the three that are hearing the omnibus autism cases, are Special Masters Hastings, Campbell-Smith, and Vowell -- Campbell-Smith being a hyphenated name, so there isn't a confusion that we have four.

The remaining special masters are hearing these jurisdiction cases as they come up.

MR. SCONYERS: Vince, you may have said but I just missed it. Is there any estimate for when the Cedillo and Hazelhurst cases are going to be decided?

MR. MATANOSKI: I don't know. The record is closed in those cases. The briefing has been done for a while. It would be any day now.

MR. SCONYERS: Other questions for Vince?

(No response)

Thanks very much.

MR. MATANOSKI: Thank you.

MR. SCONYERS: Tom, do we have you on the phone?

MR. POWERS: (Via telephone) Yes, I'm here. Can you hear me okay?

MR. SCONYERS: Yes, I think we can hear you okay. Thanks very much for making yourself available and for making this presentation. We love hearing from you. We would like to get your perspective on the autism hearings from the Petitioners' Steering Committee's standpoint.

Agenda Item: Report on Autism from Petitioner's Attorney

MR. POWERS: As always, I appreciate personally, and I know other members of the PSC appreciate, the invitation that we get regularly to speak to you all and to give an update and to answer questions.

For the Omnibus Autism Proceeding, I can just

fill in a little bit more background detail on the issues that Vince discussed. I was able to listen in on his presentation. He really covered the main topic areas.

Yes, the Cedillo, Hazelhurst, and Snyder cases from 2007 have concluded, although in the Snyder case Special Master Vowell did issue an order recently inviting the parties, if they wished to submit any reply post-hearing briefs -- that is, one final round of what would be a relatively narrowly focused briefing in that case -- the opportunity to do so is open for about another three weeks.

In Cedillo and Hazelhurst, as Vince described, the record in those cases is closed. I don’t have any greater insight than Vince does on when we might see decisions. It could be any day, at least in those first two cases. Then the clock begins running after about the end of the third week of September in the Snyder case, given the possibility of a little bit of additional briefing.

There were questions on the second round of cases, which were held in May and then again in July. Those cases have concluded in terms of the presentation of evidence. We received, as I think Vince described, a

version of corrections to the transcript.

One question that I get a lot from the families that I represent and from people following the progress and the program -- and maybe some of you have this -- is why there is such a long period of time in these cases after the conclusion of a hearing for opinions and decisions to come down. I get that question particularly from people who are used to the jury system, where one presents the evidence, the witnesses testify, they are cross-examined, the lawyers argue, and then a group of people go into a room and come back out within hours or maybe days with a decision. Here it takes months.

One of the big issues is that the transcripts of these hearings, particularly in the general causation cases in the Omnibus Proceeding, are incredibly large. You are looking at three-week trials. The transcripts often involve very technical testimony, with scientific and medical terms. It takes a careful review of the paper transcript compared to the audio recording to make sure that the paper transcript, which is the actual record of the proceeding and is the record that’s going to go up on appeal -- that the printed transcript coincides with what

was actually said in the room by the witnesses while the record is open.

Both sides, the Department of Justice and petitioner's counsel, view what are essentially drafts of the transcript and we sit down and listen -- having tried the case for three weeks, we then sit down and listen to it all over again via the audio recordings, with a copy of the draft transcript next to us, and make any corrections and changes. Sometimes they are minor, but sometimes they are significant. There are sometimes blocks of testimony that are either not transcribed at all or that contain substantive errors that would affect the quality of the record that these important decisions are hinging on.

So we are in the process of doing that. The Department of Justice has looked at the transcript and suggested their changes from the thimerosal hearings that were held earlier this year, and now we on the petitioner's side are going through the same thing. When that is all done and a final transcript is filed, we will get a schedule to brief these and argue the evidence on paper for review by the special masters.

I do assume that everybody understands, but with

new folks we should be very clear: Each of the three special masters that sat in on these hearings heard all of the evidence in all of the test cases, but each of those special masters has one case that he or she will be writing an opinion and offering a decision in. So although Special Masters Hasting, Vowell, and Campbell-Smith all sat in the room and they all heard everything that the other person did, there certainly can be differences in their ultimate opinions as to causation in any case, and even if they agree one way or the other, there might be different reasons, based on the record in the individual case that they are hearing.

The decisions, when they do come down, are going to be read carefully by the parties and possibly taken up on appeal, even if all three special masters come down with the same ultimate decision, either awarding compensation or not awarding compensation. But it's important to keep in mind that ultimately we will have six specific decisions in six different cases, from the first round and the second round of test cases, that will be rendered in the OAP.

So that's where we are in terms of the hearings on general causation and the first round and the second

round of test cases. It is true that there will not be a third round of test cases. What has been described -- if you are familiar with some of the docket materials from the Omnibus Proceeding, right about now, September of 2008, was set aside for what has been called the MMR-only test cases. Vince alluded to it, but I can give you a little more detail.

The basic idea is that in the MMR portion of Cedillo, Hazelhurst, and Snyder -- the MMR evidence developed in those cases, and the general theory of causation, that the persistent live measles virus was a triggering agent for neuroinflammation leading to the symptoms of autism -- that causative role of the measles virus in those cases last year is essentially the same role for the measles virus that would have been advanced if these cases had gone to trial in September. That being the case, there really was no substantive difference between the evidence that would have been put on for general causation in the MMR-only cases and what was already presented in the combined thimerosal-MMR cases, and so the decision was made, to save the parties and the court significant time and resources, that there was no need to

put those hearings on. Everybody agreed that they would be canceled.

So the test-case process is completely done. From the PSC's perspective -- and we have communicated this to the Department of Justice and to the special masters -- there are no additional theories of general causation that would be advanced, and so the general-causation process, in terms of selecting test cases, presenting theories, and putting on general-causation evidence, is essentially concluded. Now we are awaiting decisions in the first round of cases and awaiting the opportunity to conclude the briefings and the presentation of arguments in the second round of cases.

I want to also talk about the activated cases.

Before I do that, I was curious as to whether anybody had any questions about where we are with the Omnibus Proceeding and the test cases that have already gone on.

(No response)

Hearing none, we can talk about the activated cases.

I'm not going to reiterate everything Vince said,

except to say that that accurately describes the process, in terms of notices going out to the petitioners' attorneys saying, in these particular cases where your firm is representing somebody in the Omnibus Proceeding, please send us your medical records so we can evaluate whether the case, in our opinion, is timely filed.

I think the best way to look at this from the petitioner's side -- how we see this process playing out -- is that there are going to be a significant number of cases where, when the medical records go in, it's obvious from the medical records that the case is timely filed. Sometimes it's a very easy decision to make. For example, if a child was 3 or 3½ years old at the time the claim was filed, it's virtually certain that the claim was timely filed. It would be very unusual to see symptoms of autism in the first one or two months of life, except in the most severe early-onset sort of classic autism cases. So there will be a set of cases where it's obvious from the medical record that the case was timely filed.

In those instances, as Vince noted, the Department of Justice communication to petitioners saying, "Yes, it appears that your case is timely filed. Of

course, we reserve our right, if we see anything further in the medical records, as more records are produced, to change our position on this, we would still want to contest it. But based on everything you have filed so far, it seems that you are timely."

Those are the easiest ones.

From the petitioner's perspective, there is another set that is unfortunate, but easy also. These are cases where a petition was filed more than three years from the actual date of diagnosis of an autism spectrum disorder. I know that a number of petitioner's attorneys who have filed those cases have voluntarily dismissed the cases, sometimes even without filing a medical record. They review the medical records, understanding -- and I'm not going to get into the arguments, but there are a lot of arguments about the relative unfairness of the limitations period under the act, compared to the limitations periods that would normally govern an injury claim by a minor under the law of the individual states.

But those arguments aside, the reality is, you have a 36-month window. For a claim filed more than three years after the date of diagnosis, those, I think, DOJ very

quickly flags as being untimely, and a lot of petitioner's attorneys will be voluntarily dismissing those.

That is going to leave a big number of cases in the middle, cases where there is an argument to be made, based on the medical facts and the medical circumstances of that individual child's presentation of symptoms -- the timing of the symptoms, the nature of the symptoms, the timing of the shots -- where there is going to be a fact dispute about when the first symptom or the first manifestation of onset of autism occurred. In some cases it's going to take expert testimony. It's going to take live hearings, the presentation of evidence from both sides.

What becomes a big issue down the road -- and this intersects a little bit with the interim-fees issue and also an appellate issue that Vince was describing -- in those cases where there is a fact argument to be had about whether a case is timely filed, the burden is on the petitioner to show, through the presentation of expert witnesses and testimony and medical records and lay-witness testimony, like the parents and caregivers who have information about onset -- putting those cases on is an

expensive endeavor. If there are a couple of thousand of these -- I don't know whether there might be a couple of hundred or a couple of thousand, but assuming that there are a couple of thousand of these contested timeliness hearings, it's going to very, very quickly turn into an extraordinarily expensive proposition for the petitioners and the families to assume. The case that is up on appeal on the jurisdictional issue and its application to interim fees -- under the law right now, all of that time and all of the expert expenses and out-of-pocket expenses that the petitioners would need to invest to prove that their claim was timely -- if they lost and the claim was found to be untimely, under the current interpretation of the law in the program, none of that money is compensable.

So you are going to be confronted with families who believe they have timely claims and the attorneys attempting to represent them, who are going to find it very, very difficult -- unless there are interim fees available in these disputed jurisdictional cases, they are going to find it very, very difficult to assume the financial burden of pursuing those cases all the way to a conclusion, knowing, under the caw law right now, that that

is literally all out-of-pocket.

So that case that is up on appeal is a critical case as applied to the Omnibus Proceeding. Rather than a handful of cases that might be affected by that decision, we are looking at hundreds, perhaps a couple of thousand cases that will be affected by that decision.

It really goes -- and it’s a critically important issue -- to how the act is substantively and perceptively treating the families who are in the program. So if you file a case in good faith, believing that you are timely, and then are forced to litigate that and ultimately lose, the few attorneys that are willing to pay that money and carry those costs out-of-pocket for years -- that number might shrink, faced with the burden of cases and the expense that you see as these cases get activated and we move forward.

Again, I’m not arguing one side of the issue or the other, but just letting people on the ACCV know that the case that is up on appeal is going to be something that is closely watched by both sides. It has huge implications for cases in the Omnibus Proceeding in particular, because there are so many of them.

MS. BUCK: Can you tell me which case that is?

MR. POWERS: Is that Key or Kay, Vince? Is Vince there?

MR. MATANOSKI: Kay.

MR. SCONYERS: Vince says Kay.

MR. POWERS: Kay. I couldn't remember if it was Key or Kay.

MS. BUCK: How is that spelled?

MR. POWERS: K-a-y.

MS. BUCK: Thank you.

MR. POWERS: I want to highlight that, because, as I said, that's going to be critically important.

MS. BUCK: What you are saying, Tom, is that that's going to change the whole system, the way it has been done before, in terms of attorneys' fees being paid despite the outcome?

MR. POWERS: No, no, no. If you have a case where timeliness is in dispute and --

MR. SCONYERS: It's a jurisdictional issue.

MR. POWERS: It's a jurisdictional issue. The case law right now in the program is that if a petitioner and DOJ get into an argument about whether a case was

timely filed --

(Telephone call temporarily interrupted.)

MR. SCONYERS: Tom, I think we lost you.

MR. POWERS: (Intermittently interrupted) -- but just on timeliness -- if the petitioner loses -- even at the end of that case, because it is deemed to be outside the jurisdiction of the program, and if you are outside the jurisdiction of the program, the program does not have the jurisdiction --

MR. SCONYERS: We are losing you. I think you are saying that the program doesn't have the jurisdiction to award those costs and fees.

MR. POWERS: -- as I said, that's where the intersection of interim fees and the timeliness issue occurs. It's going to be tremendously significant to anybody who has a stake in the Omnibus Proceeding moving forward.

On the more general issue of interim fees, the Petitioners' Steering Committee -- and this is something that we are doing internally at this point, but are about to really engage the respondent's side in this discussion -- we have been going back and forth about

interim fees. As Vince described, in general, the petitioners' bar and the respondent, with some involvement occasionally from the chief special master, subsequent to the Federal Circuit decision allowing interim fees, we have been working together to come up with what will make the most sense in terms of the efficiency of the program, but also in a way that is going to, obviously, as advocates, protect the interests of our clients.

The PSC right now is putting together a very substantial interim-fee petition on the general-causation omnibus cases. The handful of firms that have been actively involved in developing and presenting that evidence over the last six years are about 98 percent complete in terms of putting together a petition seeking the interim reimbursement of the time and the expenses that have been incurred, essentially through the end of the thimerosal tests cases this past July.

We are working so far -- and I hope it continues to be this way -- in a cooperative way with respondent's counsel to see if we can agree on everything that we can agree on in terms of what is reasonable to be compensated, the amount of time, the type of activity, the rates, and

all of those details -- to reach as much agreement as we can before having to involve the special master and resolve any disputes about those areas in the petition where there is disagreement.

Like Vince, I am somewhat of an optimist. I'm hoping that by talking a lot and conferring and working as much out as we can in advance, before involving the court and using the court's resources, we will be able to reach a stage where both sides are comfortable with an interim-fee award and a cost award for the Omnibus Autism Proceeding. From the petitioners' perspective, again, for six years now, a handful of us have been not only, obviously, putting in thousands of hours' worth of time, but also hundreds of thousands of dollars of out-of-pocket expenses to do the work on these cases, and would be seeking to be reimbursed for that, in the spirit of the act that is, in part, designed to provide an attractive and fair avenue for families who are seeking compensation to pursue those claims.

So we are looking forward to working with DOJ on the interim-fee issue, again specifically in the perspective of the Omnibus Proceeding.

Those are the primary issues that I have updates on. Coming after HHS and DOJ and all, there is the danger of redundancy. But I do want to take the opportunity to answer questions that people might have and provide any further detail that folks might want information on.

MR. SCONYERS: Thanks, Tom.

Are there other questions for Tom at this time?

DR. FISHER: No, but thanks.

MR. SCONYERS: We really appreciate your taking the time and making the presentation.

MR. POWERS: Thanks very much.

MR. SCONYERS: We are exactly on time for our break, so let's take a break and recommence at exactly 3:00.

(Brief recess)

MR. SCONYERS: Our next agenda item reads "Vaccine Safety Agenda: Update on Vaccine Safety Workgroup, Public Engagement, and ACCV Role." We appreciate Dr. Dan Salmon, from the National Vaccine Program Office, being here to talk with us, in general, about where vaccine safety activities are heading, and specifically how this commission relates to that.

Dan, thank you very much.

Agenda Item: Vaccine Safety Agenda

DR. SALMON: Thank you.

I have been asked to give an update on two issues. One is the NVAC Safety Working Group and the other is the public engagement process. I'm going to kind of take a step back and start from the beginning, because we have several new members, and I don't want to presume that you are familiar with what was presented at earlier meetings.

I'm going to address these issues separately, so that there is time for questions in between. While they are related, they really are separate activities. I would also encourage people, if you have questions, to feel free to stop and ask me a question before I finish. I would be happy to address them at that point as well.

Our office is the National Vaccine Program Office. We are in the Office of Public Health and Science, which is the Office of the Assistant Secretary for Health. We were created in the same legislation that created the Injury Compensation Program and the ACCV. Our responsibility is to coordinate federal vaccine activities.

So we are kind of a quarterback office within HHS. Then we work with nonfederal partners.

As the Injury Compensation Program and the secretary are advised by the ACCV, we also have an advisory committee. That advisory committee is the National Vaccine Advisory Committee. The NVAC provides advice to our office and to the assistant secretary for health, who is the statutory director of the National Vaccine Program, on issues surrounding vaccine policy.

NVAC has a working group in vaccine safety. That working group includes many NVAC members, but it also includes a bunch of other persons that are consultants, who bring other expertise to the group. I think currently we have 17 members of the working group. They are really a great group. They are very esteemed people, very well-trained people in a broad range of disciplines that are important for vaccine safety, ranging from neurology to biostatistics and epidemiology, pharmacoepidemiology, maternal and child health. It’s a great group of people.

They have two charges. I’m going to talk briefly about both of those charges.

I should mention that Tawny Buck is one of the

members of our working group. At any point, Tawny, you can feel free to jump in and correct me if I get something wrong or add further detail if you would like.

There are two charges of the working group. The first is to look at CDC's Immunization Safety Office research agenda and provide feedback in terms of content and priorities. The second is to look at the vaccine safety system more broadly and to develop a white paper outlining what the optimal vaccine safety system would look like, to optimally detect and prevent adverse events and ensure public confidence in vaccines.

I'm going to talk more about the first charge, because that's what they are working on now.

Based on an IOM recommendation, CDC's Immunization Safety Office is developing a research agenda which is intended to guide their research activities over the next five years. Before coming to the NVAC, they went through a very extensive process to put this research agenda together. They had a series of simultaneous expert consultations, which is CDC talk for getting a bunch of their experts together and getting ideas about what sort of research they should be doing.

The NVPO then sponsored a meeting with vaccine experts in different agencies within HHS. Those experts provided advice to CDC in terms of what areas should be on their research agenda. Then the National Vaccine Program Office sponsored a meeting with vaccine companies, where their representatives came and provided advice in terms of what sorts of issues would be important for CDC to study.

Based on this series of meetings, as well as a lot of internal discussion within CDC, they developed a draft research agenda. This draft agenda was provided to the NVAC Safety Working Group. What the working group was asked to do was to look at the content and say whether anything was missing, whether they should be studying something that was not on the agenda, whether there was something on here that shouldn't be on here, and then, secondly, to look at prioritization. This is what the working group is focusing on, on this point.

The general process that they have taken is to break into subgroups. They have taken the research agenda and they have cut it into pieces. They have taken the working group and cut the working group into pieces, so that you have three or four people looking at one or two

areas. That's just a much more manageable process to try to get through such a comprehensive document.

After the subgroups are done with their work and write draft recommendations, it's going to then go to the larger working group, who will review it and make comments and suggestions and changes. Ultimately, once the working group is done with the content and prioritization, it then goes to the full NVAC. The working groups don't make recommendations to the assistant secretary. It's the larger committee, the NVAC, that does.

So this is what the first task of the NVAC Safety Working Group is focusing on. It's fairly specific. It includes research questions and outcomes and vaccines. It's really kind of the details.

The second task is to take a higher-level approach and look at the system more broadly, to answer the question of what the system ought to look like, so that the infrastructure is there to do the sorts of studies that need to be done. That second task won't start until the first task is complete.

Very closely related to this is the issue of public engagement, which I will get to in a minute. As I

have described the process that the CDC went through in developing this research agenda, what I didn't describe to you is a process of hearing the opinions of the public. That's what I'll talk about when we get to public engagement.

But before I get to that, I just want to stop for a minute and see if anybody has any questions about the ISO research agenda as it relates to the working of the NVAC Safety Working Group or other questions about the NVAC Safety Working Group.

DR. FISHER: The timeline. Clearly, you don't want it to take you two years to get your agenda.

DR. SALMON: I think they will have the agenda complete within five years, at which point -- I'm kidding. It really is a huge process, and there has been a tremendous amount of effort that has gone into it.

Related to the timeline is the issue of public engagement, which I'll talk about in a few minutes. The working group is very, very cognizant of the importance of hearing from the public. While they are thinking about these issues, they don't want to go too far along their thought process until they hear from the public. That's

part of why these issues are really entwined.

My sense is that they will probably have some sort of draft in early 2009. They will probably present that draft to the NVAC in the spring of 2009. Typically, the way it works with the NVAC is, you present a draft at one meeting, you get comments, you make revisions, and then at the next meeting you provide a provision that's voted upon. My guess is, it will be spring of 2009 when the first draft comes to the NVAC and then it will be voted upon the fall of 2009. That's my sense of the timeline.

I'll tell you what. It has taken a long time to do this. It has been a tremendous amount of work. What I will say for both CDC and the NVAC is that people have really taken this task seriously and put a lot of thought into it. When I look at the questions that the NVAC Safety Working Group is asking, they are really asking some very, very thoughtful questions and taking their responsibility very seriously.

So while it has taken a fair amount of time to do this, I'm optimistic that the final product will be worth the wait.

MR. SCONYERS: Dan, I think we had several

presentations at our June meeting that covered the agenda and the topics a little bit. For those who weren't here, I think we can get those slides and make them available to you, which will give you a little bit more background. Dan has given you some good background here, but there is a bit more meat in our last meeting. We can get those to the members.

DR. SALMON: You can also find the draft agenda on CDC's Web site, if you want to take a look at the document. I think it's a 50- to 70-page document, but if you are interested, you can look at what the draft research agenda looks like.

Any other questions on the Safety Working Group?

(No response)

I'm going to move on to the public engagement process.

It was recognized both by the working group and the NVAC, as well as the Department of Health and Human Services, that it was important to hear from the public in this area, specific to the ISO research agenda, but also to vaccine safety -- and vaccines, for that matter, more broadly. Our first meeting of the NVAC Safety Working

Group was April 11. By legal requirements, working groups are not required to be open to the public. However, we wanted to be open and transparent, and we made the working group meeting open to the public, not because we had to, but we wanted to. We wanted it to be an open process.

So we announced it in the *Federal Register*. We had it scheduled in a large room in Washington so that if people wanted to come they could come. In fact, we had tremendous interest from the public. We had about 100 people show up. We had an extended period of comments from the public. We had even more people that wanted to give comments.

In some ways, that's a good thing, because it shows a real interest by members of the public to be involved in this process. The challenge is, how does the group get its work done when there are so many people that have such strong opinions? Having a working group meeting is probably not the best way of hearing what people think.

Additionally, public comment at a meeting in Washington is going to get one section of the public. It's going to get people who are interested enough to come to Washington, D.C. and spend a day in a room to give five

minutes of comment. But a lot of people aren't going to go through that process. People who are impacted by issues of vaccine safety -- it may be important to them.

Therefore, we felt as the department, and the NVAC Safety Working Group strongly felt, a need to have a more open and engaging process to hear what the public thinks and feels and their values around vaccine safety in general and the ISO research agenda in particular. This was very strongly requested of us from the Safety Working Group.

So we have, in government terms, very quickly put together a process for public engagement. I say "government terms," because I think we started focusing on this in April and it's now August, and we are hoping to have our first meetings in October, which may not seem fast. But, believe me, for the government, this is really, really quickly.

We have worked through an organization called ASTO, which provides a mechanism and a way of bringing in a neutral group who are experts in public engagement. That group is called Keystone. They focus on ways of engaging the public and hearing the issues of values from the

public. We have completed the contract with ASTO, and they are writing a contract with Keystone.

The basic plan is to have three meetings across the country with the general public and one or two meetings with stakeholders. When I say stakeholders, that has been defined broadly as groups that have a primary interest in vaccine safety.

We are still fairly early on in the process here. I'm going to share with you what the group has been discussing, but with the understanding that none of this is set in stone. People are still thinking through the best process to do this. When I say people are thinking through it, we have a group within HHS that is providing ideas in this regard. Dr. Benjamin Schwartz from our office is really taking the lead on this. Ben worked very extensively with the public engagement process when the department was developing priorities for influenza vaccine in case of a pandemic. He is kind of our resident expert on public engagement when it comes to vaccines.

We also have several members of our Vaccine Safety Working Group that are a part of the steering committee. The three members we have who are working with

us are our two public members, Tawny and Trish Parnell. Trish is the mother of a child who has a vaccine-preventable disease and the founder and executive director of Parents of Kids with Infectious Diseases.

You all know Tawny, so I don't think I need to give her background.

The third person is Jim Mason. Jim is a former director of CDC and former assistant secretary for health. So he kind of brings the wisdom of having been formerly at a very high level within government.

These three persons are working as liaisons between the NVAC Safety Working Group and the public engagement process. The reason we want to have them involved is to make sure that the needs of the working group are met in this process, so that in the end the working group hears from the public what it is important to them, as they deliberate on this research agenda.

So the game plan at this point is to have three public meetings. Two would be intended to include parents of children from the general public -- kind of the average mom and dad. How we are defining children is still being debated. It's probably going to be under 18 years of age.

As we know, we now vaccinate adolescents. But the thinking is that you want to kind of focus it on parents, because there's where most of our vaccines are being given. However, that is still being discussed and it hasn't been decided upon.

For the third public meeting, we will probably go to an area where there is a lot of vaccine hesitancy. We have seen, based on a number of indicators, that there are certain areas geographically where you see a lot of parents that are particularly concerned about vaccines. The thinking is that it would be very interesting and perhaps informative to try to go to a community where you see very high rates of vaccine hesitancy.

So the intent is to have two meetings with the general public and then one meeting with a group that is of the public but particularly concerned about vaccine safety.

MS. CASTRO-LEWIS: Just a quick question regarding the stakeholders meeting. Are you planning to include the organizations that represent diverse populations, like organizations that represent African-American communities or Hispanics?

DR. SALMON: So the question, just to repeat it

for everyone -- and please correct me if I don't get it quite right -- is whether or not the stakeholder meetings will include organizations that represent minority populations and other special populations. The way it's being defined right now, it's organizations that have a primary interest in vaccine safety. My guess is that probably most of those organizations would not identify themselves as having a primary interest in vaccine safety.

We are still discussing how we go about identifying those organizations. I think there are probably going to be a variety of approaches used. I'm sure that we will put some sort of public notice out, so people who are looking can find it. But we will probably reach out to others and ask them to reach out to others. We really want to get a broad approach.

DR. ISKANDER: (Via telephone) Dan, this is John Iskander, on the phone.

The question brings to mind that there are a number of, for example, liaison representatives to the Advisory Committee on Immunization Practices that represent various -- to sort of oversimplify things -- minority groups that might fit both sorts of definitions. The

National Medical Association is one example.

DR. SALMON: I think the NMA, for example, would probably say they do have a primary interest in vaccine safety, and they are a representative of a subset or minority population. They are African-American physicians.

I think people are open to other suggestions. If you have a suggestion, you are certainly welcome to make it. One of the hats that Tawny wears is her ACCV liaison. You are welcome to, if you have suggestions, make them now or I can also offer Tawny's email address -- just kidding, Tawny. You can also make recommendations to her. She has keenly been aware of the interest of this advisory committee as we have had these discussions.

I think what we want to be careful with is that we want to include groups that really have a primary interest in vaccine safety. If someone says, just an interest in vaccines in general, you kind of end up with every group. What group doesn't have an interest in vaccines, given that almost every population receives vaccines? The intent of including stakeholders is to really try to keep it focused. So I think the effort has been not to include every organization under the sun,

because you would end up with an exceedingly long list of groups.

MS. CASTRO-LEWIS: At least include some organizations that are looking out for the health of their own populations. That includes vaccine safety. That, I think, is worth thinking about.

DR. SALMON: I think that's good food for thought. The next time we discuss this, I can personally mention your suggestion.

MS. BUCK: I would comment, as a member of the working group, that it would be good for folks to know that the whole group is really, really committed, as Dan said, to this idea of vaccine safety. We have struggled mightily with some of the items on the scientific agenda and things that aren't on there. Subpopulations and special populations are definitely an area we have looked at.

Also in terms of public engagement, just to reiterate what he said, there is this really big commitment to looking at vaccines and their safety, understanding that safer vaccines sort of meet the needs of all these interested parties, but also understanding that for this group to really do work that is credible and be accepted by

the community, the public engagement piece is really important.

As he indicated before, we are moving as quickly as we can. It's probably not as quickly as we would like. But I am confident that what we have going so far feels very comfortable to me. I think we are on the right path.

DR. SALMON: Thank you, Tawny.

I just have to say, Tawny has been a really fantastic working group member. She has been very committed to this and very thoughtful and has really contributed quite a bit.

When we talk about timing, based on our discussions with Keystone, I think these are probably meetings that are going to take place in October and maybe early November. We should be getting reports soon after. September, and back to school, is not a time to get parents to come and spend a day discussing vaccines. If we hold the meetings in October, the beginning of November, we get reports in December. Then the working group needs time to really think about what they have heard. This is what puts us into early 2009 before any sort of report is possible.

We plan on inviting the working group members to

attend these public engagement processes.

MS. GALLAGHER: I just was wondering if you could explain to us what plans you have in place of reaching out to those who make vaccines. They are clearly a big stakeholder in the whole process. Is that going to be part of the public meetings or is there some other mechanism that you are using?

DR. SALMON: The question was, how will vaccine makers be engaged in this process, because they clearly have a very important role? The answer is, several ways.

One was, NVPO sponsored meeting where we invited representatives from all of the U.S. companies that make vaccines that are routinely used in children in the U.S. They were all invited and sent one or two representatives. We spent the better part of a day, where they provided their insights and what areas they thought were important for vaccine safety. So that’s one way.

Secondly, the NVAC has by statute members of pharmaceutical companies that make vaccines on the NVAC. In fact, two of those representatives are on the NVAC Safety Working Group. So both in the working group and then when it goes to the full NVAC, they have an

opportunity.

Additionally, there is the ISO research agenda on the Web. Anybody can submit comments to the working group. We have received comments.

Lastly, I think they would be included as an organization that has a primary interest in vaccine safety.

So there are multiple places where their input can be listened to. They clearly have an important role.

However, I also want to stress the point that a function of the NVAC is to make sure that stakeholders are included in the process, and industry, by statute, is identified as one. But this is not a process that by any means is being driven by industry. The majority of the members are not connected to industry. In fact, most of the working group is not people who are primarily vaccine safety -- or even vaccine researchers. Several of the members of the working group were former members of the Institute of Medicine's Immunization Safety Review Committee, including their chair, Marie McCormick, who is a professor of maternal and child health at Harvard University.

So there is a role for industry, and it's

important that the working group hear what they have to say, but it's not by any means a process being dominated by industry.

MS. GALLAGHER: I didn't mean to suggest it would be dominated in any way. I just meant that there is a very important role for people who make the vaccines that literally save children's lives every year. Clearly, they have to be also listened to in this process, because I think they can give a lot of help to what you are doing and your goals, because I think they share so many of them with you.

DR. SALMON: Your point is well-taken. By suggesting that they weren't dominating the process, I wasn't suggesting that you were suggesting that they were.

MS. GALLAGHER: I was afraid it was a pejorative comment, so I just wanted to come back and say that we share many of the same goals. Children's health is our primary aim as well.

DR. SALMON: Your point is very well-taken. It's really remarkable how much work is done by industry in the area of vaccine safety. Your point is very well-taken.

Any other comments or questions?

DR. HERR: I don't want to presume that you haven't thought about this already. Obviously, we work with the people who make the vaccines, but we also deal with the people who buy the vaccines. So make sure that you are including insurance companies. They are going to be interested in safety as well. As I said, as the purchasers of the vaccines for a lot of the kids, we need to make sure that they are on board and they are interested, because we want them to pay for them.

DR. SALMON: The question, just to repeat it for those on the phone, is to make sure that the perspective of those that purchase vaccines are considered. This is really one of the wonderful things of the NVAC. It's set up in such a way that the many stakeholders are brought to the table for discussions like this. AHIP, the Association of Health Insurance Plans, has a representative at the table at the NVAC.

By having this be a part of the NVAC, it really makes sure that a broad spectrum of stakeholders in the immunization enterprise are included.

Any other questions?

(No response)

Thank you for the opportunity to update all of you on this. I look forward to doing so again in the future.

MR. SCONYERS: Thanks, Dan.

I'm going to ask Michelle to get some of the presentations from June out for those of you who weren't here for them. I think that will give you a little bit more background on the whole program.

We shortchanged Dr. Marion Gruber last time and have put her back on the schedule to give the excellent presentation that she has prepared on thimerosal in vaccines. Dr. Gruber is from the Center for Biologics Evaluation and Research at the FDA.

Agenda Item: Thimerosal and Vaccines

DR. GRUBER: I appreciate the opportunity of giving this presentation again. I realize we were pressed for time in our June meeting. I summarized a lot of issues, and I think some of the messages that I intended to communicate might have been lost.

The presentation that I'm going to be giving today has really not changed from the presentation I gave in June, with the exception of the date. For the people

that already heard this discussion, be patient. For others, have mercy on me. The reason I'm saying this is that any time somebody from the Food and Drug Administration gets up and talks about thimerosal and thimerosal preservative, there are usually critical questions, critical comments. They are all very well acknowledged and appreciated. I by no means claim that I have done or involved myself in doing research, active research in the laboratory, in humans on thimerosal.

What I'm doing here today is giving you an overview of what I think is the most relevant literature and the most critical activities that have been going on in the last decade that concern themselves with thimerosal preservative, not only in vaccine products, but perhaps also in other drug products.

What I would like to do today is to provide an update regarding the regulatory actions that the government has taken concerning thimerosal preservative in vaccine products. In this context, I would like to discuss some of the activities within the federal government regarding thimerosal preservative in vaccines. I'll touch on the Food and Drug Modernization Act of 1997. I would like to

talk a little bit about the studies that the Public Health Service has initiated evaluating potential health effects from exposure of children to thimerosal preservative in vaccines.

I would like to briefly review the conclusions that the Institute of Medicine has drawn after their evaluation of pertinent data. I'm referring to IOM reports from 2001 and 2004.

Last but not least, I would like to speak to thimerosal preservative in currently U.S.-licensed vaccines or, perhaps better, the lack thereof.

Before going into this discussion, I would like to explain what preservatives are. Under our Code of Federal Regulations -- that's 610 15(a) -- they are defined as constituent materials. They are not active ingredients. They don't have adjuvant effects. They don't work as antigens to enhance an immune response. They are compounds that kill or prevent the growth of microorganisms, particularly bacteria and fungi. They are used, when added to a vaccine vial, to a final formulated vaccine, to prevent microbial contamination in the event that a vaccine is accidentally contaminated. That could occur with

repeated puncture of multi-dose vials.

In the past, vaccines that were licensed in the U.S. were really formulated in multi-dose vials. Usually you have 5 or 10 mL. If you had a dose that was comprised of .5 mL, you would go repeatedly in and out of these multi-dose vials. There is risk to that, because you could introduce environmental pathogens. That really has happened in the past, before preservatives were added to vaccine vials. It has occurred that vaccine vials were contaminated with bacteria. That actually has led to some public health disasters. That is, subjects who received vaccines did die as a consequence of the pathogens that grew inadvertently in these vaccine vials.

There are also situations where preservatives are really not added to the final vaccine formulations, to the multi-dose vial, but they are a component of the manufacturing process, to really ensure sterility, to prevent microbial growth -- column chromatography, column washes. This component is added to the column washes. That’s really not a wide practice anymore, but it used to be that manufacturers did do that.

So the United States Code of Federal Regulations

requires -- it's really our regulation; it's the law -- the addition of preservatives to multi-dose vials of vaccines because of these consequences that can occur if you don't that I just summarized. There are a few exceptions. Some of the live viral vaccines do not have thimerosal, but they are not formulated in multi-dose vials.

I want to get back to this a little bit later because of certain activities that the government has engaged in to really look at this regulation a little bit more closely.

I talked about preservatives. I'm turning to thimerosal, because thimerosal is the most widely used preservative in vaccines, or used to be the most widely preservative in vaccines. What is it?

It's a substance that is based on mercury. It's an organic form of mercury. As I stated, it was contained in U.S.-licensed vaccines since about the 1930s.

We already covered this. The primary purpose was to prevent microbial growth during storage and use of the vaccine vials. Some manufacturers used it in the manufacturing process.

Thimerosal contains about 50 percent of mercury,

occurring in an organic form, and that is ethylmercury. For all the non-chemists among us, including myself, just keep in mind that there are different forms of organic mercury. It's going to be very critical to what I'm going to be talking about in a minute. Thimerosal contains an organic form that is called ethylmercury. Many childhood vaccines contained this form of mercury at a concentration between 12.5 and 25 µg/dose. That mainly pertained to the influenza vaccines that were licensed in 1945; whole-cell pertussis vaccines, these combination vaccines -- diphtheria, tetanus, and whole-cell pertussis vaccines -- licensed in the 1940s; then the acellular pertussis combination vaccine that was licensed in 1991; hepatitis B vaccines; and *Haemophilus influenzae* type b vaccines, licensed in 1987. All those are formulated in multi-dose vials, and they did contain thimerosal preservative.

We already talked a little about the organic forms of mercury. Just for completion, mercury exists in three forms. There is the organic form, and there are actually two, methylmercury and ethylmercury. Ethylmercury, again, is the form in the thimerosal. Then mercury also occurs in mercuric salts and as elemental

mercury.

In the environment, it is actually pretty ubiquitous. Ninety-five percent of environmental mercury resides in soil. It can be released into the environment by burning fossil fuels. There has been about a threefold increase in environmentally available mercury due to increases in power-plant emissions and in industrial uses over the past century.

So as you can see, we are exposed to mercury. It’s around us.

It’s deposited on the surface of bodies of water. Elemental mercury can be then converted back to organic mercury. That is the methylmercury organic form. It’s not the organic form in thimerosal preservative. It’s methylmercury. Bacteria do do this. This organic form of mercury then enters the food chain, because it’s taken up by fish. So levels in fish increase as ascend the food chain.

The principal source of human exposure for organic mercury is fish consumption. The organic form here is methylmercury. There have been calculations that a can of tuna contains about 28 µg of methylmercury. I cannot

tell you how big the can of tuna was. It's just some estimate. I assume it's the little things that you can buy in the store.

There are other sources of mercury. It could be in breast milk, if the woman consumes tuna sandwiches. Cosmetics, dental amalgams, vaccines, of course, can all contain a form of mercury. The form in vaccines is the thimerosal preservative, which has ethylmercury in it, 50 percent.

The concern around thimerosal comes from the fact that mercury -- and it is well accepted and well understood -- methylmercury is a known neurotoxin. The toxicity of methylmercury was first recognized during the 1950s and the early 1960s. There was industrial discharge of mercury into what they call the Minimata Bay in Japan. That lead to a widespread consumption of mercury-contaminated fish.

Epidemics of methylmercury poisoning also occurred in Iraq in the 1970s, when seed grain that was treated with methylmercury fungicide was accidentally used to make bread, homemade bread.

During these epidemics, fetuses were found to be

more sensitive to the effects of methylmercury than adults. Maternal exposure to high levels of methylmercury resulted in infants that exhibited severe neurologic injury, while the mother showed few or no symptoms.

So this is what created the concern.

Because we have an organic form of mercury -- that is, methylmercury -- and we have the other organic form, ethylmercury, that is in thimerosal preservative in vaccines -- since they are both organic forms, people thought the toxicity may be related; they may be similar. So these concerns were raised.

Of course, thimerosal had been used as a preservative in some vaccines since the 1930s.

During the 1990s, then, additional vaccines were licensed and they were added to the routine childhood immunization schedule, and they contained thimerosal as a preservative. Then, in 1997, the FDA Modernization Act. That FDA Modernization Act required the agency to compile a list of drugs and foods that contained intentionally introduced mercury compounds, and we were supposed to provide a quantitative analysis. The analysis that the FDA did at this point really was not restricted only to

thimerosal preservative in vaccines; it was all other drug products -- nasal sprays, ophthalmic products. It was really a very comprehensive analysis. It was blood products, sera -- all of these products were evaluated.

Of course, under this Modernization Act, the FDA carried out a comprehensive review of the use of thimerosal in childhood vaccines that were on the market in the 1990s. That review was carried out in 1999, almost 10 years ago.

What FDA did at that point was to evaluate the amount of mercury that an infant might receive in the form of ethylmercury from vaccines under, at that time, the U.S.-recommended childhood immunization schedule. We compared these levels with guidelines for safe intake for methylmercury.

You might think, why did we do this? We have two different organic forms of mercury. We have ethylmercury and we have methylmercury. Why did we take methylmercury guidelines? There is a difference. Vaccines are given as episodic doses. They are a few and apart. It’s controlled. We know how much ethylmercury is in the vaccines. The methylmercury guidelines were really issued to give an idea about safe intake of methylmercury from

oral consumption, such as fish. It's daily intake, whereby you really don't know what the exposure is. But the FDA was sort of stuck with using these guidelines because there were no ethylmercury guidelines at this time.

We realized the uncertainty. It was probably not perfect, what was done. But at that time it was thought that the toxicities and the toxicokinetic profiles for ethyl and methylmercury were sufficiently similar that we could do that.

Over the last 10 years, there were additional studies conducted, and ethyl and methylmercury are really quite different.

Anyhow, in doing so, by looking at the guidelines for safe intake for methylmercury, it was found that the maximum cumulative exposure to mercury from vaccines in the at that time recommended childhood immunization schedule was within acceptable limits for methylmercury exposure guidelines set by some agencies, such as the FDA, the WHO, the Agency for Toxic Substances and Disease Registry. However, depending on the vaccine formulation used and the infant weight, some infants may have been exposed to cumulative levels of mercury from vaccines during the first

six months of life that exceeded the EPA guidelines for safe intake.

So calculations were performed, and it was thought that -- basically, what people did was, they added up the ethylmercury concentration in the at that time recommended childhood vaccines. An infant would get these vaccines at 2, 4, and 6 months of age. They added it all up and they found it was a cumulative exposure to ethylmercury of about 187 µg. That again exceeded the EPA guideline.

The emphasis here is on cumulative exposure. At that time we really didn't have data to see that actually infants can clear ethylmercury from the system. At that point we were assuming that ethylmercury is taken up and stays in the body.

Despite these findings on the levels of ethylmercury from childhood vaccines, the review that was conducted by the FDA in 1999 could find no evidence of harm from the use of thimerosal as a vaccine preservative, other than local hypersensitivity reactions. Of course, what they did was a literature research. They hadn't had a lot of studies looking at, of course, thimerosal preservative

and potential effects in infants at that time.

As a precautionary measure, and because it was thought that the elimination or reduction of mercury in vaccines was feasible, there was a joint statement issued by the Public Health Service and the AAP -- that's the American Academy of Pediatrics -- that urged that thimerosal should be removed from vaccines as soon as possible. The PHS started to collaborate with investigators to initiate further studies to better understand the potential health effects from exposure to thimerosal in vaccines. The FDA, in the Center for Biologics, started to write letters to vaccine manufacturers in 1999 and again in 2000 where we encouraged manufacturers to develop new vaccines without thimerosal as a preservative and/or to remove or reduce thimerosal from existing U.S.-licensed vaccines.

So between 1999 and 2001, there were several childhood vaccines reformulated without thimerosal as a preservative. These included two hepatitis B vaccines and a DTaP vaccine. The way that was achieved was by reformulating these vaccines that were initially in multi-dose vials into single-dose vials.

As data became available, these were reviewed by experts. There were several public forums, which I have listed here, such as the Workshop on Thimerosal in 1999. The Advisory Committee on Immunization Practices had two meetings on this issue in 1999 and 2000. As I mentioned earlier on, the Institute of Medicine Immunization Safety Review Committee did in July 2001 and 2004 examine the available evidence. I would like to talk about this a little bit.

The Institute of Medicine, in 2001, did a review to assess whether there was a relationship between thimerosal preservative exposure from childhood vaccines and neurodevelopmental disorders, such as autism or other attention-deficit hyperactivity disorders, speech or language delay. They looked at the evidence available in 2001, and they said, we cannot really conclusively say that the evidence is there or not. We have to say at this point that the evidence is not adequate to either accept or reject a causal relationship between thimerosal exposure from childhood vaccines and these neurodevelopmental disorders.

They strongly urged additional studies to

establish or reject a causal relationship. They also concluded that removing thimerosal from vaccines was a prudent measure in support of the public health goal to reduce mercury exposure where feasible.

In 2004, they issued their final report. They examined the hypothesis that vaccines -- in particular, the MMR vaccine, as well as thimerosal preservative-containing vaccines -- if these vaccines are causally associated with autism. In this report, they incorporated new epidemiological evidence from the United States, from Denmark, from Sweden, and the United Kingdom, and they also evaluated studies of biological mechanisms -- that is, *in vitro* studies and animal data available at that time -- to find if there is somehow a causal relationship between vaccines and autism.

The committee concluded in 2004 that the body of evidence actually favored rejection of a causal relationship between thimerosal preservative-containing vaccines and autism. They stated that data from well-designed epidemiological studies that examined thimerosal-containing vaccines and autism consistently provided evidence of no association between thimerosal-containing

vaccines and autism, despite the fact that these studies utilized different methods and examined different populations.

There were other studies and reports and analyses that claimed that there were findings of an association. The committee at that time reviewed all these data and found that the studies had serious methodological flaws and they were non-contributory with respect to causality. Other experts in the field did reexamine these studies and supported the findings of the IOM.

What needs to be pointed out is that in 2004 the Institute of Medicine did not address the hypothesized link between thimerosal-containing vaccines and other neurodevelopmental disorders. That's not what they looked at, because there were not really data at that time. This hypothesis was further evaluated in other studies, such as those conducted by the Centers for Disease Control. One of these studies was published in late 2007. It's a study by Thompson *et al.*, who really looked at a possible association of thimerosal preservative in vaccines and neuropsychological functioning of children that had early exposure in their lives. They looked at over 1,000

children from 7 to 10 years of age. They found that there was no such association.

Other studies in Canada looked at similar endpoints also came to the same conclusion.

So much for the epidemiological data.

Since 1999, vaccine manufacturers actually have made substantial progress in removing thimerosal preservative from U.S.-licensed vaccines, as I indicated, for pediatric, adolescent, and even the adult populations. Since 2001, all vaccines that are routinely recommended for children 6 years of age -- that really includes children up to 6 years of age -- which are manufactured and licensed for the U.S. market contain either no thimerosal preservative or they contain trace amounts. Sometimes these are defined as less than 1 µg mercury per dose. Here we say less than .5 because of the actual concentration of trace amounts that we still see in some of the U.S.-licensed vaccines. They are all under .5 µg. That's why this value is listed here.

The list is long. I will show you a table in a minute. I just want to point out that it includes DTaP, hepatitis B, *Haemophilus* b conjugate vaccine, pneuomococcal

conjugate vaccine, inactivated polio vaccine, the MMR vaccine, and the varicella vaccine. Rotavirus vaccine is another example.

So the maximum cumulative exposure that I was talking about that an infant of 6 months of age might have received from childhood vaccines really was decreased from 187 µg to less than 3 µg of mercury.

There is always a caveat. A couple of years ago, the influenza vaccine was recommended to be given to infants. An infant can receive a thimerosal-containing influenza vaccine at 6 and 7 months of age. Because they don't receive the full human dose like we do, .5 mL -- they only get half of the dose -- they would get 12.5 µg of ethylmercury, if you want to put it this way, at each visit, at 6 and 7 months. That would then result in a maximum exposure of 28 µg.

Is that good enough? No. I think we should continue the drive of taking thimerosal out of vaccines. We have actively engaged vaccine manufacturers in meetings that we have with them. You know that over the last couple of years, we have licensed quite a number of influenza vaccines. Most of them are really indicated for

populations 18 years and up. Right now there is only one vaccine that is licensed for infants 6 months of age and older. That is Fluzone. We have this other live-attenuated vaccine, FluMist, that is indicated for children 2 years of age and up. That does not contain thimerosal. Fluzone comes in both, thimerosal preservative-free and thimerosal preservative-containing formulation.

We are urging the manufacturers to increase the amount of thimerosal preservative-free influenza vaccines. As a matter of fact, when we are talking to the recently licensed manufacturers, which really have to have a pediatric assessment, now that that's the new law, we urge them to make formulations of influenza vaccines that are thimerosal preservative-free. That, of course, is achieved by formulating these vaccines in single-dose vials.

I'm talking a little bit here about preservative-free and thimerosal-free. I think the difference is perhaps understood now. Preservative-free simply means that thimerosal is not used as a preservative. If it's used as a preservative in a vaccine, it has to be at a certain concentration to exert an antimicrobial effect. That's usually .01 percent, or 25 µg. Preservative-free

means it's not used as a preservative, but trace amounts may be in the vaccine. These are residuals from the manufacturing process.

Thimerosal-free means no thimerosal can be measured. It has been sufficiently removed or the vaccine has never come in contact with thimerosal, neither as a preservative nor as part of the manufacturing process.

This shows, for people who are on the phone, the thimerosal content in U.S.-licensed pediatric vaccines. As you can see, the overwhelming majority of childhood vaccines are free of thimerosal. There are some that contain trace amounts. Then, of course, there are the influenza vaccines that come in formulations that either contain thimerosal as a preservative or they are thimerosal-free.

As for the childhood vaccines, we also have engaged in efforts with vaccine manufacturers to remove thimerosal preservative from vaccines that are indicated for adolescents and adults. We have now all hepatitis B vaccines for adolescents and adults that are available only in formulations that are free of thimerosal or contain trace amounts. The same goes for the tetanus and

diphtheria toxoid vaccine. We have recently licensed a number of combination vaccines, Adacel and Boostrix, as well as the Menactra vaccine, neither of which contains thimerosal. The same goes for Gardasil.

In summary, I would say that thimerosal has been removed or reduced to trace elements in U.S.-licensed vaccines, as I indicated, for children, adolescents, and adults. The exception is the influenza vaccine. We are working with the manufacturers to increase the supply of thimerosal-free formulations of influenza vaccines.

We also have engaged as a working group at the FDA, taking a look at that regulation that I showed you at the beginning that requires a preservative to be present in multi-dose vials of vaccines. We have been approached by several manufacturers who suggest that there is an alternative methodology to really prevent and/or alleviate the risk of contamination of a vaccine vial with bacteria. There are certain adaptors that you can put on a multi-dose vial. They are showing us data that they don’t have this contamination with bacteria anymore. So we are actually engaged with several vaccine manufacturers now in looking at these technologies to see if this is a real valid

alternative to the use of preservative in vaccine vials. So that is another effort that we are engaging in.

That, I think, concludes my presentation.

MR. SCONYERS: Do we have questions for Marion? The slides that she has been through are in your blue folders. Are there any questions?

It's good that we could get the full presentation, because there is a lot of data in there. We did give you short shrift last time. So thank you for coming back and doing it.

Hearing none, thank you very much.

We are going to move on to our next agenda item. In your notebook you will have seen an article discussing a meeting that was held to talk about mitochondrial disorder and the relationship to encephalopathy claimed as a result of vaccination. We have Dr. Walter Koroshetz from the National Institute of Neurological Disorders and Stroke to tell us about that meeting.

Agenda Item: Report from the Workshop: Mitochondrial Encephalopathies: Potential Relationship to Autism?

DR. KOROSHETZ: I'm Walter Koroshetz. I'm the deputy director of the National Institute of Neurological

Disorders and Stroke at NIH. I'm here to talk to you a little bit about a conference that we held in June. At the conference, there were members from CDC, FDA, Vaccine Safety.

The conference was basically bringing together two groups of physician-scientists, one group which concentrated primarily in caring for children and doing research in mitochondrial diseases, and the second group, people who see children and do research in autism.

The question that we posed to the group was, what is the potential relationship between mitochondrial encephalopathies and autism? So this was not really aimed at the vaccine issue, but basically trying to get at this bigger question, which has been raised by literature that I will talk to you about: Whether or not some children with autism may have a disorder in their mitochondria as a contributing factor, even a cause, of the autism.

The agenda of the meeting:

- To talk about mitochondrial diseases in general, particularly with regard to their genetics and the pathology that they cause. As you will see, for people who are not involved in mitochondrial disorders, it's quite

complex. There are important nuances that are worthwhile understanding if one is going to think about this area.

- The second question was to talk about potential overlap between mitochondrial dysfunction and autism. That's actually what got this whole thing started, because there are people who have thought that there is some overlap here. So we would talk about what that level of evidence is.

- The next question, which is clearly important if you are thinking about whether mitochondrial disorder related to autism: How would you test for that? You can't answer that question without knowing something about how you test for mitochondrial disorders. That was the reason for this topic

- As you will see, this series of topics raise more questions than they answer, so the next issue was, what are the research opportunities and challenges?

- In addition we did have a section here, as we got these people together, to talk about what the triggers are that are known to cause deterioration in mitochondrial diseases.

If one is thinking about, for instance, something like vaccines -- do vaccines cause autism through a mitochondrial mechanism -- is there some lesson that could be learned from what we know about what triggers mitochondrial diseases that get worse or not? This is important, because there are known triggers of mitochondrial disorders.

Does that make sense? Interrupt if you have questions. It's a little complex.

The general rationale is that there have been reported potential ties between mitochondrial disease and autism spectrum disorders, autism spectrum disorders being the large group of disorders which have autistic features. They basically are that there have been reports of children who are diagnosed with autism spectrum disorder who are then at some point found to have a mutation that affects mitochondrial function.

So we will be talking about the genetics of mitochondria with this piece of evidence in mind.

The next one is somewhat related, but, as you will see, there is a little bit of differentiation here. A number of the physicians who are taking care of children

with mitochondrial disorders have, seemingly by coincidence -- but, of course, it's not coincidence -- found that their siblings sometimes have autism or autism spectrum disorder. Because of the way mitochondrial disorders are inherited, even when you can't find the mitochondrial disorder in that child, it's presumed to be there. We will talk about why that is. So the fact that you can have siblings, one with a mitochondrial disorder and one with autism, is evidence, even if you can't find the mitochondrial mutation, that the mitochondrial problem is the root cause.

The last piece of evidence: There have been a number of genetic studies that have been done in autism, and a few of them have come up with associations between genes and autism, and in a rare example those genes have been thought to be related to mitochondrial function.

So those are kind of the general categories of evidence that we are talking about which are the links.

You can see from the papers here that there have been some reports going back into the early 2000s. In the first one, Pauline Filipek was at the meeting, who reported in 2003 two children with mitochondrial enzyme

abnormalities found in muscle. Kids had hypotonia, a moderate increase in lactic acid, which we will talk about, and motor delay. These children had autistic features.

There is a syndrome reported of children with hypotonia, seizures, autism, and developmental delay by Filano. These kids are thought to have problems with their mitochondria. Some of them have been found to have deletions in their mitochondrial DNA.

There is another report of children, three cases, with a known mitochondrial mutation in the mitochondrial DNA, which had autistic features. One of these children deteriorated after a viral infection, which, as we will talk about, is not uncommon in children with mitochondrial disorders.

This child deteriorated with autistic features. There was another report of one case of autism with a mitochondrial RNA mutation in muscle. The sister of this child, who presumably has the same mitochondrial DNA, which we will get to, had brain lesions which are characteristics of a mitochondrial disorder.

The tricky one is a study that came out of Portugal in 2005, where they looked at about 125 children

with autism and they measured lactate in the blood and some enzyme tests in the muscle, and thought that about 7 percent of the children had mitochondrial abnormalities. But they did not find genetic mutations in any of these children.

There are some other papers, but these are the major papers that have been published over the last couple of years. You can see that all of them are two or three cases, except for this last one, which is about 125 and narrowing it down to about 7 percent.

But we will talk about some of the issues, particularly with the last paper. The ones that have the mutations are the ones that we feel most secure about. But there are problems, as we will talk about, with making the diagnosis based on a measurement in the blood or on an enzyme test in the muscle. So that last study is still, I think, a question mark for many people. But it’s clearly the kind of thing you want to know.

This is an example of a 4-year-old boy with a history of normal development until 18 months of age. At 18 months, he loses expression of language and language comprehension. There is a gradual increase in disruptive

behavior, hyperkinesis, self-injurious behavior, and mild motor clumsiness, but no ataxia, normal lactate in the blood. He has a sister who has Leigh's disease, which is a known mitochondrial disorder that occurs in young children and is inherited due to a mitochondrial mutation. It's presumed that he would have that same mutation. That's indeed what happened.

This is a single case, but a single case can demonstrate what this potential tie is.

This is another example, which is a little more complex. Basically, we have --

(Discussion of slide off-mic)

The reason I put this out there is to demonstrate the complexity of the problem. Even in the genetic, which I mentioned to you is the one kind of test that we are most secure about, it is maybe not possible sometimes to make these diagnoses. Even though we think that mutation is there, we can't find it. We will talk a little bit about how that happens.

This is an example of a report from a genetic study where they claimed to see an association between a gene that is involved in mitochondrial function in a large

autism genetic study.

The general gist of what people are thinking is that autism spectrum disorder -- this large group, pure autism, smaller group -- that mitochondrial diseases, which are either described as definite, probable, or possible -- there is probably some overlap. But we really don't understand the extent of this overlap.

The reason the problems that I described to you in the setup occur is that the mitochondrial DNA is in your mitochondria, and your mitochondria are basically ancient bacteria that invaded cells many millions of years ago, and they have lived within the cells. What they do is, they generate the energy in the cell. Some of the DNA in the mitochondria is related to these bacteria that invaded cells millions of years ago. When the cells divide, the mitochondrial DNA comes to the child through the mother's egg, the ovum, and not through the father. The mitochondrial DNA is inherited through the mother.

In most of the mitochondrial disorders that are really well known -- that is, a mitochondrial DNA mutation -- you have this maternal inheritance. That's what I was explaining to you before. That's the simple

part.

The complex part is that over these millions of years, most of the proteins inside the mitochondria -- the DNA from the mitochondria was transferred to the nucleus. There is a portion which we know pretty well, which is the mitochondrial DNA, but the majority of the proteins in the mitochondria are coming from the nuclear DNA. That inheritance is much like any other inherited disorder.

You have a combination of two different types of inheritance that can occur with mitochondria. So we have to look, when we think about mitochondria, at the big numbers of genes that are in the nucleus and we have to look at these particular mitochondrial genes.

Over these millions of years, the other thing that happened is that human beings evolved out of different races, and there are certain mutations in the mitochondria that are related to the race that you originated from. One sign of confusion has been that some of those mutations -- because people didn’t realize that. They were thought to be mutations that caused disease. They are not disease mutations at all. It’s the fact that you are related to somebody from Finland and the other guy was related to

somebody from Greece. The mitochondria -- one theory of why this happened is because the mitochondria are central to how you generate heat. People living in hot countries had one type of mitochondria, because they wanted not a lot of heat to be made out of mitochondria, and people living in cold environments wanted a lot of heat to be made out of mitochondria. That's one of the reasons that might have caused that.

So that's another complicating factor to think about in mitochondrial genetics.

This is a picture of the mitochondria. The reason they are important is that mitochondria allow you to use the energy and oxygen to make chemical energy for the cells. You need oxygen to breathe. The reason is because your oxygen is going to your mitochondria and your mitochondria are making energy. That is, as you can imagine, incredibly essential to cells in the brain -- anywhere.

The other problem is that the price that you pay for using oxygen is that the electrons in oxygen, which are the ones where you are getting a lot of the energy from -- if they get free, they are incredibly dangerous. In the

mitochondria, as they function, the electrons are taken in from the oxygen, and there is a small leak in which these free electrons get loose from the oxygen and loose from the mitochondria. The cell has to sop those up, or they can be quite dangerous.

The third thing that's important in terms of mitochondria to know is that when a cell is ready to die, one of the signals that tells the cell it's going to die is a signal that comes out of the mitochondria.

For these reasons, you can easily see why mitochondria will be very, very important in all cells in your body, and particularly the ones that are metabolically active, that require the most energy. Of all the cells in your body, the ones that require the most energy are the ones in your brain. So many mitochondrial disorders affect brain function and muscle function. The same thing -- you need a lot of energy to run your muscles. Muscle disease is quite common.

But mitochondrial disorders will affect other cells as well. Not uncommonly, they will affect kidney, liver, nerves, muscles. Many parts of the body can be affected by mitochondria. The general rule is, if you have

a kid that has diseases, and it seems like they have 10 diseases instead of one, you think a mitochondrial problem is the cause.

That's one peculiar thing about autism. That's not entirely the case with autism. There are certainly in autism some GI problems that have been reported. There is hypotonia, and there are seizures. Those are the kinds of sources of overlap that you see with mitochondrial disorders and autism.

In terms of mitochondrial diseases, what you look for is evidence of abnormal mitochondria. If you can nail down certain things really specific for it, you can call it a definite diagnosis. But there are many children who have these complex disorders, and there may be something wrong, but you are not entirely sure if it's mitochondria. Sometimes they are given a diagnosis of probable, possible. There are a lot more probable and possible cases than there are definite.

But even in mitochondrial disorders -- forget about autism -- it's sometimes very hard to nail down that the mitochondria are the problem. We will get into a little bit about why that is.

But for mitochondrial disorders, most present before age 5. In the ones that we know about, they have a very high mortality when they present in childhood onset. But there is a lot of heterogeneity in mitochondrial disorders.

This is just an example of all the organs that can be affected by mitochondrial disorders. Lactate is often talked about. Lactate is basically a chemical that is made when your cells switch from using mitochondria for energy into using glycolysis, which is another biochemical pathway. It doesn't produce as much energy, but it's very quick. When you exercise, you produce lactate. If you go to the doctor's office and they put a tourniquet on to draw blood and make the veins pop out, that is enough to cause the muscles in your arm to generate lactate. You will get lactate high in your blood if you use a tourniquet to draw blood.

One problem, say, in the Portugal study is that we don't know how they drew the blood. If they put tourniquets on these kids and some kids were struggling, they are going to have a high lactate because of that. It's a normal thing. If you run a marathon, your lactates

are astronomically high.

The other thing is, when you activate you brain, your lactate goes up.

What they try to do is get tests of lactate when the child is at rest or they get spinal fluid lactate and see if it's elevated. That would be something where you would worry about a mitochondrial disorder, if you got a high lactate in a really resting child.

What I mentioned before was that doctors give kids diagnoses of definite and probably. They do a whole bunch of tests. The diagnosis really depends on how all the pattern comes out. They measure lactic acid in the blood, amino acids in the blood, organic acids in the urine, spinal fluid lactate, pyruvate. They do muscle tests, where they take a biopsy of the muscle and look at it under the microscope, look at the mitochondria. They do assays on the enzyme function in the muscle, to actually test enzyme function of the mitochondria in the muscle. Then they do the DNA testing. Some of these will come up positive; some will come up negative. That's what determines how sure you can be about the diagnosis.

In some severe cases, you have these lesions in

the brain, in the center of the brain. On both sides you see these lesions. These are very characteristics of a mitochondrial disorder, Leigh's syndrome.

One other thing to know about the mitochondrial disorders -- here is a picture of the mitochondrial DNA. Here's a picture of how you are inheriting DNA from your mother.

The other point to mention is that -- remember I showed you that the kid had 11 percent of the mutation in his blood, in his urine? The reason that is, is because if you inherit mitochondria from your mother, some of the mitochondria may actually have normal DNA in it. Some will have abnormal DNA. When the egg then divides, the abnormal mitochondria might actually go into one of the child eggs, not the other one, and so any cells that come from the one that didn't get the bad DNA will be completely normal. The ones that came from the abnormal dividing egg will have a certain load of abnormal mitochondria. That is what we call heteroplasmy. That means that some cells in the body may have no mutations and some of them may have a lot of mutations. Some cells may have some, but not a lot. So your mutation load can differ because of the way the

maternal DNA is inherited.

That's a big problem, why we think in that child they could not find the DNA in the tissues they looked at. But they suspect that the kid has the mutation that was associated with his neurologic problem. The problem is, you can't go into the brain and get DNA out. Maybe that's the only place in that boy where you have the abnormal mutation. So that creates a real problem. You can't just draw blood, check the genes, and get the diagnosis in all the cases. You have to sample multiple tissues, which creates a big problem if you want to study a population. You have to do muscle biopsies, spinal fluid, skin biopsies, hair. It can be quite invasive. That's going to be a problem that we are going to have to overcome.

This is just the child we talked about.

The point of this slide -- we talked about inheritance, either due to problems that are also DNA mutations in the nucleus that affect mitochondria -- we mentioned that -- what we talked mostly about are the mitochondrial DNA defects. That's what we know most about. There are also many conditions that can affect mitochondrial function. The Minimata Bay problem with

mercury exposure that we talked about, that potentially is due to the fact that mercury actually affects the mitochondria. Certain infections can affect mitochondria. Certain toxins can affect mitochondria. Certain drugs affect mitochondria.

Some people think that the major mitochondrial disease is aging, that the reason why cells age is because the mitochondria are developing all these problems over time, and that actually leads to aging of the cell.

Reye’s syndrome was not an uncommon problem. Kids with high fevers got aspirin and would have severe liver failure and die. That was due to the fact that the infection and the aspirin somehow affected the mitochondria in the liver.

Then there is a syndrome that looks like Parkinson’s disease, caused by a drug, which is a drug that -- people were trying to make heroin, and they ended up making something else. It killed the cells in their brain that produce dopamine. So they look like they have Parkinson’s disease. It was basically because that drug poisoned the mitochondria in the dopamine cells in the brain.

So there are certainly toxins that can affect mitochondria.

These are just examples of kinds of enzyme abnormalities that can cause mitochondrial disorders. In a muscle biopsy, what they look for are these abnormal mitochondria. This area here is called ragged red fibers, a common sign of mitochondrial disease in muscle biopsy.

There is a whole algorithm for evaluating mitochondria biopsy tissues that doctors use for kids who are thought to have mitochondrial disease.

In brain, you can do some studies to get a chemical signal of lactate in the brain. This may be important down the line in trying to look for the link between autism and mitochondrial dysfunction in the brain. MR spectroscopy -- that’s basically this peak here of lactic acid in the brain, which you can see in this particular way of doing MRI.

These are the kinds of tools we talked about at the conference. If we are going to try to look for this, how would we do this?

In terms of the triggers that we know about worsening mitochondrial disease: Seizures are known to

occur in mitochondrial disorder kids when they start to do poorly. Infections -- very commonly in Leigh's disease, which I mentioned, which causes those holes in the brain. Kids get really bad about three to four days after onset of a febrile infection. About 70 percent of kids with Leigh's disease actually get worse around the infection.

What we don't know is whether it's the fever that causes the problem or whether it's the inflammation that causes the problem, or maybe both. As I mentioned, heat is generated by the mitochondria. When you have a fever, your mitochondria are really working hard. Although they are producing less reactive oxygen species, they are really stressed by a fever. Whether or not some of the inflammatory products that you have when you have an infection can trigger mitochondrial disorder we are not sure of, but that's a possibility.

Kids with mitochondrial disorders get worse when they are dehydrated and when their caloric intake goes down. If you have a kid who has a diarrheal illness or he's throwing up and he's not eating and he has a mitochondrial disorder, that's a big problem. Often doctors, if a kid gets something like that, bring him into

the hospital and put him on IVs, give him fluid, glucose in the vein, so that they don't get into trouble.

There are some medications that will affect mitochondrial which are common: valproic acid for seizures, some antibiotics, HIV drugs that will affect mitochondrial function.

The research direction that we thought about -- we thought about two major areas. One is a targeted approach, which is to look at children with autism spectrum disorders that have overlap with mitochondrial disorders. They have hypotonia, epilepsy, developmental delay, and maybe a family history. The idea here is that if you could create a subset that has mitochondrial disorders, this is what it might look like. Let's go after that and study the mitochondria as in-depth as you would if you had a kid who had seizures and mental retardation, liver problems, muscle problems, where you would suspect a mitochondrial disorder.

That, however, would be invasive. It would require getting muscle biopsies, doing spinal taps, skin biopsies, getting urine samples, cheek samples, looking at all the tissues you can sample for mitochondrial DNA abnormality. Getting an MR of the brain in a small child

usually requires some kind of anesthetic or hypnotic agent. You would do deep sequencing of mitochondrial genes. So this would be an intensive study. You couldn't do this on a large population, but on a small group you could and see if you really find anything.

You would have to have a control group. That's another big problem. You are doing so many tests that the odds are, just by chance, some of these tests are going to be abnormal. So you would want to have a control group to know that it is really different in these kids than it is in a control group.

The second way is do more of a survey approach. This gives you less definitive information, but, as in the Portugal study, it gives you a sense of what kind of overlap you are really talking about here. You would want to draw the blood in an appropriate fashion. You would have a control kid who doesn't have autism, where you are sampling the blood, making sure that in the two groups there is or there is not a difference. You want to look at the amino acids in the blood. Also you would look at some urine studies. Those would be fairly simple to get -- maybe swab some check samples to look for mitochondrial

mutation.

This would be more superficial. You would expect that you would see something here. Then you would have to follow that up. It wouldn't be definitive. The first one would be more definitive, with a small group of patients.

The problems I think we talked about. It's really hard, because of the problems that we mentioned about the DNA not being in all the cells. The other thing I didn't mention is that some of these abnormalities occur at certain time periods, like when a kid has an infection. The kid gets bad and has mitochondrial disease. You see big lactate. Three months later, when the kid is doing well, everything is normal. If you got your test then, everything would be normal, and you would miss it, except for the DNA. So timing is going to be very important.

One thing we think of is -- as I mentioned when I described one of the children, he was doing well and then he started to lose language, so he is deteriorating. So that, you would think, if you had an autism group -- you would want to get them when they deteriorate, to look for these kinds of -- and that actually makes it a little harder to do. You really have to know when that's

happening and have a good way of assaying it and getting the kids in in time.

There are lots of things you have to control for, because, as I mentioned, caloric intake, fever, level of muscle activity are all going to potentially affect the tests you are looking at.

In general, if I had to summarize, I would say that the data that is out there says that there is definitely at least a small group where kids are presenting with what looks like autism, but there is a mitochondrial disorder at the bottom of it. Now we need to know how big a group that is. As I mentioned before, because of the complexities, it's not going to be entirely simple. But it seems as though it's really worth pursuing.

Hopefully, I presented how complicated it is, but not so complicated that the take-home points are not understood. I'd be happy to answer any questions.

MR. SCONYERS: Thank you.

DR. BERNSTEIN: You mentioned that 50 percent of the mitochondrial disorders typically onset before the age of 5. For the other 50 percent, is it throughout the lifespan at different times or are there typical times?

MR. SCONYERS: Let me just repeat it. The question is, if 50 percent of mitochondrial disorders have an onset before age 5, what about the other 50 percent? Is it throughout the lifetime or at specific times?

DR. KOROSHETZ: It tends to be dropping continuously with age. Childhood is the highest onset. The older you get, the less chance it's going to show itself -- with the caveat being that some people think that Alzheimer's and Parkinson's may be related to mitochondrial disorders. With these aging diseases, the jury is still out. But if it turns out to be true that Parkinson's is due to mitochondrial disorder, that would certainly cause an upswing in age. That's a hypothesis.

The one thing I should mention with regard to vaccines is that because most of the children get worse after an infection, the doctors who take care of kids with mitochondrial disease are all very high proponents of vaccines, because the worst thing that would happen would be that the kid could get a bad viral -- they had taken care of hundreds and hundreds of kids. They had not seen -- they said this -- they had not seen vaccine-related problems, except maybe in a few cases here and there.

Their general recommendation is to have their kids with mitochondrial disease vaccinated.

MR. SCONYERS: We were interested in this topic because of the Sarah Pauling (phonetic) case and the published article that correlated her mitochondrial disorder with the onset of her autism, as a result of a vaccine-induced event. Can you comment about the conference and any discussions or conclusions that may have been reached there?

DR. KOROSHETZ: We really did not go into any specific cases.

MR. SCONYERS: I understand, not specific cases, but just the mechanism.

DR. KOROSHETZ: I think that in terms of the hypothesis, there are triggers. Fever is a trigger. Inflammation is a trigger, either alone or together. The issue in vaccine cases is, is it possible that fever and inflammation related to vaccine are related to making a mitochondrial disorder worse? The question of autism -- that would be the first level, whether vaccines make mitochondrial disorders worse. That might be worth collecting data on. I think the vaccine safety group was

thinking of that.

The third-order question would be, if there is a mitochondrial disorder that causes autism, is that potentially made worse by inflammation? You can't really answer the second question until you answer the first one.

Does that make sense?

DR. FISHER: Just a comment. In that specific case, I believe that the father, who is a neurologist, proposed that the vaccines caused the mitochondrial disorder. I don't think we have any basis for that speculation, do we?

DR. KOROSHETZ: No, not that I know of. Mitochondrial diseases are usually caused by mutations.

MR. SCONYERS: Any other questions, comments?

(No response)

Thank you for that presentation.

We are close to the end of our time. I'm going to call on Dr. Bernstein, if I may, to save her presenting tomorrow. Dr. Jessica Bernstein is here from the National Institute of Allergy and Infectious Diseases, sitting in for Barbara Mulach, who is usually here with us. We had a brief conversation. I think she has a brief update for us.

This will allow her not to have to give it tomorrow.

Agenda Item: Update on the NIAID Vaccine Activities

DR. BERNSTEIN: I have a few things to report on from NIH.

One is that NIH and the CDC recently -- just this week, in fact -- released a program announcement soliciting grant applications for research on vaccine safety. You can find more information on the NIAID Web site, which is niaid.nih.gov. If you go to the vaccines section, you can see links to the program announcement. There are two funding mechanisms through which is offered.

NIAID also recently launched a Web portal on vaccines. That includes sections on vaccine research that is being conducted and understanding vaccines. Again, you can get to that through the main NIAID Web site, niaid.nih.gov.

I also want to mention that the National Institute of Mental Health issued to requests for public comments on behalf of the Interagency Autism Coordinating Committee. One pertains to the coordinating committee's draft strategic plan for autism spectrum disorder research. The deadline for that is September 30. The other pertains

to priorities for the Interagency Autism Coordinating Committee -- priorities for the IACC Services Subcommittee. That deadline is September 19.

The information for public comment on those is available on the NIMH Web site, nimh.nih.gov.

I also have some information on that. If you want to see me, I can give you the direct link to the Web site for the public comments on that if you would like.

That's all I have.

MR. SCONYERS: Thank you.

Are there any questions for Dr. Bernstein?

(No response)

Thanks.

At this time, operator, I would like to take the opportunity for any public comment.

OPERATOR: At this time, we will begin the question-and-answer session. If you would like to ask a question, press *1 on your touchtone phone. Once again, that is *1.

One moment, please.

(No response)

At this time we do not have any questions in

queue.

MR. SCONYERS: Are there any other comments or questions that anyone on the commission or anyone in the audience has at this point?

(No response)

I would like to ask that we convene at 9:00 tomorrow rather than 8:30, as we were originally scheduled to do, just so that people have a few minutes extra to get some breakfast and pack up and get over here. We will commence at 9:00 and we will plow through our morning agenda and get done with that.

Anything else this afternoon? Then we will start up again in the morning. Thank you very much.

(Whereupon, at 4:47 p.m., the meeting was recessed, to reconvene the following day at 9:00 a.m.)