DEPARTMENT OF HEALTH AND HUMAN SERVICES

ADVISORY COMMISSION ON

CHILDHOOD VACCINES (ACCV)

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P R O C E E D I N G S

Agenda Item: Welcome and Chair Report, Charlene Gallagher, Chair

MS. GALLAGHER: Good morning everyone, and welcome to the meeting. I would like to start out by having all of the commissioners introduce themselves, and we have three new commissioners today and we have three commissioners who will be taking office for the next meeting so I'm also going to ask them to introduce themselves. I am Charlene Gallagher, the chair of the Commission, and I am the industry representative currently.

MS. DREW: Good morning, my name is Sherry Drew. I am the co-chair of the Commission and I am the person representing petitioners' attorneys.

MS. WILLIAMS: My name is Michelle Williams and I am the unaffiliated attorney.

MR. KING: I am David King and I am a parent of a child.

MS. PRON: I am Ann Linguiti Pron. I'm a pediatric nurse practitioner representing health professionals.

DR. SALMON: Dan Salmon, National Vaccine Program Office.

MS. CASTRO-LEWIS: Good morning, I'm Magdelena Castro-Lewis and I represent the general public.

MS. HOIBERG: Good morning, I'm Sarah Hoiberg, and I'm a parent of a vaccine injured child.

DR. HERR: Tom Herr. I'm a general pediatrician.

MS. SAINDON: I'm Elizabeth Saindon with the Office of the General Counsel.

DR. EVANS: Geoffrey Evans, I'm Director of the Division of Vaccine Injury Compensation and Executive Secretary to the ACCV.

MS. GALLAGHER: And now would the members or the projected members who are sitting in the audience please come up and introduce themselves?

DR. DOUGLAS: I'm Charlene Douglas, representing Public Health.

MR. SMITH: Jason Smith, going to be joining the ACCV as the industry representative.

DR. FEEMSTER: Kristen Feemster.

MS. GALLAGHER: And Dr. Feemster is a pediatrician.

DR. FEEMSTER: Oh yes, I'm sorry. Yes, a pediatrician from Philadelphia.

MS. GALLAGHER: Thank you. And now I welcome everyone to the meeting, and I would like to turn my attention initially to the minutes.

Agenda Item: Approval of October 2010 minutes: Charlene Gallagher, Chair

MS. GALLAGHER: And I wonder if I hear a motion from anyone as to the minutes of the September meeting.

DR. HERR: I have a question of a correction. On the first page, third paragraph, where it says, "Dr. Fisher stated that rotavirus does not cause severe diarrhea," I think we're probably talking at that point of the rotavirus

vaccine. Are we talking about rotavirus causing diarrhea? It does cause diarrhea.

MS. GALLAGHER: Yes, we'll have to get that clarified, but I think usually we have a motion and then we have discussions, and then we have a vote. So I'm inviting a motion --

DR. HERR: Move to approve.

MS. GALLAGHER: Thank you very much.

WOMAN: Seconded.

MS. GALLAGHER: All right, so now we have --

DR. HERR: Remember my comment.

MS. GALLAGHER: Okay, now we have a discussion of the minutes as written. We had gotten some comments from the members who were on the Commission during this meeting and have since gone on, and we've incorporated them into the minutes and I've reviewed the new drafts and I think that was all done appropriately, if everybody else agrees. And so then this one suggestion about the severe diarrhea. As I was --

DR. HERR: Here she comes.

MS. GALLAGHER: Oh good, excellent. We'll have Dr. Fisher let us know what she thinks of paragraph three. Good morning.

DR. HERR: You're on the hot seat already. We had a question about the minutes.

DR. FISHER: Yes, I see the minutes. I read that.

DR. HERR: Do you mean the virus or the vaccine?

DR. FISHER: Well both. My point was that the way it read it seemed like everyone who got rotavirus had severe diarrhea, and I thought that was an overstatement.

DR. HERR: Okay.

DR. FISHER: Timing is everything, right?

MS. HOIBERG: Do you want it to say that it does not always cause severe diarrhea, because this says it does not. Do you want to say it doesn't always cause severe diarrhea? Because right here it looks like it doesn't cause it at all, the way it --

DR. FISHER: Yes, no, I didn't mean that either. I didn't mean it as never, I meant that it's a spectrum of illness. How's that?

MS. GALLAGHER: You just missed the introduction, so just introduce yourself briefly.

DR. FISHER: Hi. Meg Fisher - sorry to be late -and I'm a pediatric infectious disease doctor in New Jersey.

MS. GALLAGHER: Okay, so I think that we agree that that paragraph should be that rotavirus does not always cause severe diarrhea.

DR. FISHER: Perfect.

MS. GALLAGHER: Any other corrections or comments on the minutes? All right. All in favor of approving the minutes please raise your hand. Anybody opposed?

(Minutes approved.)

Okay, the minutes are approved. Thanks. Now I would like to move on to a report from the Division of Vaccine Injury Compensation. Dr. Geoffrey Evans will provide that for us.

Agenda Item: Report from the Division of Vaccine Injury Compensation (DVIC), Geoffrey Evans, M.D., Director, DVIC

DR. EVANS: Good morning everyone. Good morning especially to the new members. I'm going to begin just by talking about the highlights of the agenda, which you see on the slide. Following my update of the Division of Vaccine Injury Compensation we'll hear an update from the Department of Justice Vaccine Litigation Office. And then following the agenda we'll have - following that we'll have the review of Vaccine Information Statements and then updates from some of our ex officio members from the National Vaccine Program Office, from the Stanford Disease Control Immunization Safety Office.

Then NIH following lunchtime and then from CBER's Biologics Office from Dr. Marion Gruber, and then we'll have an update from Sarah Hoiberg on the Communications and Outreach Workgroup, and then we'll be discussing a petition for adding an injury to the vaccine injury table. And tomorrow morning we'll be receiving several clinical updates from our medical staff. So those are the highlights of the agenda, and we will be getting the correct presentation put on the telescreen here in just a second. Actually I could just use my handout. So this is part of my evaluation. My team has to be sure

that I can react on the spot to a different slide presentation. Okay. Now that's what I just went over on the various topics, and we'll start with this slide.

I'm going to pretend that some of you have never seen this slide before or seen this data before so I'll take a couple of extra minutes to go over this. This only goes back to fiscal year 2004, of course. These data on filings started in fiscal year '88, or actually '89 because it began October 1st, '88. But in terms of the history for the past six, seven years you can see a trend where two things are happening very clearly. One, the number of non-autism claims are going up and the autism claims are going down. And there are only - we've only received two claims this past year whereas in stark contrast the non-autism claims have increased significantly from an average of about 160, 170 from 2004 to 2008 to now we're receiving an average of over 300 claims and last fiscal year we received over 400 claims. And we are at this rate, I am calculating we're on the march to get about 450 claims.

So this reflects the fact that we are now covering influenza vaccine, which is no surprise, and it's given in much larger numbers than any of the other vaccines that we cover under the program. So it's not that influenza vaccine is particularly reactive or not safe or anything, it's just the basic fact that over a third of the vaccines of the hundreds of millions of vaccines given in the country are influenza vaccines. So, and with that of course has come the shift starting in 2007 from most vaccine claims now being filed are alleging injury in adults versus for the many, many years prior to that they were filed on behalf of children.

So going to the next slide, adjudications. You can see that we've been very busy, and of course been very busy in terms of adjudicating claims. Again, we're on a trend of equaling if not exceeding what we did last year. Actually, we're on about the same pace now altogether. And there's really no real big differences here and you'll see in fiscal year 2010 we - the one, the first autism claim was compensated. It's probably on this autism proceeding.

Now someone asked yesterday at the orientation about settlements versus concessions versus noncompensable claims and the trends and so on, and I think that this slide, which is a direct result of this particular commission, you know, some of the members who are retiring or are still on. I want to make you better understand exactly what is going on in terms of decision-making. So you can see that over the past three years, and actually the past four or five years, that the settlement rate has been rather high. It was, I would say, 2004, 2005 around 40, 50 percent, and since then it has now been in the 70 to 80 percent range. So many claims now filed in the program are compensated on the basis of litigated versus settlement. A concession rate has been between 10, 15 percent over the past three years, concession meaning that after HHS, our office, reviews the medical records we make a determination that the claim fits the Act in terms of entitlement to compensation and we recommend that compensation be granted.

In the cases, where we don't and it goes on to a hearing before a Special Master in the US Court of Federal Claims, then it could be compensated on the basis of a court decision. You can see that those, the percentages of that

have also stayed fairly the same, although this particular fiscal year you can see that there are now more court decisions so the inference being that perhaps more claims are being defended. You know, that's a trend that we'll continue to look at but this is a snapshot of where we are in terms of concessions, court decisions and settlements. And again, a very, very busy several years in terms of the numbers of cases that are - that are going through.

In terms of petitioners' awards, the fiscal year 2010 represented the largest amount of outlays. It was $189 million altogether, and we're on track again to possibly even exceed that. It is a fact that the four or five largest awards in program history have occurred within the past fiscal year. There are a number of reasons why that is. We've actually had several questions thrown at us by people downtown wanting to know why it is that the individual awards are getting higher. And I'm not an economist, but it does have to do with Treasury rates, interest rates, annuities, the market and the valuation of these kinds of things, and that's something we certainly can explain further if the Commission is interested in a particular agenda item, to go through what exactly are the factors that do influence how a claim is finally paid and the amounts that go into an annuity.

DR. HERR: I think we really should look at that, realizing that with the increase from 2009 to 2010 of perhaps only 40 percent or 30 percent in the number of claims paid, also realizing that there's also an average of a three year gap from when claims are filed to when they are paid, and that we're now having more filings this year than we've had in the past, it's going to be even greater

outlays down the next three years. I think we ought to have an idea of what's going on.

MS. GALLAGHER: Okay, I'm making a note and that'll be one of the things we'll put on the agenda for the next meeting.

DR. EVANS: Yes, and just to clarify something Tom just said, although for the record we state that overall the average time for a compensable claim from filing to being compensated is three to four years, you'll remember that Mark Rogers has repeatedly presented data that show that for the last several years you're talking about turn-around rates, averages now of perhaps a year to a year and a half and some as quickly as eight to 10 months. So that has significantly changed, so - because of the litigation, litigated risk settlements that are going on.

Going further, this is where the trust fund is currently, at $3.29 billion. Interestingly, this was, if you'll remember over the past year or so in meetings, this was something that was steadily increasing but has now slowed down its increase. Again, we're talking, because of current interest rates and also not significant - not insignificantly, the fact that the outlays have increased significantly. So we still are in our positive zone in terms of we're taking in more per year than compensating, but it has dramatically changed and this number is staying just below $3.3 billion but it continues to go slowly. It's certainly a very sizeable protective amount of money for the kinds of claims that are going to be facing the program in the future, an insurance policy as it were.

In terms of significant activities, I attended the National Vaccine Advisory Committee meeting in Washington along with Charlene Gallagher, representing ACCV, and we'll hear more about that from Dan Salmon during his National Vaccine Program update. That was on February 15 and 16. Last week I had the pleasure of going down to Atlanta and attending Advisory Committee on Immunization Practices meeting, a meeting by the way that can easily be accessed by anyone in this room and actually anyone around the world who has a broadband or even a slower connection, I'm told.

The technology that CDC provides in that global communications center where the meeting is held is very impressive, and you can hear most anything said and watch the slides and watch the discussion. And that is the lead body for vaccine policy recommendations in this country with both American Academy of Pediatrics, American College of Physicians, and American Academy of Family Physicians and so on, all coming together and advising CDC and the Secretary on immunization policy. So that's a meeting that if you're interested I would certainly recommend you tune in from time to time.

And at that meeting I had a couple of questions. They certainly wanted to know about the Bruesewitz decision which Mr. Rogers is going to be discussing briefly. They also wanted to know if Japanese encephalitis vaccine, which they are considering recommending for young children for travel, could possibly be covered under the ACIP. And I pointed out to them, reminded them that it takes a general use recommendation by CDC before a vaccine is covered under the compensation program. It can't just be for a small group of children

who are traveling, and so the program doesn't cover travelers' vaccines, it covers a general use recommendation and it also has to have an excise tax imposed. So in that case, that vaccine would not be covered. Also that same week we had the Bruesewitz decision by the US Supreme Court.

DR. HERR: Geoff, just to get back again - I'm sorry. You said that the trust fund actually went up still this year from 2009 but we had, according to your statement here, we had $98,000 in revenue or income, which includes the tax - $98 million, I'm sorry, you're right, $98 million, almost $99 million of revenue to the fund by tax and interest but we paid out $190 million. How does that end up still with a plus?

DR. EVANS: Well I looked at the data and how it is on the website of the Treasury Department, and it didn't comport with my sense of what the trend has been all along. I mean, if you look at that, that's for a one-month period of January 2011 and we were supposed to have taken in nearly $100 million, and that doesn't make sense. So that's the reason why I chose simply to put the bottom lines for the two different dates and then try to make sense of that in the future. But I knew that one of our more observant members would spot that in the book and ask me that question so Tom, you get the prize. That's perfectly understandable. So we'll try to make sense of that, but that would be an extraordinary amount of increase, and that would - you know, if you project it out $100 million for one month, and go from there. So, anyhow -- .

As I usually do, I read for the listeners on the phone the points of contact. Anyone interested in writing the program can write the National Vaccine

Injury Compensation Program. The address is 5600 Fishers Lane, Parklawn Building, Room 11C-26, Rockville, Maryland 20857, and our toll free line for information and materials is 1-800-338-2382. And I urge everyone to visit the program website, which is at www.hrsa, h - that's h-r-s-a.gov, and then slash vaccinecompensation, one word, www.hrsa.gov/vaccinecompensation. And those who wish to provide public comment or participate in the Commission meetings should write our principal staffer, Ms. Andrea Herzog, at the same address in the Parklawn Building, or call her directly at 301-443-6634, or e-mail her at aherzog@hrsa.gov. And with that I will end my presentation.

MS. GALLAGHER: Thank you. Now I would like to invite Mr. Mark Rogers to give us the report from the Department of Justice.

Agenda Item: Report from the Department of Justice (DOJ), Mark Rogers, J.D., Deputy Director, Tort Branch, DOJ

MR. ROGERS: Good morning. Welcome to the new members, and welcome back to the - well I won't call them old, but previous continuing incumbent members. It's a pleasure to be here. I'm Mark Rogers. I'm a Deputy Director in the Torts Branch, and the vaccine program is almost exclusively what I do. And I will try and move slower through this than usual for the benefit of the new members. Just as an overview, what I try to do is give you a snapshot, a relatively recent snapshot of how the litigation has been going. And our timeframe is generally from the last meeting of this Commission to about a month ago, so that our administrative folks can put together data.

On the personnel side, we've - two paralegals have left us and two have come in. We have a trial attorney who is leaving shortly and we have nobody in the pipeline coming so we'll be, if things go as I expect, down one attorney in about two months. On the statistics side we show one autism case, and again I know that Dr. Evans showed two, but the timeframes are slightly different. There are going to be differences between our numbers. This question comes up again, now and again, but that's the reason. We have a different timeframe.

And also, we pivot off the judgment. The judgment - this is a litigative process at heart and for any claim to be paid, for any claim to come to an end in this process, a judgment is entered. There's one exception, and I'll get to it. But 95 percent of the cases end with a judgment. That's when the case is over. It's entered by the Court of Federal Claims when there's been no appeal within 30 days of the Special Master's decision. So in our program Special Masters decide the cases, the Court of Federal Claims enters judgment, and there's a possibility of appeal to the Federal Circuit, which is relatively infrequent.

Okay, we have one autism case. They are fading to a dot. We took out a couple of slides that talked about them, as they fade into our rear view mirror, except for - and it's significant - processing attorney's fees. We are working through the cases and they won't go to final judgment until we have processed them, processed the attorney fee request.

Non-autism cases, you've heard, they're trending higher. They continue to trend higher. And the cases are moving, the percentage of adult

cases is increasing. I have a busy slide. Again, this pivots off judgments entered in the program. There were 69 since our last meeting that were compensated, 118 total cases adjudicated, of which 69 were compensated. Of those we counted six concessions by HHS. That's where they determine that compensation is appropriate and the case immediately moves to the issue of how much.

In those cases, those six conceded cases, all six were resolved by a proffer. And we'll get to the definition of a proffer. It's close - it's got a lot of - it's similar to a settlement with an important difference. The important thing at this point is, it's resolved by a handshake. That's where the parties agree as to what the damages should be.

There were 63 cases that were not conceded by HHS. That's where we file a Rule 4 report that says no, we don't think compensation is appropriate and we give our reasons - legal, factual, whatever. In those cases - and again, these are resolved cases during this time period - 63 of them were not conceded. One, there was a decision awarding damages. What that means is the Special Master decided what the damages should be. For the most part a decision will resolve a difference between the parties as to what the damages should be, but I suspect this one - I didn't look at it - it also could be where the damages are set by statute and the Special Master just enforced the statute. And of course that's most commonly a death case, $250,000. The parties really can't disagree, it's determined by law, but the Special Master decides it based upon that law. It's not really a contested issue.

We have the decisions adopting proffers. Here we've got a proffer again. That's where the parties have agreed as to what the evidence shows, and the Special Master has decided to adopt it and make that the Special Master's decision, an amicable result.

And then 56 were resolved with a stipulation. That's a settlement, that's an agreement between the parties as to what the damages should be. The Special Master's role in that situation is generally just to approve the agreement. It looks good to the Special Master, the Special Master approves it. It doesn't always happen. The Special Master - well what always has happened is the Special Master ultimately approves the agreement. What happens sometimes is the Special Master will convene a status conference and ask about the agreement to satisfy the Special Master that it's fair. There were 49 cases that were not compensated, that were dismissed without compensation. Fifteen of them were non-autism cases, and 34 were autism cases.

Now the statute provides an avenue out of the program that doesn't result in a judgment if they withdraw. Petitioners may withdraw their petitions. And if they do it under certain conditions - mostly a time condition, they have to give the program a certain amount of time to work - they can withdraw without prejudice to pursue a private, civil action. During this reporting period five non-autism cases went out that way and two autism cases were withdrawn.

Some terms, and I'll spend a little more time with these in deference to the new members. When we say "adjudicated" what we mean is a judgment's been entered, the case is over as far as the court's concerned.

There's some ways you can attack a judgment or re-open a judgment, but they're very, very narrow - fraud, a mistake, something of that nature. The court is very protective of its judgments. They should be generally final. That's the next definition. It's a final decision wrapping up the case.

Compensable, that's where petitioners have received compensation. There are three ways generally for a petitioner to receive compensation through the program. One is when HHS concedes the case and as I mentioned before we immediately go to damages and culminating in an award of damages and finally a judgment entered by the Court of Federal Claims.

The second is a settlement. Now settlement is a handshake between the parties supervised by the Special Master, where the parties have agreed - they have two different positions and they've agreed to compromise them in some way, where both are satisfied. That's the essence of a settlement. Both parties have a position, they are different and they've agreed to compromise them. That's a settlement. A decision is when the parties cannot agree and it goes to the Special Master to resolve the difference. That's what we mean by a case that's decided by the Special Master.

A conceded case we've talked about before. That's where HHS on initial review, having seen the medical records they believe are necessary, decides this is a compensable case under the program. We've already talked about settlement. Negotiated agreement is a shake of hands reduced to a

writing, and that writing is called a stipulation, and it's filed, and the case is generally over.

Decision - that's when the Special Master finishes the case at the Special Master level. And when there's been a settlement the decision is to approve the settlement. Where there's not been a settlement it's a decision to resolve the differences of the parties. But one way or another, the Special Master stamps the case at the very end with how he or she has resolved it. That starts the 30-day period, the 30-day clock for either party if they're unhappy with the decision to appeal to the Court of Federal Claims. Now if it's been resolved by a handshake and a settlement, there's never an appeal. Never say never but I can say it here. If there's been a comprehensive settlement of the case there can be no appeal. Now there may be a settlement of only part of the case and then there's an appeal of the part that wasn't settled. But that's unusual.

Non-compensable case dismissed. It can be dismissed for legal reasons, it can be dismissed because the Special Master has determined that the vaccine, that the injury has not been caused by the vaccine. A proffer - a proffer is like a settlement in that there's a handshake between the parties. They agree. But with a proffer what they're agreeing is what the evidence would show. They're not agreeing - in effect it resolves the case, and I'll get to the distinction. They're agreeing to what the evidence shows in the case, which will drive the Special Master's ultimate decision.

The most common situation for a proffer is when the life care planners for both sides have sat down together and agreed as to what the

medical needs are of the injured individual. Then we'll file a proffer before the Special Master. The Special Master really doesn't have a case or controversy before him or her. They approve the proffer. That becomes a Special Master's decision.

The distinction is one of internal processing at mostly the Department of Justice. The Department of Justice approves all settlements. With a proffer there is no settlement. There's nothing to approve. The Special Master is the authority that's approving what has occurred by deciding based upon that agreement and what the evidence shows. It's a little nuanced, but a proffer can be a little faster because it doesn't require as much internal processing at DOJ. Sounds like a lot of bureaucratic complexity, but it actually makes a difference and can shave a couple of weeks off the process, and so the Special Masters are happy with it, the parties are happy with it, it does not violate any of our rules within the Department of Justice on approving settlements.

This is a wire diagram and I'll just spend a couple of minutes with it. The case starts with a petition, it's initially reviewed by HHS, and then either not conceded or conceded, so with the statistics that most track down the left side of this chart. If it's not conceded, the parties start talking immediately about whether we can settle this, or whether the Special Master has to decide it. Again the numbers, the center of gravity, sides over to the left side here with the settlement. If the parties can reach a comprehensive settlement, settling all the issues and file a stipulation, there's a final decision by the Special Master approving that, the case is over.

If the Special Master has to decide the case, it starts taking more time. There's more friction in that process just because it's a matter of scheduling some sort of proceeding to resolve the matter. And the Special Master either decides that the case is compensable or noncompensable. If it's not compensable you have a final decision dismissing the petition that can be appealed. These are proceedings before the Special Masters. If the Special Master decides this is a compensable case, it moves over to damages.

And then on the damages side, on the right side, or a conceded case comes immediately, goes immediately down the right side of the chart here. Either way, when the parties start talking damages, again, the first issue is can we settle this. Most of the cases run through the middle if there is a settlement. Or, there's a proffer.

So you see where proffer shows up over here on the right, it generally does not show up on the left. Rather, the way we resolve the case on the left is just a comprehensive settlement. It has to be approved by both HHS and the Department of Justice because at heart we haven't agreed that any compensation is appropriate except by means of that settlement agreement. That's why there's a little more processing involved.

DR. HERR: But you're saying, Mark - excuse me, this is Tom Herr - that this seems to be an increasing trend, though, that we're moving over to the left side rather than the right side?

MR. ROGERS: The trend is to the left, yes. The trend is to the left, hard left, and when we're forced over to the right, a proffer.

DR. FISHER: Before you switch to the - can I ask one other question? This is Meg Fisher. Of the conceded cases, are most of those table injuries, or can you give us an idea of about more than half table or - we're going to talk a lot about the table.

MR. ROGERS: Maybe, Doctor, my recollection - and it's off the top of my head - is that it's about 50/50.

DR. FISHER: So you could still get to a conceded case without it being on the table?

MR. ROGERS: Yes.

DR. EVANS: I would say probably over 50 percent are table concessions. It's still at this point. There are just relatively few vaccines and adverse events for which there is cause - you can actually prove causation or have causation as fact, information and literature. So that would be my guess, and it would be three-quarters, one-quarter.

MR. ROGERS: The most accurate thing I can say is, I see them occasionally but I haven't counted them. Now appeals. The case is only over if the parties don't appeal. And on that front we have three cases that were recently decided by the Federal Circuit. That's at the highest level. They can and have gone to the Supreme Court, one case, one vaccine case has gone to the Supreme Court. That was the White Cotton case. It's been some time.

So for the most part, the Federal Circuit is the court of last resort in our cases, as a matter of practice. We had three cases decided since our last meeting, the Davis case, which was a statute of limitations case, and that was a

case as I recall where the Federal Circuit ruled that the argument that petitioners were raising had been waived because it had not been raised before the Special Master. And Rodriguez and Riggins were fees and costs cases, and in both those cases the Federal Circuit affirmed the decisions below.

In all three cases the appeals had been brought by petitioners. I know that was a question yesterday about the frequency of the appeals by each side.

DR. HERR: How did - can you go more into specifics of Davis, of the statute of limitations, versus Cloer, that you got later on?

MR. ROGERS: Davis, the primary argument was that the statute of limitations was unconstitutional, and the Federal Circuit ruled, well, you've waived it, but they went on to say, you know, we've held that it is constitutional. So that was the gist of Davis.

DR. HERR: Okay, so this was - it was - I'm just trying to understand the decision that you have here, that it was, the petition was affirmed, that it was - that the appeal was denied.

MR. ROGERS: Yes, I'm glad you asked. What happened here was, the Special Master dismissed the case as untimely. It was appealed to the Court of Federal Claims, which affirmed that decision saying the dismissal was right. Then this appeal to the Federal Circuit, which, too, affirmed the decision that it should be dismissed. Affirm means agree with the court below.

DR. HERR: Yes, but it didn't really say who brought it, and how. Thank you

MR. ROGERS: Okay.

DR. FISHER: I thought - I thought when it says petitioner affirmed, or at least I thought - I thought when it said petitioner affirmed that it would be the opposite.

MR. ROGERS: Okay.

MS. HOIBERG: These were - these were actually, affirmed means that they were - that they held up the decision.

MR. ROGERS: Yes, when you see “appellant” that means the person bringing the appeal.

MS. HOIBERG: Right.

MR. ROGERS: “Affirmed” means the appeal was not successful.

DR. HERR: So the fact that it says “appellant: petitioner” means the petitioner brought the appeal forward?

MR. ROGERS: Yes. And it’s - maybe we could be clearer than our use of colons and semicolons, but there’s a colon, meaning the appellant was petitioner. You know, the tyranny of the slide, trying to get it all in there. Maybe we could put captions above, we bringing the appeal. We’re victims of our own jargon. Okay, does that make it clear?

DR. HERR: Yes, I’m just kind of going on to the next one, because isn’t the next one you guys? Wasn’t the respondent then the appellant?

MR. ROGERS: No. No sir. In Rodriguez and Riggins.

DR. HERR: Oh, I’m thinking Cloer.

MR. ROGERS: Oh, Cloer. The appellant was originally the petitioner.

DR. HERR: Oh, okay.

MR. ROGERS: But the petition for rehearing en banc was filed by the respondent. But the original appellant, the initial decision was dismiss the case. Petitioners appealed, the Court of Federal Claims affirmed. I'm 90 percent certain of that, and I'm 100 percent certain that the Federal Circuit overturned that decision and then Respondents sought rehearing en banc.

MS. HOIBERG: For the new people, Mark, could you explain what en banc means?

MR. ROGERS: Yes, absolutely. When a case is appealed to the Federal Circuit it's assigned to a three judge panel, and that panel decides the case for the full Circuit. It's called a panel decision. And virtually all the time that's the end of the matter. There's an avenue, though, for an aggrieved party, someone who's unhappy with that panel decision, to ask that the full Circuit review it personally, not just with this one panel, all of them. It is very, very rarely granted. The full Circuit does not want to hear every case. It would be hopelessly bogged down were it to do it regularly.

So the full Circuits will only do this in an unusual case, and they had deemed this to be an unusual case that they want to hear en banc, that is, the full, every judge who's sitting at the time. So they vacated the lower, the panel's decision. The appeal now is reinstated to be heard en banc. Is that helpful?

Now these are the pending cases before the Federal Circuit. They're all headed to the three judge panel. We never know who the judges are going to be until the morning of the hearing. Now of these, the appellant was the petitioner - we have petitioners because there are multiple - in all of them except one and that is Knight. Or two. Knight, Rotoli and Porter. I say one because I know they're related cases. The same issues are raised. So two of these were brought by respondent to the Circuit, the rest by petitioners.

And three cases were just decided by the Court of Federal Claims. In all of those the petitioner was the appellant, brought the deal, unhappy with the Special Master's decision. In two of them, the Court of Federal Claims said you know, I want the Special Masters to think more about this. That's what a remand is, it's sent back to the Special Master with - usually with instructions. Here's what I'm concerned about, here are the questions I want answered. And in one of them the decision was affirmed.

MS. PRON: Can I ask a question, going back?

MR. ROGERS: Yes.

MS. PRON: Can you give us an example of why the respondents appeal? It's the government that needs to respond.

MR. ROGERS: Yes. The easy answer is, the government's unhappy with the decision below. There are any number of reasons that we would be unhappy with the decision. What makes us most unhappy, I think I could say, is when we think that the law has been misapplied. When we think there's an important issue of interpreting this statute that's going to have effect

on other cases, that in the hierarchy of things, that's pretty high. There also can be policy considerations. This Act should be interpreted in this way because it's consistent with the policy of imperatives of Congress.

So the things that concern respondent the most are issues that are going to keep coming up, not just this case. I'm not going to characterize my petitioner's appeal, but generally it's that particular case that they're concerned about by the nature of the beast. Does that help?

DR. HERR: I'm sorry, we should all go to law school to do this thing, but - decisions by the Special Masters, while they discuss policy so to speak, they don't set up case law, right?

MR. ROGERS: Right.

DR. HERR: So a decision that is uncomfortable by the government only becomes case law once you appeal it, right?

MR. ROGERS: This is arcane, but a Special Master's decision is not precedential as to other Special Masters. The other Special Masters may or may not go along with that. I hate to say a stitch in time saves nine - but if one Special Master decides a case in a way that we think is wrong from a programmatic standpoint, we know the other Special Masters are watching, and furthermore another situation is that we can't get an issue higher than the Special Master except by appeal to the Special Master's decision. So we may consider an issue important within the Special Master's decision, and know that the only way to get it to the Federal Circuit is by appeal to the Court of Federal Claims following the process.

So what you'll find in report after report that I give, is that by far petitioners are appealing the cases and we are not. You will see one or two at most. Usually there are none, and I got tripped up at the last report because I just automatically said, "We don't have anyone." We did have one. It's unusual for us to appeal and there's a recognition that cases should start and finish before a Special Master and that should be the end of it. And you should only appeal if there's an issue worth appealing.

Okay, these are the pending cases before the Court of Federal Claims on appeal. And here again you see that all but one were filed by petitioners and then the Heinzelman case - well, I just won't comment on it. It's - because it is pending appeal. We have no cases scheduled for argument before the Federal Circuit. With the Court of Federal Claims we have one, and that's the Graves case. That was a case brought by petitioners.

This was a request that this Commission made a couple of meetings ago. It asked us to take our stipulated settlements and break them down a bit so that you could get a snapshot of what kinds of cases are being settled and how quickly it's taking to settle them. The time period here is from when the petition - the stopwatch starts with the filing of the petition and it stops with the filing of the stipulation. There's still more to do after that, but it's for the most part out of our hands.

And these are the cases. You'll see, there are the three and four year cases, the two year cases, then as Dr. Evans was pointing out, quite a few just over a year. And as I've mentioned before, for a case to proceed from

petition filing to stipulation within a year and a half requires in our experience everything to have worked right. We had to have gotten the petition that was immediately capable of review by HHS, the parties have to turn to immediately to agree on a settlement and then process it through to the filing of a stipulation. This is - we're still working on trying to shorten this period but I think we're right at the very best we can do with that timeframe.

Okay, we've got some real quick ones in there. I'm not quite sure what happened with the double print there on one of those but I'm not the one to ask. There you have it. Now one thing I did was, I asked the attorneys in every case that took three years or more what happened, why did it take three years or more. And I can't go into individual cases but the trend is consistent with years and years and years of experience with this program starting from the very beginning.

The predominant reason for a long time period from petition to filing of the stipulation is that the record was not completed. There were additional medical records to file, there was a search for an expert, there are requests by the petitioner for more time to document the case, for timed (?) information. Occasionally a case will look like it's going to trial and then shift over to settlement. The trial process takes longer and if you go down one road and then shift to another, those periods generally have to be added to each other and that will stretch it out. Occasionally a case will go into an omnibus type processing where they're being aggregated by the Special Master because the issues are the same with other cases. In our experience that is a source of delay.

Are there any questions about the settlements? I was asked to talk briefly about Bruesewitz, and what I'll try and do is, I'm not going to discuss - I mean, it's a long decision that speaks for itself. I'll try to put it in a nutshell. And the case turned on the interpretation of one provision in the Act, and that's Section 22(b)(1). It's a preemption, there was a preemption issue, and what preemption means is when the federal government has spoken through legislation in an area, it generally preempts state law. It pushes it aside, if you will. Not always, but when the Supreme Court says it does, it does and that's what happened here.

What the Supreme Court did is, it did two things. It said, it interpreted this provision and determined ultimately that it preempted state law in the area. Now the statute, you have the language of the statute: "No vaccine manufacturer shall be liable on a civil action for damages arising from a vaccine related injury or death." This is a statement of preemption, that manufacturers shall not be liable. That's the general rule. Then it has a condition. If the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings. The two parties' positions turned on the meaning and effect of these various sections of this provision.

The petitioner's argument was that the last clause, even though the vaccine was properly prepared and was accompanied by proper directions and warnings, was incidental. That is, the meat of the provision was that a vaccine manufacturer shall be liable. They will not be liable if the injury resulted from side

effects that were unavoidable. Their argument was, if we can show that they were avoidable, this provision is not operative. There is no bar. This a civil action for damages.

The manufacturer's response was, no, this last provision is what's important here. If the vaccine was properly prepared and accompanied by proper directions and warnings, the vaccine manufacturer shall not be liable even if the injury or death resulted from side effects that were unavoidable. The manufacturer's argument was, if the vaccine is properly prepared, then the side effects were unavoidable. So it hinged on which of those two views was consistent with the purposes of a vaccine act.

The Supreme Court held, and reduced it to the gist, I believe, of the decision. There's certainly far more in the decision, which is far more eloquent than I'm being. But if a manufacturer could be held liable for failure to use a different design, the word "unavoidable" would do no work, meaning, it removes that from the Act. And so the Supreme Court held that the vaccine Act preempts design defect claims under state law.

So the correct way to read this according to the Supreme Court, is that if the vaccine is properly prepared, accompanied by proper directions and warnings, no vaccine manufacturer shall be liable for injuries that were unavoidable.

So that's the best I can do. It's like one of those -- it's like the picture of the Statue of Liberty that you've got to stare at and stare at until it finally emerges. It's a very difficult issue, and I would say there were two views

and two interpretations of this Act that the Supreme Court had to parse through and decide which interpretation furthered the purposes that Congress had in mind when it passed this Act, and they decided it in favor of the manufacturers for a broader preemption provision and shield from liability for design defects. I hope that kicks the can a little further down the road for you, and believe me, I've been staring at it a long time.

MS. HOIBERG: This is Sarah Hoiberg. Wasn't one of the main fears the Supreme Court had was that if they ruled in favor of Bruesewitz that it would open up a huge door, like Pandora - actually opening Pandora's box for the autism cases to come in or for really for that matter any case that had not been successful in vaccine court to come in and claim that there was an issue with a better vaccine out there for their child.

MR. ROGERS: I know that that was - those arguments were made. What drove the Supreme Court I really couldn't articulate better than they do. I think it boiled down to the purposes of the Act, and what the meaning of this provision was.

MS. HOIBERG: It was not a unanimous decision.

MR. ROGERS: It was not. Well with that I hope I've anticipated your questions and covered what you'd like to hear. As I've said before, before other constituted commissions, if there's more information we can give you, let us know. If the information we're giving you is starting to get boring tell us that and we'll compile it in a different way. We're here to please.

DR. EVANS: Mark, this is Geoff Evans. You referred to Cloer rather briefly, and I know that this was brought to the attention of the Commission previously. What is your best sense of the timing of where this is going to go and when we could reasonably expect a decision on which is probably one of the more important if not the most important case that's now facing the program?

MR. ROGERS: We're pending scheduling of the argument. It's a - it's tougher for the Federal Circuit to get all their judges in one place than to put together panels. We've been in touch with our appellant section and they're guessing this summer that we'll have the hearing. How long it takes them to decide the case after that, again, all bets are off. I would be surprised to see a decision - I guess I wouldn't be surprised to see it before the end of the year but I'd be surprised to see it much before that, and more likely early next year.

MS. GALLAGHER: Mark, I was wondering, for the benefit of the new commissioners, if you could just give a very brief thumbnail sketch of what the statute of limitations issue in Cloer is? Because I don't think they necessarily followed it or are familiar with it. I hate to put you on the spot that way, but --

MR. ROGERS: No. The issue is when does the statute start running. And the statute itself says, "from the first symptom of a vaccine-related injury." The respondents' position has been that that's what it appears to mean, that it's the first symptom of what is finally alleged to be a vaccine injury.

The argument that developed with the panel was, well, it's not a vaccine-related injury until the medical community relates it to the vaccine, and so the statute of limitations doesn't run until the medical community is relating

that symptom with the vaccine. So that's how I would reduce it to a nutshell. Again, you'd have to read their decision. I know I'm not doing justice to it, but that's how I understand it.

MS. GALLAGHER: Right, and I just wanted them to understand why you felt that it was an issue of general importance for the program, and I think that nutshell description does it. When exactly does this time period that's well-defined begin to run, and that could swing significantly with the two interpretations.

MR. ROGERS: Yes.

MR. KING: I have a question.

MR. ROGERS: Sir.

MR. KING: Hi, Dave King. On looking at the appeals slides I noticed that most of them from the petitioners seemed to be around entitlement, but there are some that have to do with fees and costs. And so what I'm trying to understand is a couple things. One, are the fees and costs, is that increasing as a trend in terms of petitioners filing an appeal? And if so, do you know what might be driving that? I don't know the answer to the first question, though.

MR. ROGERS: It is increasing. A source of increased litigation within the Avera decision, which appears to authorize the award of interim fees. And with the award of interim fees, the number of total awards has gone up significantly because conceptually it means you can have more than one award of attorney's fees in the same case. Depending on how many you have, that increases the number of awards significantly. And the Shaw decision rules that

those decisions are separately appealable. So you just have more decisions from which can be appealed. So yes to the first question, and that's one of the explanations I would give.

MR. KING: Are there other explanations you would give?

MR. ROGERS: Not that I would give, and really none that occur to me as I'm sitting here. Interim fees does not explain it all, but it's the most significant.

MR. KING: Okay, so there is a growing trend and it's possible that the reason is that there are more opportunities for it and therefore we see more. Is that a safe assumption?

MR. ROGERS: That's correct.

MR. KING: Is there - is it also possible that it's because people are arguing over the fees and that they don't feel that they're being compensated enough?

MR. ROGERS: I wouldn't be comfortable characterizing it that way.

MR. KING: I don't know. I'm just trying to find out.

MR. ROGERS: I couldn't say.

MR. KING: Is there any way for us to begin to find that out?

MR. ROGERS: The best way would be to look at the decisions themselves because the decision is the most authoritative pronouncement by the Special Master as to what's happened and what the parties are saying, and you know, I'd hate to generalize because there are a variety of reasons. Sometimes the disagreement is over what's legally permissible to pay as a fee. Sometimes

it's the reasonableness of the level of fees, and whenever the parties disagree and the Special Master has to decide, you have the potential for one party or the other to be displeased with how the Special Master resolved it.

So I guess if you track that, pull that thread to the end, the increase in the number of appeals is directly related to the displeasure of the parties bringing those appeals, which is generally petitioners, to the Court of Federal Claims. It's a disagreement with the Special Master's decision.

MR. KING: It's the Special Masters, then, that determine the fees and costs, is that correct?

MR. ROGERS: Yes sir.

MR. KING: Got it. Okay, thank you.

MS. GALLAGHER: Thank you very much, Mark. Right now I would like to depart from the agenda just slightly because I'm told that Joyce Somsak is here. She's the Associate Administrator of the Healthcare Systems Bureau and she has some remarks and presentations today.

Non-Agenda Item: Remarks and Presentations, Joyce Somsak, Associate Administrator, Healthcare Systems Bureau

MS. SOMSAK: I'm here on a pleasurable occasion, to represent the Secretary and extending congratulations and appreciation to the members of the Commission who have served us for so many - so long a time, so well, and are going to be rotating off the Commission. And the three people who are here today are Charlene Gallagher, who is our current chair, and Dr. Margaret Fisher,

who is our professional, and Magdelena Castro-Lewis, who has also been our prior chair as well as being a representative of the general public.

And the legislation establishing the Commission is very specific in the important role that this Commission plays in the program, and insuring that the issues that are discussed that were weighing in with people who are very concerned about this issue. So by serving on this Commission, the members who have done this so long and so well have proved that for us. They've had - they've shared their expertise, they've shared their passion, they've shared their dedication in terms of it. So on behalf of the Secretary we want to really express our appreciation.

But in addition, to the three members who are not here who had the most - the longest running every appointments to our Commission, I'd also like to thank Jeffrey Sconyers, who was our chair for many years, and Miss Tawny Buck, and Tammy Tempfer, who probably definitely exceeded what anyone could reasonably expect in their dedication to serving on this Commission. So I want to thank them as well. And hopefully they're listening and understand how much we appreciate them.

But now I'd like to give a plaque to our current people here. First, Charlene Gallagher, congratulations. (Receives plaque.) And Magdelena, congratulations. (Receives plaque.) And finally, Dr. Fisher. (Receives plaque.) And we also have letters of appreciation as well from the - for your work on the COmmission. So thank you very much. And I also want to extend to the new folks, Michelle and David and Ann, you have really outstanders here to look up to

in terms of working on the Commission and given their contributions over the past year. So we appreciate your willingness to serve as well. And I can't leave out the people who are standing here, right? So thank you very much and I will try to let you go back to business.

MS. GALLAGHER: Thank you. I think it's now time to turn to the Vaccine Information Statements. The Commissioners have the copies in their book, and I believe that Jennifer Hamborsky is on the telephone.

So which one would you like to start with, Jennifer?

Agenda Item: Review of Vaccine Information Statements, Jennifer Hamborsky and Skip Wolfe, Centers for Disease Control and Prevention (CDC)

MR. WOLFE: Dr. Evans has asked us to begin the presentation with a brief summary of how the development process for VIS has worked. Should we do that first?

MS. GALLAGHER: Oh yes, that would be extremely helpful for the new members. Thank you very much.

MR. WOLFE: Sure, and I did send a hand-out. I assume you all got copies of that, that goes over the process. Up at the top, it says "Producing a Vaccine Information Statement."

MS. GALLAGHER: It's in the handouts, tab six for those of you who are trying to find it.

MR. WOLFE: So I'll just go through that briefly, and then I want to say a couple of words about the interim Vaccine Information Statement. So

whenever there's a new vaccine licensed or whenever there's a substantive change in recommendations for an existing vaccine, we have to either create or update the Vaccine Information Statement for that.

And it's sort of a several-step process. The first part of the process is the drafting process, and CDC is the designated agency within HHS to be in charge of producing the VIS's, so somebody here, usually Jennifer or me, will draft a VIS, in the existing format and based on whatever the HCIP recommendations are, and we'll do that in consultation with the CDC subject matter experts who are usually the authors of the ACIP segment.

Once we get a draft that the subject matter experts are happy with, we move to the second phase of the development process, which is the consultation phase, and there we're required, mandated by law to have four, basically four reviews. One is with ACCV, which is what we're doing today, the second is with FDA, and usually what we do, we'll send them a draft by e-mail and get their comments back by e-mail.

The law also states that we should develop these in consultation with appropriate healthcare provider and parent groups, and we usually do that in what we call a consultation meeting, which sometimes in the past we've actually convened a meeting. Usually it's a conference call like this where we'll just bring all the people from different groups, like the American Academy of Pediatrics, the American Academy of Family Physicians, parent groups like the PTA, bring them all together and discuss the VIS's like we're doing here. And then fourth, it needs to be published in the Federal Register for a 60-day public comment period.

And there's no specific order in which these steps have to take place. Usually we go ahead and put it in the Federal Register and are taking the 60 days of public comment while we get the other three reviews. Once we've gotten the comments from all of these different reviews then we will redraft the VIS, again, in consultation with CDC subject matter experts. Most of the comments we get we'll accept. Occasionally we'll get a comment that the SME's will say no, we can't do that for this or that reason. So we're not required to incorporate every comment we get from the groups we get reviews from, but we usually do.

And then finally, the updated draft will go through a CDC clearance process. Once it clears, we'll finalize it and post it on the website, and put one more notice in the Federal Register, which is not for comment, just a notification that the new VIS is available.

So that's the mandated process to produce a final VIS. A problem with this - and I think it's a problem that the people who wrote the law back in 1986 didn't anticipate, 1986 when the law written and then 1991 when the first vaccine information materials were published, there were only four vaccines by the law, BPP, MMR, polio and adult PD. And the recommendations were pretty stable so you could publish a VIS and be confident that it would be good for quite awhile. Now, 20 some odd years later we have 15 VIS's and six more if you count travel vaccines and other non-injury table vaccines, so 21 total, and the recommendations are changing all the time.

So a problem that has arisen is that recommendations can change more quickly than we're able to produce VIS's, using this multi-month process that it takes to do it. So to deal with that, and to comply with what we believe is the spirit of the law, is that we need to get this important information into providers' and parents' hands as soon as possible, we came up with the idea of an interim VIS, which is basically what we do is produce, go through the first step of the process where we consult with the CDC technical experts, get a cleared up CDC, and publish an interim VIS as quickly as we can and then at the same time start the development process I just described to produce a final document.

And another - and a problem that has come up related to that is that sometimes, like the recommendations keep changing. We wind up with the interim VIS's for sometimes several years, which is unfortunate, but sometimes just the way things work out. So I wanted to go through that just to explain where the idea of the interim VIS came from. It's an idea that the purposes is to be able to get the information out quickly, proceed with the mandated process while we do that. And right now we're considering writing a proposal to get a provision for interim VIS's added to the law to actually make it official. So any questions on the development process?

MS. PRON: Yes, I have a question. This is Ann Pron. My question is then, does the interim VIS, is it the one that gets posted and distributed and handed out to patients or are both available then?

MR. WOLFE: No, the interim, that's - yes, the purpose of the interim is to be able to get that posted and handed out to patients while the final one is still in development, so the patients will have access to that information.

MS. PROM: So it replaces the other, the old statement that's been going through the whole process temporarily?

MR. WOLFE: Yes, when there's an update, yes.

MS. PROM: Thank you.

MS. GALLAGHER: Any other questions on the process? All right, should we turn our attention then to the statements that we're supposed to look at today? Would you like to start with Hepatitis A, the first in our binder?

MS. HAMBORSKY: I just wanted to tell the members real quickly, the main changes from the version that you currently have to the existing version is the statement about the indication for people in contact with international adoptees, and then there was a change to post-exposure prophylaxis. Those were the only two changes for Hep A.

DR. FISHER: This is Meg Fisher. I usually get to start, and I have to say for this one I thought it was just fine as it's written, so let the record show I had no suggestions.

MS. GALLAGHER: Anybody else have any suggestions? Dr. Herr?

DR. HERR: Yes, I have some questions again on who should get Hepatitis A vaccine and when, and I - maybe I'm wrong but I guess my

assumption of the ACIP recommendations was that all children beginning at age one year.

MS. HAMBORSKY: That's on the first one.

DR. HERR: I know but it doesn't quite - it implies all children through that, as opposed to the catch up and things like that of children who were not immunized at that time, and if you try to include that in the one down below that says children through 18 years of age, if there's a disease in that area, I mean it's just a little confusing.

DR. FISHER: This is Meg Fisher. I think it is confusing because I think the recommendation was a little bit wishy-washy. So catch up or when the recommendation changed in 2006 to recommend universal immunization for children age one to two, catch up was optional and catch up has always been optional. However, if it's a child who would be at increased risk that catch up should occur and I think that's the way this is written and it doesn't say you can't get it if you're just catching up, but these are the ones that should be targeted.

DR. HERR: Would it be incorrect or wrong to add, to change the first statement to "all children beginning at age one"?

DR. FISHER: That would make catch up not optional.

DR. HERR: Okay.

DR. FISHER: I'm sorry. I didn't mean to interrupt you. Is that Skip Wolfe?

MR. WOLFE: No, that would be an easy change to make, if that would help make it more clear.

DR. HERR: And the question of - I know that there's a question at the state level of what they were going to want to pay for or not pay for. But that doesn't always follow what ACIP's recommendations are so the fact that what the states are saying should be done for catch up or not catch up and what they will provide under their budgets is different than what ACIP recommends in the best scenario. And as I understand the best scenario, it does include catch up. But I guess that's open to interpretation.

MS. DREW: This is Sherry Drew, and I'm just speaking about paragraph number six, or section six, where they talk about the vaccine program. And I think we discussed this with respect to a VIS that is actually in effect. People who believe they may have been injured can't file a claim by calling this phone number. They can find information on filing a claim, but I don't think we should give them the impression that they can file a claim by making a phone call.

MR. WOLFE: Oh, good point. I seem to remember discussing that before, and maybe we just forgot to add that nuance in this statement.

MS. DREW: Okay. It's true also in the next one, in section seven, which is the same wording needs to be corrected.

MR. WOLFE: Right.

MS. GALLAGHER: This is Charlene Gallagher. I believe that we already agreed that wording maybe a couple of meetings ago, so if you could just pick up on whatever wording we all came to agreement on, that would be great.

MR. WOLFE: Yes, sorry, I think I just cut and pasted this from another VIS. I must have lifted that from the wrong one, from a draft.

MS. GALLAGHER: Okay, should we move on then to the second one?

MS. HAMBERSKY: And with this second one, there's a couple things. The main changes to the existing one were the changes in the recommendations for the age indications, and then there also was a statement that the vaccine safety people came out about syncope. And then we also got some additional comments from the subject matter expert that are not incorporated in the version that you got, and all that is, is in section three in the bulleted section, this language about intervals between Td and Tdap. And that information about the intervals has been taken out. And then also in the last bullet where it says "healthcare workers under 65," the age indication has been taken out because the new recommendations are just all healthcare providers. So now it just says "healthcare workers who have direct patient contact in hospitals."

DR. FISHER: Great. That was actually my comment, was that the intervals had to be - should be taken out of there. So that means under the adolescent one where it says "waiting at least five years" that's not going to be in there, and for the healthcare workers, a two-year interval, you're taking that two-year interval out as well.

MS. HAMBORSKY: Correct.

DR. FISHER: Perfect. And those actually were my - this is Meg Fisher - my main point. My other one was kind of a minor one. If you look at moderate and severe problems, the swelling, severe pain and tenderness in the arm is listed as both a moderate and a severe.

MR. WOLFE: I'm trying to simplify this for a lay audience. One of those is whole limb swelling and the other is - I forget the term now - the other is - -

DR. FISHER: One's supposed to be brachial neuritis?

MR. WOLFE: No.

DR. HERR: A little redness, a lot of redness.

MR. WOLFE: Sorry?

DR. HERR: A little redness, a lot of redness.

MR. WOLFE: Yes, there's a name which escapes me at the moment. It's actually two different adverse events, but they sound similar.

MS. HOIBERG: This is Sarah Hoiberg. Shouldn't it say redness and swelling at the site of the injection? I know that the bullet about it says pain at the injection site but shouldn't it say redness and swelling of your arm, or of the injection site? Because if you - your whole body has redness and swelling, I would think that that would be a major allergic reaction, so maybe it needs to be a little bit more specific to the fact that this is, we're talking about the injection site?

MR. WOLFE: In which - which one are you --

MS. HOIBERG: It's on all of it. It never says "redness or swelling at the injection site."

MR. WOLFE: Oh, I see, yes.

MS. HOIBERG: Pain, but pain where? Pain throughout your entire body? Pain just on your arm? So it needs, we need to say that it's at the injection site.

MR. WOLFE: Yes, thank you, good.

MS. HOIBERG: You're welcome.

DR. FISHER: This is Meg Fisher again. I guess I'm just being dense here. I honestly don't get the difference between extensive swelling in the arm where the shot was given and swelling, severe pain and redness in the arm where the shot was given. I'm presuming you do, and you're trying to distinguish one from the other, one being moderate and one being severe, but it - I mean, I think if I have trouble figuring it out probably many people are going to have trouble figuring it out.

MR. WOLFE: We can go over that again with the subject matter experts.

MS. PRON: This is Ann Pron. I see that there's a differentiation made in parentheses under mild, moderate and severe in terms of whether it interferes with your activities and whether it requires medical attention. Is that supposedly the difference?

MR. WOLFE: Yes, so it is a similar reaction but just more severe in one case. And then I guess you could make an analogy between a mild fever and a high fever.

DR. HERR: Changing the subject, Ted, this is Tom Herr. In the "Why Vaccinated" again - I seem to focus on that part - if we're looking under tetanus, diphtheria and pertussis and at least the tetanus and diphtheria is saying that okay, we can - these are why to get immunized, why to get vaccinated, and we include death in those two, I don't know why we don't include death and encephalopathy in children, in infants, with pertussis. You know, "it can lead to." I mean, we talk about broken ribs. In infants, it can be devastating.

MR. WOLFE: And it's more common than tetanus and certainly diphtheria.

DR. HERR: Yes.

MR. WOLFE: Okay.

MS. HAMBORSKY: They may have some updated data now from California for that.

MR. WOLFE: But it's always been a risk.

MS. HAMBORSKY: Right, but they may - that might be why it's not in there.

MS. HOIBERG: This is Sarah Hoiberg again. I'm looking at the side effects now. These are all - now the risk with the Tdap, you know, the one that contains pertussis, couldn't that still at some point - have we not had any

problems with encephalopathy or seizure disorder with that particular - with the pertussis-containing vaccines? I'm just wondering because anything else --

MR. WOLFE: We can check with the safety people, but these are based on the information that's in the ACIP recommendations.

DR. EVANS: Skip, this is Jeff Evans. I know after Tdap was licensed in '96 for use in infants, and then TDaP followed after that, that there was - that they kept the language the same initially, but then I think the language was adjusted to reflect the fact that you have an older age group, you don't have - or evolving neurological disorders which are an issue for infants under a year of age are not an issue for older children and adolescents, so I think the language has now been changed so that these kinds of precautions are not for children in the older age group.

DR. WOLFE: Right, and some of those precautions that were based on a reaction after a previous dose has applied it. The phrase I was groping for awhile ago just occurred to me. The difference between those two, extensive swelling. One is extensive limb swelling, the other is arthus reaction. So they're actually two separate things but they're very similar and it would be hard to explain the differences in a document like this.

MS. HOIBERG: Well so then maybe put it under one and not the other.

MR. WOLFE: Well because one is more severe than the other.

MS. HOIBERG: I see where Meg's having a problem, and I have a problem with it because it says "moderate problems" and under the Tdap I see it

says “extensive swelling of the arm,” and that’s under moderate. And then on the - under severe it just says “swelling.”

MR. WOLFE: We’ll run those two by the subject matter experts again and see if we can hammer out something that’s a little bit more descriptive.

MS. HOIBERG: It just sounds like the one on the --

MR. WOLFE: Yes, it sounds less severe than the other one.

DR. FISHER: This is Meg Fisher again. I definitely would not have anticipated that was an arthus reaction, so yes, I would redo it. Talk to the subject matter experts again to really see if there’s a different way to say it that - because as a pediatrician or someone giving this vaccine if the parent asked me what that was I would have trouble describing it. It didn’t strike me as an arthus reaction.

MR. WOLFE: Okay, we’ll try to make it sound worse.

DR. HERR: Skip, one last thing, and I understand that this is for older children, but the reason I would still include the information on infants on pertussis complications like we did for the influenza vaccines, that it’s important to immunize for influenza because we’re also protecting children under six months who might be exposed. So you want to limit the exposure to those children. Likewise, I think it’s important when we’re talking about immunizing older children against pertussis that we bring back why it’s important to protect the infants.

MR. WOLFE: So we’re talking in the section one, like it’s --

DR. HERR: In the “Why Vaccinated,” right.

MR. WOLFE: Okay. Good.

MS. HAMBORSKY: Any other comments?

DR. FISHER: We like them.

MS. GALLAGHER: We don't appear to have any other comments around the table now.

DR. HERR: Thanks for the frequent feedback.

MR. WOLFE: And thanks a lot for your input, as always.

MS. GALLAGHER: And we appreciate you going through the process for the new members. That was very helpful.

MR. WOLFE: Good, thanks.

MS. HAMBORSKY: And then hopefully at the next meeting - we didn't get a chance to share the preliminary results but in the past couple of months our communications group has done several focus groups of the VIS, so hopefully for the next meeting we'll have some summary points for that.

MS. GALLAGHER: That would be great. Thank you very much. All right, now checking my agenda it would appear that it is time for a break. So I would say if we could try to get back around elevenish. I know we're running about five minute behind but I'll just steal some time from the break. Thank you very much. We'll be back in about 10 minutes.

(Brief recess)

MS. GALLAGHER: We're going to have the update from the National Vaccine Program Office.

Agenda Item: Update from the National Vaccine Program Office (NVPO), Dr. Dan Salmon, NVPO

DR. SALMON: Thank you for the opportunity to speak with you today. Dr. Evans asked that I give kind of a detailed description of what the National Vaccine Program Office does, particularly for the benefit of the new members that may be less familiar with us. So I'm going to start from the beginning and provide a fairly broad overview. I'm probably going to look to my left more than my right because I think my right had heard much of this before so please don't think I'm being rude. I'll try to focus also somewhat on issues that I think would be of interest to this Commission so I'll highlight things which seem to be more relevant to the domains that you work in.

So the National Vaccine Program - and there's a lot of NVP's here so work with me because I'm going to draw the distinction that's often confusing. But the National Vaccine Program was created by Public Health Law 99660, which is the same law that created the Injury Compensation Program and the HDCV, and that created the National Vaccine Program and the National Vaccine Advisory Committee. And the goal of the National Vaccine Program is to ensure federal assets are coordinated with the dual goals of preventing infectious diseases, the sequelae and morbidity that can follow that are vaccine preventable, so the goal of effectively using vaccines and at the same time preventing adverse events from vaccines. So it's a dual goal of both prevention of disease and prevention of adverse events.

When the National Vaccine Program was created the Assistant Secretary for Health was designated by the department as the director of the

National Vaccine Program. Additionally the department created the National Vaccine Program Office, and that's NVPO, and that's where I work. So the National Vaccine Program Office is the office or arm of the Assistant Secretary for Health that tries to carry out the functions of the National Vaccine Program. So the National Vaccine Program is made up of the agencies and departments that have assets within vaccines. So within the Department of Health and Human Services that includes primarily FDA, NIH, CDC, HRSA, also Indian Health Services, in some situations CMS, HRQ, and then other non-HHS departments, primarily USAID, the DA and the DOD. So in many ways we're a policy office. We're a coordinating arm. Our job is not to make sure -- .

MS. SAINDON: Could you say what those acronyms mean? I'm not sure if everybody knows every one that --

DR. SALMON: I'd be happy to, thank you. So we'll get away from the alphabet soup. The agencies that we coordinate, primarily CDC, the Centers for Disease Control and Prevention; NIH, the National Institutes of Health; FDA, the Food and Drug Administration; HRSA, I think you're familiar with; CMS is the Center for Medicare and Medicaid Services; IHS, Indian Health Services; departments, the VA, Veterans Affairs, and Department of Defense, DOD. And I will try to refrain from using acronyms as I go on.

So we're in many ways a quarterback policy office. We're not responsible for doing everything that needs to get done to prevent diseases that are vaccine preventables, that prevent adverse events. Thank you.

MS. GALLAGHER: And if you would just mention a few of the commissioners, particularly on page five of the red book, thanks.

DR. SALMON: I'd be happy to. So it's been pointed out to me that in the National Vaccine Plan, which I'll talk about in a minute, and page five is our directory of alphabet soup, so that might be helpful as you look at these different acronyms.

So our job at NVPO is not to make sure all these things get done. Looking at Dr. Mulach around the corner, I mean NIH does a tremendous amount of work in vaccine discovery, from basic laboratory research to clinical trials. NVPO does not do those things but our job is to make sure that the efforts across the federal government are coordinated in that regard. So we're a policy office. We're a fairly small policy office. The director of NVPO is Bruce Gellin, the deputy director is Mark Grabowsky, my job is the director of Vaccine Safety, so the coordinating function that NVPO plays is what I do in vaccine safety. I'm responsible for coordinating federal assets in vaccine safety. So this is the focus of NVPO.

And then we have NVAC, the National Vaccine Advisory Committee, which is our advisory committee, and it's similar to this Commission in many ways. It makes recommendations on vaccine policy to the Assistant Secretary for Health, who's the director of the National Vaccine Program, and with the dual goals of prevention of infectious diseases through vaccines and prevention of adverse events. But the focus is policy, right? So for example the Advisory Committee on Immunization Practices makes recommendations on who

should get what vaccines under what circumstances, and who shouldn't. And that would be a practice focus, where our Advisory Committee is focused more broadly on the policy issues.

So let me stop there, and that's kind of the broad overview of what NVPO does, our responsibility, how we were created, and our advisory committee. And I'll stop there and I'll get into some more specifics, but in case anyone has any questions I don't want to bite off too much before I move on.

MS. WILLIAMS: This is Michelle Williams. Do you also coordinate with the stockpile, the national stockpile?

DR. SALMON: So that would be a part of the larger effort to control infectious diseases through vaccines. The stockpile is mostly in CDC's domain so there could be issues, for example, where one of the issues that the NVAC is focused on historically is ensuring adequate supply of vaccines, and a part of that would be a stockpile. So again, NVPO doesn't run the stockpile, it doesn't tell CDC how they should run the stockpile, but we will look at the broader issues often through our Advisory Committee of how does the stockpile fit into ensuring adequate supply of vaccines. So that's a good example to exemplify what we do and what we don't do.

MS. WILLIAMS: Thank you.

DR. SALMON: Sure. Any other questions before I move on? So one of the things that Congress told us to do when they created our office is to create a National Vaccine Plan, and the first plan was created in 1994 with the goal of making sure that federal efforts in vaccines were well-

coordinated and there was strategic vision and it was a plan for what our nation's National Vaccine Program should do in the future. And it's nice for me to come to you with the next revision of that plan, which is this red book. So this was actually just released at our NVAC meeting I guess a few weeks ago and this is the most recent, the new National Vaccine Plan.

I'll walk you through this just a little bit. I appreciate you pointing out that page five has all the acronyms. I teach a class on vaccine policy and I've learned in that setting not to use documents because it drives people crazy so I'll try to remember that when I'm here speaking with you. So if you look at this, there's really two areas.

So there's five goals to the plan. Goal one is develop new and improved vaccines - I'm looking on page 10. Goal two is enhance the vaccine safety system, goal three is to support communications to enhance informed vaccine decision making, goal four is to ensure a stable supply of access to and better use of recommended vaccines in the U.S., and goal five is to increase the global prevention of disease, of death and disease through safe and effective vaccination.

And I think you'll find that goals two and goals four are really what relate probably most directly to this Commission. I mean, there may be other parts that relate and communications probably relates to some extent as well, but that's really where this is probably most relevant to your work. So looking at goal two - and I'm turning now to page 22 - so there's a number of objectives, objective 2.1 through 2.8. And I'll walk you through those briefly because it really

highlights the vision of the National Vaccine Program or the departments and agencies responsible for vaccination in terms of what we believe we can and should be doing to enhance the vaccine safety system.

Let me take a step back and tell you a little about the development of this plan. It was no easy task and it was not quick. It took about three, three and a half years for this to get written. It included broad reaching and discussion with stakeholders, with public meetings, we had the Institute of Medicine review and earlier draft of this, we engaged the NVAC multiple times on this, so this was a very large and long endeavor. It wasn't something that was done hastily or quickly, and the intention is to have our long-term vision. So it's a rather comprehensive strategic plan.

So goal two, the first objective is to develop or ensure a vaccine safety scientific system that focuses on high priority areas. And these strategies include 2.1.1, which is developing a scientific agenda to increase and recruit scientists and clinicians and improve methodologies, laboratory, epidemiological and statistical. And in fact one of these recommendations came out of the Institute of Medicine, which was to develop a national scientific agenda. And I'll talk in a few minutes when I get to the NVAC about a scientific agenda that was developed for the Centers for Disease Control.

But what this is calling for is a safety scientific agenda that goes across the government. So in other words, we want to have a clear outline or a clear strategic plan in terms of what safety questions should be studied and what are the highest priorities. And this will help ensure that we have a

comprehensive and systematic approach to answering outstanding questions. And I think this is relevant to what you folks are looking at, because ultimately fair and equitable compensation is based upon the best available science.

Objective 2.2 talks about advances in manufacturing science and regulatory approaches, and this is really focused on the licensure process.

Objective 2.3 looks at enhancing the timely detection and verification of vaccine safety signals. So vaccine safety signals are something that comes up that may warrant further investigation and this is an area where people often misunderstand what a signal means. A signal could arise from a variety of sources. It could be a bunch of reports that come out in VAERS passive reporting system, it could be something that comes out in the media or comes out through looking at Internet blogs or surveys of parents, it could be a very interesting case that's published in a clinical journal.

So initially a signal comes up. A signal is something which seems interesting, which seems worth studying further. And then that signal is verified. In other words, it's looked at more closely and determination is made of well, what - does this really deserve or warrant further investigation.

And sometimes they do and sometimes they don't. The idea is to capture a broad range of things as signals so that you're being very sensitive and you're picking up anything you might possibly want to investigate further. But then you have to figure out, well is this something that really warrants further investigation.

Moving on to 2.4, to improve the timeliness of the evaluation of signals and in particular two times are highlighted, when high priority new vaccine safety concerns emerge, or when a new vaccine is recommended, as an extension of recommendations or a public health emergency such as an influenza pandemic. So this is kind of a sequential process. Something odd pops up or unusual, and you examine it and say, well should we study it more.

And if the answer is yes and you want to do so vigorously and quickly, the next objective, 2.5, is to improve causality assessment of vaccines and related adverse events following immunizations. In other words, now that you've investigated some of them, the ones that warranted investigation, to figure out whether or not it really is caused by the vaccine.

And this is an important distinction here, because lots of bad things happen to people every day and if you vaccinate everybody today, every bad thing that happens tomorrow happened a day after vaccination, whether that be heart attack or a hurricane in the Gulf. So bad things happen to people every day and unfortunately bad things happen to young children, especially in the first two years of life when we give a lot of vaccines. So we know that there will be lots of young children that are vaccinated, and then an adverse health outcome or an adverse event following immunization happens.

And the key to safety science is to figure out, well did that happen by chance alone or was that caused by the vaccine, because we know these things will happen anyway but we need to figure out was it just because these things happen in the population or is it because the vaccine caused it. And

objective 2.5 is to focus on whether in fact the vaccine caused the adverse event, based on the science that's done previously.

2.6 is to improve scientific knowledge about why and among whom vaccine adverse reactions occurred. So if in fact in some cases we do the science and we say yes, this vaccine caused this adverse event, or this adverse reaction, well why? And how? And among whom? What was the biological mechanism? How did that bad thing occur? And is there a subpopulation that's at increased risk? Maybe there's a certain genetic component, maybe somebody had a previous illness or illness at the same time. But it's not enough to just say yes, this vaccine sometimes causes bad things to happen. We need to go the next step and we need to figure out how it happens, why it happens, and among whom.

MS. HOIBERG: Can I stop you right there?

DR. SALMON: Sure.

MS. HOIBERG: This is Sarah Hoiberg. Where you're talking right in here about assessing whether the risk is specific, if it's - well anyway, that's 2.63 - I personally have never received a phone call from you guys asking to look at my daughter for what happened to her, why it happened to her. I know a few of my constituents who also have vaccine-injured children who have been compensated by the program have never been contacted to say we'd like to find out what happened, we'd like to study your child. So who are you looking at?

DR. SALMON: Yes, so that's a great question and so one of the concepts that NVPO has been working on - I'm going off on a bit of a tangent

now to answer your question - but would be to enhance a vaccine safety biobank or repository with clinical information. And there's a very small biobank that's run by CISA which is a network of clinical academic centers that look at rare adverse events and try to understand the pathophysiology. So a lot of what would be done in 2.6.3 is done by CISA - CISA, the Clinical Immunization Safety Assessment Center Network, thank you. I'll get better at that, I promise.

So this is the kind of work that these centers do. There's six academic centers across the country that try to understand the biological mechanisms, and they have a very small biobank. Biobanks are hard to put together, they're hard to run, and they're not inexpensive. And one of the things that our office has helped try to coordinate is to expand that biobank working with NIH and FDA and CDC, and also including HRSA, to see how we can do better in that regard. And one approach that we've discussed is trying to get cases that have come through the compensation program.

But it's not easy. I mean, it's not easy for a lot of reasons. A couple of them is that there's confidentiality issues, so your name can't be given to somebody because you were compensated through the program without certain levels of consent. Also, when you want to collect biospecimens often you want to collect them very soon after the health outcome occurred. So in fact the Injury Compensation Program for many of these things may not be the best place to get cases, because by the time you come to the program and it's been figured out whether or not the vaccine may have caused the adverse reaction, that may be months or years after it occurred.

MS. HOIBERG: So what are you doing to educate doctors about vaccine injury? Because if you educate them about vaccine injury, then they're going to be looking for it and they'll be able to supply you with children or adults that have suffered an injury and therefore you will be able to do your research because vaccine injury is not something that's really talked about because it's shoved under the rug and considered in most parts not really to happen, then you're not going to be getting information that you need.

DR. SALMON: So there's a whole other goal, and I'll mention that this probably isn't the most interest to this Commission but to some extent in your example it probably is, there's a goal on communication. I think it's goal three, support communications to enhance informed vaccine decision making, and that does include communication with providers about vaccine safety. And I'd have to double check but I think there's also mention in the goals for the National Vaccine Injury Compensation Program about informing stakeholders about the existence of the program.

MS. HOIBERG: Okay, thank you.

DR. SALMON: Does that answer your questions? Okay. So 2.6, objective 2.6, to understand the why and among whom for vaccine adverse reactions, goal 2.7, to improve clinical practice to prevent, identify and manage vaccine adverse reactions. So once you've figured out that they occur and you've figured out among whom and why, to then try to prevent them and then to manage those adverse reactions as much as possible.

And then lastly, 2.8 is to enhance collaboration of vaccine safety activities, and this relates to the sort of work that NVPO does, to make sure that there's collaboration broadly across federal agencies, departments, and with non federal partners, to improve information and data sharing, and to develop standardized case definitions. So this is a fairly brief summary, although not that brief, of the work that's in the National Vaccine Plan in vaccine safety, and it characterizes the spurts of work that not only do we do now but we want to do more of and we want to do better.

MR. KING: Question. So thank you for outlining this by the way. The - this kind of tells us what the goals are. How do we find out what the how we achieve those goals are?

DR. SALMON: That's a great question. You know, it's almost like I set that up, but I didn't. So we're in the process of developing an implementation plan for this, and there's certain high priority items which will then have implementation that's written for. So this says what needs to get done, but as you've articulated it doesn't say how you do that. And that's what the implementation plan will do.

MS. HOIBERG: Who's helping you with that implementation plan?

DR. SALMON: Well we're working as NVPO typically does with the agencies and departments that are a part of the National Vaccine Program, and we are developing that implementation plan now.

DR. FISHER: Dan, following up on one of - Sarah's idea, which I think is a neat idea and I wish we could access or have easier access to people

with vaccine adverse events, VAERS might be the other way to do it. So there, there's not as much the confidentiality clauses or the confidentiality problems. If there was some addition on VAERS that gave you the ability to give consent to have yourself studied or your child studied, or even gave you the contact for how you might get that next step, because I think it's a great point.

I mean, we'd all rather have a double blind control study that would pair people who don't have the event with people who do have the event. But it might - if there is some genetic something or if there is, you know, as we get more proficient with the genetic background of people it would be nice to have a group of those people - I don't mean, people aren't stockpiles, but to have their names or their contact information, or just a registry. And I think the problem with the compensation is probably the fact that we do need to protect confidentiality but with the VAERS there might be a way that on an ongoing basis you could enroll those people.

DR. SALMON: I agree with you completely. It's certainly something that we're exploring. It would still require a consenting process because people who have made a voluntary report, there would have to be some sort of consent that would say can you be recontacted. And typically for a biobank you want a lot of information. You want certain types of samples depending on what you're studying and what the outcome is, and you also want a medical history. And typically you want the two linked. So you want to say, well we have protocols for these rare outcomes, and for people that experience that outcome with some standardized case definition within a specified time

period we will collect certain specimens, and then we'll get their medical histories and they're linked together.

And you know, this is something which one of the groups that NVPO works with is called the Federal Immunization Safety Task Force. It's a group of feds that focus on vaccine safety. It was established by Secretary Leavitt in 2008. And when we looked at how we can improve the infrastructure for vaccine safety a biobank was one of the areas that we thought was most important because studying very rare things is really hard and having, collecting cases prospectively allows one to eventually collect enough cases that you can do these studies.

So we looked at other ways. Injury Compensation Program is one potential source for cases, VAERS is another, we have a number of very large, active surveillance systems like the Vaccine Safety Datalink, like PRISM's, the Center for Medicaid and Medicare Services - I hope I got that right, it might be Medicare and Medicaid, I'm sure it's CMS. And the VA, the Department of Defense, using these large surveillance systems may be another place.

Another potential source we've looked at is clinical trials because even though they're not terribly large so you may not get very rare adverse events persons that are in clinical trials are studied really carefully and you have all sorts of information that are collected as a part of those clinical trials. So the points you're raising are important ones and ones that we're thinking through as we think about how to really establish a robust vaccine safety file bank.

DR. HERR: So are you going to develop the candy store wish list, you know, if I could this is all that I would want?

DR. SALMON: Right. It's not a short one.

DR. HERR: Yes. And then you sit down with the practicality of what can I afford and how can we get this done.

DR. SALMON: Yes, there's no question that there's enormous price and planning implications.

MS. CASTRO-LEWIS: And what is the timeline for the development of an implementation plan?

DR. SALMON: We're working on it now. I think we're hoping to have it complete within the next six months. Don't hold me to that but that's my understanding is that within six months that would be complete. But we're not writing an implementation plan for every strategy and objective in here because you could imagine that would be a book. But rather, we've identified high priority items, and for those high priority items we'll write implementation plans.

MS. PRON: Yes, hi, this is Ann Pron. I did receive some information through an e-mail which said also that you would be having national meetings with - regional meetings to work with stakeholders. Who exactly will that be?

DR. SALMON: That's exactly right, and Sarah Landry from our office is coordinating those, so there's a series of I guess regional meetings that are being put on. I think one's in Denver, one's in Chicago. I see Barbara nodding. I think there's a third one that's scheduled. But the idea is to get input

from stakeholders and to try to do so on a regional level. And that will help inform the development of the implementation plan.

MS. PRON: How are those stakeholders identified and invited?

DR. SALMON: We're a part of the Office of the Assistant Secretary for Health and the Office of the Assistant Secretary for Health also includes regional health administrators so different parts of the country are grouped into regions and those regions have a fed that works with the state and local health departments. And it's kind of the liaison between the federal government and the state and local health departments, so those regional health administrators are helping us work to develop these meetings, and they're bringing in local organizations to gain input. So that's kind of the mechanism that we're using. Does that answer your question?

MS. PRON: Well not completely, but how does one find out about - just through the coordinator, the administrator?

DR. SALMON: Regional health administrators. So I'm sure that - although I haven't checked - that our website has information on these meetings. And I'd be happy to, the next time I come to the ACCV at your next meeting provide you an overview of what those meetings entailed, how they were put together.

MS. PRON: The reason I ask is because I guess we sent out to our organization a link to the plan, the immunization plan, and right away I got a response from someone that says oh, I'd like to be, you know, NetMap's representative and involved in that. But I don't know if NetMap is going to be

contacted or how we would even put that as an organization, decide, you know, how, who would go and all that.

DR. SALMON: Sure, so Jennifer if I forward to you some information on this could you forward it to the Commission? We'd be happy to provide you more information.

MS. PRON: Okay great, thank you.

MR. KING: I have another question. Going back to the point that Sarah had brought up that Dr. Fisher had also commented on, so of the cases that have been resolved my understanding is that number since the inception of the program is somewhere around 2,500. I think that's an accurate - is that correct? - or something along those lines I saw on a slide yesterday.

So of them, some of them have been where it was conceded that in fact there was an issue. And I don't know if that number would be statistically relevant but in order for them to be conceded there has to be a massive amount of data that has already been provided. Now I don't know whether, from privacy issues, whether the names of the individuals can be removed, but is there a way to analyze all of that data and see if there is a common set of characteristics somewhere within them that might bring something up?

DR. SALMON: This is not the first time this suggestion has come up. In fact it's come up repeatedly over the years, thinking that the reservoir of cases that have been compensated in the program have a unique value in terms of trying to clinically examine them and see if there's any patterns. For all the reasons that have been talked about, it's certainly something that can be

challenging to do, and what I'd like to suggest is that we postpone that question until tomorrow.

Rosemary Johann-Liang, our Chief Medical Officer, is going to be providing with her staff a clinical update, and she is also involved right now in a series of clinical projects utilizing some of the cases and I think it's a better time in the context of that discussion to talk about some of the difficulties in examining seizure cases, for example, encephalopathy cases, which have their own complexities as a group. It's a good question that you asked, David, but it is a - there's some pluses to trying to take a look at these groups of children who have chronic seizure disorders and encephalopathy and there's some commonalities that really don't lend themselves well to trying to make some kind of a - to discern some kind of a trend out of them and I think that Rosemary is in a better position to discuss that.

MR. KING: So that will be a question for tomorrow.

DR. SALMON: If I could draw your attention to one other part of the plan, on page 35, objective 4.8, and Geoff may want to comment on this more because whereas the safety goal, I was very involved in writing that goal, this was really, I was not directly involved in but I'll mention it to you because it relates very directly to your work. But again, on page 35, objective 4.8, the strength in the National Vaccine Injury Compensation Program and the Countermeasures Injury Compensation Program.

And there's four strategies here, increased knowledge about the programs among all stakeholders, which I think relates to your point; to

assure the programs are responsive to evolving science including regularly updating vaccine injury compensation table. And this is where there's a real clear link between the work of this Commission and the program, and the work of vaccine safety science, because the better science we have the more complete the science, the quicker the science, the better the causality assessment, then the more accurate the table is.

4.8.3, continue to insure fair and efficient compensation for vaccine-related injuries; and objective or strategy 4.8.4, examine alternative approaches and evaluate and implement those deemed optimal for adjudication of VICP claims for illness not included in the table to the extent permitted under applicable law.

So let me stop there for a minute, because this is as much as I was going to talk about the National Vaccine Plan. But I've given you a lot of information in a short amount of time, and I think my right side's probably heard much of this before and my left side is probably going, "God that's a lot of information in a short amount of time."

MS. WILLIAMS: That's a nice presentation.

DR. EVANS: The only think I would add to what Dan just said about the strategies, those strategies reflect fairly closely what's in the strategic directions that were worked on with outside consultation In 2006 and also a little bit of the info we received from Congress as a result of the hearings earlier, before that. So these are some basic principles and goals that the stakeholders

that came to that particular meeting thought were important, and are reflected in this document, too, and things that we continue to work on.

DR. SALMON: Are there any other questions about the National Vaccine Plan? And then I'll talk a little bit about the National Vaccine Advisory Committee. Please don't be unhappy that I keep looking left. You guys have heard this all before. So the National Vaccine Advisory Committee, this is an advisory committee that makes recommendations to the Assistant Secretary for Health, as the director of the National Vaccine Program, and there are two working groups. Much of the work is done in working group, as it is for this Commission and many advisory committees and there's two that I'll make specific mention to, because I think you might be interested in them.

One was established in response to H1N1, and it's the Vaccine Safety - H1N1 Vaccine Safety Risk Assessment Working Group, affectionately known as the VSRAWG. And it's been pointed out to me that it may be one of the only Google searches you can do where you will actually only get this one item. But the charge of this working group was to look at H1N1 safety data on a regular, ongoing basis to provide independent assessment of H1N1 vaccine safety. So their focus was entirely on safety. They did not look at the burden of disease or the effectiveness of vaccination, so they didn't look at vaccine benefit. But the idea was to have a group of external experts that would provide a review of all the data on a regular basis.

So it's chaired by Dr. Maureen McCormick. She's a professor of maternal and child health at Harvard. It includes representatives from the five

advisory committees that had a role in H1N1, so that includes the ACCV - I'm sorry, it does not include the ACCV because you weren't involved in H1N1. It includes the ACIP, which is the Advisory Committee on Immunization Practices - so you're going to test me now to see how well I know all my acronyms - VRBPAC, which is FDA's advisory committee; the NVAC, the NBSB, which is the National Biodefense Security Board, which advises the Assistant Secretary for Preparedness and Response, so because H1N1 was the national preparedness part the NBSB had a role; the Department of Defense Health Board.

So there were representatives from each of these advisory committees, and then a public representative from FDA's VRBPAC, and then we brought in two other external experts that were members of the Institute of Medicine or one of these advisory committees to really make sure we had a technically, scientifically very strong group. They went through very stringent conflicts of interest criteria, they met before the Vaccine Program started, and they looked at all the different systems we had in place to monitor the safety of H1N1 vaccines.

They then met biweekly by phone throughout the Vaccine Program, and this immunization safety task force I mentioned, this is the feds that across the agencies that work on safety that were collecting H1N1 safety data, every two weeks we provided those external groups summaries of all the data. So they didn't actually collect the data, the advisory group, they didn't run the analysis, they looked at all of our data and once a month they issued reports through the NVAC summarizing those data. So NVAC meetings, like ACCV meetings, are

open to the public and this way there was a public reporting mechanism on an ongoing basis of the safety of H1N1 vaccines.

They issued maybe eight interim reports - don't quote me on that, they're on our website, somewhere between seven and nine. At the last NVAC meeting they put out their interim report which includes a summary of just about all the data we received to date. We're still waiting on a couple of things. We're combining data for Guillain-Barre syndrome across systems. That's going to take about another six months. And the pregnancy outcome data is going to take a bit longer because as you can imagine if you vaccinate pregnant women and you want to look at how their babies turn out you've got to wait awhile. So we're giving a very, very careful look at all of the H1N1 safety data. So that's the H1N1 Vaccine Safety Risk Assessment Working Group.

The other working group I would mention to you from the NVAC is the Vaccine Safety Working Group and this group was set up a few years ago. It is chaired by Dr. Maureen McCormick, Tawny Buch, who is a former ACCV member and ACCV chair, and Andy Pavia, who is a peds ID doc in Utah. It includes public reps from the four federal vaccine advisory committees, not necessarily the current public rep. Often when somebody new was coming on we took the person that had been there for awhile because we wanted people that were familiar with the advisory committees. And then a broad range of expertise from immunology and neurology, epidemiology, biostatistics, genomics, kind of all the expertise one needs in vaccine safety.

Their first task was to look at the CDC's immunization safety office research agenda so based on an IOM recommendation, CDC developed the research agenda and this working group reviewed that agenda very carefully and they looked at both content and prioritization and they did so in such a way that had very broad public and stakeholder input. So they held a series of meetings, three different meetings in three different cities where we brought in members of the public to hear their thoughts on content and prioritization, we had a small stakeholder meeting, we had a large stakeholder meeting, and ultimately NVAC issued a report that provided feedback to CDC in terms of what was on their agenda and in terms of how to prioritize their agenda. And either very recently or very, very shortly from now, that final research agenda will be posted on their website. I think it already has. If not it will be there very soon.

So this is the first task of the safety working group. They completed that in June of 2009. Their current task is to look at the safety system more broadly and to vet a white paper on how we can take advantage of new science and new technology to have a vaccine safety system of the 21st century. So they're looking very closely at the safety system and they're looking at advancements in immunology and genomics and information technology and writing a very comprehensive report on how we can take advantage of emerging and new science and resources to have the most robust vaccine safety system we can have.

They have a draft which they're putting their dots on their i's and crosses on their t's, and we're getting ready for a stakeholder meeting which will

be April 29th. That will be an opportunity for a broad range of stakeholders to look at that first draft and provide feedback to the working group on how to enhance it. In the June NVAC meeting a draft will be shared with the NVAC for deliberation and in September of 2011 we anticipate a final vote on that white paper.

So let me stop there and just mention one other thing that you've received in your notebooks, and this blue guide. A couple years back we wrote a very large document describing the vaccine safety system, and the vaccine safety system is incredibly complex. As I've used all these acronyms, these are all these different agencies and departments many of which have multiple programs and activities that focus on vaccine safety. I look again at Barbara and there must be hundreds of programs at NIH that have a role in vaccine safety.

CDC has many programs in vaccine safety, and there's huge efforts across HHS and other departments and then other non-federal partners ranging from healthcare providers to state and local health departments to consumer groups to the public themselves. And this is a really complex system, a system that has worked well over many years, but a really complex system.

So we wrote a document that described that system that's posted on our webpage, and if you look at the references in this blue book you'll see it referenced on page 11. It's the third down on the right column, "A Comprehensive Review of Federal Vaccine Safety Programs and Public Health Activities." So this 70-page document describes remarkably briefly given it's 70 pages the many programs that are out there in vaccine safety. And there's

probably a couple dozen people in the country that are interested in a 70 page document at that level of detail on vaccine safety.

But we hear often, people don't understand what we do and this was an opportunity to tell our story. We also recognize that there are a lot of people that would like a more basic understanding of the safety system, and that was the intention of this document. So it takes this 70, 80 page document and distills it into a much shorter, much briefer document that talks more succinctly, albeit with less detail, about our nation's vaccine safety system.

So let me stop there and I'm happy to take any questions that you might have.

MS. CASTRO-LEWIS: Thank you so much for this document that I think it will be very useful for the new members. I remember three, four years ago when we started I was tremendously confused who is in charge of safety, and you gave us a presentation and we had several other speakers also come in from different sectors to talk about how the pharmaceuticals, if you remember that, and many other institutions were in charge of safety and how it was coordinated, and it will be helpful to have them visit, but I'm glad it's out and I think it will be very useful for the new members.

MR. KING: Does anywhere in this blue book talk about vaccine injury compensation?

DR. SALMON: Yes, it is mentioned. I mean, it's not a major focus of this book but it is certainly included in here and I'm trying to find it. Bear with

me. I mean, it's in here. It's - the injury compensation program is discussed in here.

MR. KING: It is?

DR. SALMON: It is.

MR. KING: You don't know where?

DR. SALMON: No, bear with me one second and I'll find it for you.

MR. KING: I'm trying to find it. I found it.

DR. SALMON: Are you going to tell me where it is?

MR. KING: Page four, bullet form, HRSA oversees VICP.

DR. SALMON: Yes, there we go, thank you. And if you look at the larger document that I mentioned, it's discussed in much more detail. I think that the Injury Compensation Program is also discussed later in this document and that's where I was looking. You know, we're not - we just put this out so we're not planning on a quick revision but if anyone does have any comments on this we're happy to hear it.

So if there's no other comments or questions, let me just thank the Commission for the opportunity to share what NVPO does with you, and we're here as an ex officio at all of your meetings and we're happy to help however we can.

MS. HOIBERG: Dan, I wanted to ask you one more question. Is there any way that you could keep us updated on where you are in your plans, and then kind of give us an update every once in awhile on how you're doing with the goals and what's happening with that?

DR. SALMON: Yes, I'd be happy to. We are planning regular reviews of the National Vaccine Plan. I think it's every two or three years. I mean, if you look at how broad these activities are you can imagine that it's quite a task, but I'd be happy to do so.

MS. GALLAGHER: And can I just remind you - this is Charlene Gallagher - there is an ACCV representative to NVAC, so you can take advantage of that source of information for updates on where the plan is, because that member would be getting the information and could share it with people, and Geoff regularly attends the meetings as well. We have several different avenues to obtain further information.

DR. SALMON: Plus an ex officio (?) 00:45:39

DR. FISHER: Just to follow up on that - this is Meg Fisher - I just remember that the first vaccine plan was - came out in what, 1994, eight years after it was going to happen, and then the big criticism of it was it didn't come with any strategies so that nothing happened. So I guess we're excited that it sounds like this is going to come with strategies, and would like to just hear more about how it's actually being - not just being developed as a plan but actually being put into action.

DR. SALMON: I'd be happy to. You know, I would argue that almost everything in the '94 plan happened. The question is whether it happened because of the plan or whether it happened anyway and it just, so be it that it was in the plan. But you know, this is why we're really focused on making it actionable and this is why we're writing an implementation plan.

MS. GALLAGHER: Thank you very much, Dan, and I'm - we've always appreciated your presentations and I'm sure you're going to continue to do that wonderful job in the future.

DR. SALMON: Thank you.

MS. GALLAGHER: Next on our agenda, is Dr. Jane Gidudu on the phone? Hello? I think that our next speaker is en route to the meeting and has not yet arrived because I don't hear that she's on the telephone. So it's about five minutes to 12, so why don't we just call the luncheon break now and Dr. Gidudu's presentation is going to be slated for right after lunch. So we are now going to adjourn until 1:30 p.m. Thank you everyone.

(Lunch break)

MS. GALLAGHER: Hello everyone. Welcome back. We're continuing the meeting of the Advisory Commission on Childhood Vaccines, and our first speaker this afternoon will be Dr. Jane Gidudu, who is going to give us an update on the Immunization Safety Office, Centers for Disease Control and Prevention vaccine activities.

Agenda Item: Update on the Immunization Safety Office (IDO), Centers for Disease Control and Prevention (CDC) Vaccine Activities, Dr. Jane Gidudu, ISO, CDC

DR. GIDUDU: Thank you very much, and good afternoon, everybody. I appreciate the chance to be back here to give the update on safety on behalf of my office, the Immunization Safety Office. My name is Jane Gidudu. So I'll be giving you, in this next couple of slides, my outline is going to involve

the current safety environment, a birds-eye view. And then I'm going to give you an update on our office structure and then I will, at the end I'll give you additional scientific updates.

So the current vaccine safety environment – I hope you can all hear me – it's like drugs, no vaccine is perfectly safe or effective. Adverse events are monitored in pre-licensure studies and the number of people involved in these trials is usually large. But when the vaccine is licensed many, many people, millions of people, get these vaccines. And usually rare events that may be detected that may have been missed in the clinical trials are then ticked off after the vaccines have been licensed. So it's very, very critical to have a post-licensure monitoring and research system.

An adverse event is an undesirable health outcome that occurs after vaccination. There are two reasons an adverse event may occur. First, it could be caused by a vaccine or a vaccination process, and secondly it may be occurring after vaccination by chance. Every day people get sick, and some of these events will occur around the vaccination or at the time of vaccination by chance alone.

One of the challenges of vaccine safety monitoring is to distinguish between these two situations. So we start looking for a signal, which is basically a suggestion that there is a concern for an adverse event that is occurring, usually a number of events above what we would expect. Then next we conduct activities to see if that signal is likely just by chance alone. We may call this signals assessments. This may involve conducting special studies, analyses, or

reviewing charts and other studies and see whether really they are adverse, confirming clinical patterns on this event. If we continue to have our concern, a signal is verified or ruled out by conducting studies with proper comparison groups, to see if there is a risk for an adverse event and determine that level of risk.

Sometimes more than one study is needed to verify a signal. A much higher standard of safety is expected for vaccines because vaccines are given to healthy people, mainly children, versus drugs that are given to ill people. And vaccines also play a dual role, protecting an individual, and it also has a societal role where it's protecting many people in the community. And sometimes these vaccines are recommended or mandated in some circumstances.

So we've a strong emphasis on vaccine information, and a decision on vaccine safety is very, very important. It is an active engagement and that bucket on immunizations, like most of our groups, regardless of scientific evidence from science about vaccines and on vaccine acceptance in some people, and there's concern as well as discussions - there's a concern as well as another – as well as another concern under discussion that they're being diverted when they could be spent answering pre-qulaified questions.

There is also a perception that the public health – the public health is most concerned with the large community that impacts immunization, and is less concerned about individuals who may be harmed by the vaccines. So that is

the platform of the current safety environment in a nutshell. So I'm going to give you an overview of our Immunization Safety Office activities.

So in terms of the agencies that conduct safety, this outline here will give you most of the organizations that deal with safety. Vaccine safety monitoring is an important part of the nation's vaccination program. Many partners work together to make sure vaccines used in the U.S. are as safe as possible.

NVPO, the National Vaccine Program Office, provides direction and inter-agency coordination, while CDC conducts surveillance, research, prevention and education activities. Our partners like FDA provide largely regulatory and enforcement activities but they also do research, and the NIH conducts basic science as my colleagues may say, but it's a network of very, very many people as you can see. And we are just one of the players in the Immunization Safety Office.

And our mission is to assess the safety of vaccines administered to children and adolescents and adults. So our core scientific activities include monitoring the safety of all newly-licensed and ACIP-recommended vaccines, responding to potential vaccine safety signals that may be identified from various sources, providing technical consultation to CDC's immunization experts and other stakeholders for progressive and multi-disciplinary scientific activities. We conduct monitoring vaccine safety as well as responding to vaccine safety emergencies in the event of a mass vaccination, like more recently held a mass vaccination of the H1N1 2009 pandemic.

So it's a comprehensive approach to vaccine safety. So we conduct surveillance to detect possible adverse events following immunization in a timely way, investigation and research of possible adverse events to determine causality and risk factors to help us develop strategies for the prevention of these adverse events. And timely communication is a key activity, and education for our partners and the public.

So our main activities in our office are, there are four main projects: the Vaccine Adverse Event Reporting System, which is VAERS, the Vaccine Safety Datalink, which is VSD, the Vaccine Analytic Unit, VAU, the Clinical Immunization Safety Assessment, which is CISA. I'm going to give you some broad overview of these activities.

So VAERS is a national spontaneous reporting system for adverse events after U.S. licensed vaccines. It receives approximately – the number is high – about 30,000 U.S. reports per year which requires a report to be filed and it accepts reports from healthcare via sources including healthcare providers, manufacturers, parents, and others. It's jointly administered by CDC and FDA so it's mandated by the National Childhood Vaccine Injury Act of 1986. The first reports were accepted in 1990, CDC largely focuses on the program management aspect, and between CDC and FDA we do both part of the data management and analysis, we work together a lot. VAERS data is publicly available at VAERS and there's two sources of data there. There's one, which is one, the data you can also access there.

So what is the purpose of VAERS? It's to identify new or very rare adverse events following immunization; it's to monitor trends of all known adverse events; identify potential patient risk factors for particular types of adverse events; it is used to generate hypotheses that are then tested in other systems; and used to provide information for public health policies on vaccine safety; and it's also used to monitor vaccine lot safety, which is done by our FDA colleagues.

What are VAERS' strengths? To detect very rare adverse events that may not be detected before licensure, so as I've mentioned, it's used to generate hypotheses and it helps identify new or very rare adverse events following immunization because of the large population that it's tapping into. And it helps to determine if further investigations need to be conducted. So it monitors trends, as I've already said.

So what are VAERS limitations? This is – there is underreporting, stimulated reporting due to media attention and other factors like during the recent mass vaccination after the pandemic using complete and accurate data on this report form. There's a lack of availability of denominator data, which is a very large limitation. There's no information on the number of persons vaccinated, and there's no information on background rate on adverse events in the population.

VAERS generally, however, cannot determine if an adverse event report was coincidental or caused by a vaccine. This slide shows you some of the highlighted examples of VAERS use. I've mentioned already that during the

recent H1N1 influenza pandemic there was a mass vaccination of very many people. And I've listed references here so those who are interested can read these materials.

So in the past there are intussusceptions that many of you may be aware, where they did find in the Rotashield vaccine in VAERS, leading to the withdrawal of that vaccine in 1999. And myopericarditis was – you know, that's the smallpox vaccine, and using VAERS data, and syncope following vaccination has been seen, identified in VAERS, leading to some recommendations, especially monitoring young people for 15 minutes after vaccinations. So the materials are there for you look at.

So here's, in this slide, here's what a VAERS report looks like. The report contains information about the patient, the provider and reporter, demographics, adverse events, vaccines received, and any pre-existing conditions. Vaccination details, including vaccination location, date, vaccine type, lot number and dose number is also included here. However, reports that also contain incomplete information are accepted in this system.

We encourage the reporting as soon as an adverse event is identified, but there's no time limit to reporting. We receive reports - typically, many of them are clustered around vaccinations but a year later HIPAA has reported adverse events. You can find this data in VAERS.

So we do VAERS follow-up. VAERS does follow-up with healthcare providers on serious reports that contain selected reports of interest by phone, to obtain mainly additional medical records for review so we can make

sense of these cases, and we also look at the collected additional information, and autopsy report. A letter is sent to reporters to seek recovery status for all serious reports with known or unknown recovery listed on the initial VAERS form, twice – at 60 days and then one year later.

So how does VAERS define a serious report? It's a death, it's in box 8 from the VAERS form, some of you who know the form. It's death, life threatening illness, hospitalization, prolongation of hospitalization, persistent or significant disability, and another medical important conditions. This is under the Code of Federal Regulations, Title 21.

Well, I will move on to the next project within our office, which is the Vaccine Safety Datalink. This is a geographical map, so you can see the 10 centers that are dispersed across the U.S. So the Vaccine Safety Datalink, or VSD, is a collaborative project among CDC and ten managed care organizations. It's data on slightly over nine million persons, which is about three percent of the U.S. population with a birth cohort of over 95,000 people. It monitors and analyzes data on 65 conditions, which allows for planned immunization safety studies as well as timely investigations arising from hypotheses from medical literature and prelicensure and some of the hypotheses, as I mentioned earlier, from VAERS, and it also conducts studies based on changes on immunization schedules and introduction of new vaccines. A lot of the studies, they shift their priorities according to the new vaccines.

So what are the advantages of VSD? Now all medical encounters that are available at the sites, it allows calculation of background rates, medical

chart review is accessible, patient surveys and other types of follow-up can also be conducted for specific studies. This availability of items – that is, we can – it is available for conducting – I did studies that cannot be done in a very, very short time, they - it can't be done in let's say a week.

So the limitations of VSD are listed on this slide. The sample size may be inadequate. We take the 00:14:50 sample association between a specific vaccine and very rare events. The population, as I've mentioned, is about 9 million, and the U.S. is about 305 million, so it's a fraction of the entire population.

Vaccines administered outside the HMO setting may not be captured. When you go and receive a vaccine at Costco, or I guess at CVS, some of those cases may be missed in this database. Vaccines administered outside the HMO really are very difficult to capture. The potential for lack of demographic and socioeconomic diversity. In HMO practice as you made mention the people don't have, who do not have – who do not have insurance. There's variable accuracy of coded data used for studies. And unvaccinated populations may be very small.

So this line shows you some highlighted research. I did mention VSD has conducted several comprehensive studies that do not support causal association of events from thimerosol-containing vaccines, and the immunoglobulin and neurodevelopmental disorders including autism, which should help to further lessen concerns regarding vaccinating children. So I've listed the two studies, the second one by Price and others, I gave an update, I

think, in the last meeting here. They are all accessible, including another study which used a public database.

In 2007, the VSD rapidly conducted a study to assess the risk of febrile seizures, I've again mentioned this here in this Commission, and found that the vaccination with mumps, measles and rubella vaccine associated with those ones results in one additional febrile seizure for every 2,300 doses given compared to when separate vaccines, mumps, measles, and rubella and varicella vaccines are given.

So the next project in our office is our Vaccine Analytic Unit which uses the Defense Medical Surveillance System data. It's an active surveillance system of the U.S. military personnel, which is about 1.4 million persons. It's a relational database having demographic inpatient and outpatient data, vaccination data and also deployment information, and analyses are done on site. The Vaccine Analytic Unit assesses unusual, possibly longer-term anthrax vaccine adverse events replacing the Department of Defense's database, which conducts investigations to assess whether specific adverse events are associated with current anthrax vaccines, future anthrax vaccines and other biodefense vaccines. They evaluate other vaccines administered in the DOD populations which are critical applications for civilian public health. And here I also – it uses the same structure like VSD probably used to rapidly assess vaccines.

DR. FISHER: May I ask – can I interrupt for a second to just ask a quick question? Are those only the soldiers or does that include also the families of the soldiers?

DR. GIDUDU: I think to best of my knowledge it's the soldiers.

DR. FISHER: Okay, thank you.

DR. GIDUDU: But there is a system – I forget what it's called – that also monitors the families of soldiers.

DR. HERR: So VAERS is vaccines that are administered on just children, monitored through --

DR. GIDUDU: VAERS.

DR. HERR: VAERS.

DR. GIDUDU: We get the information from VAERS on that. So the last big group we have is the Clinical Immunization Safety Assessment Network, CISA. This is based on individualized care to study the pathophysiologic basis of adverse events following immunization, to study biologic risk factors associated with developing an adverse event following immunization, including identifying and characterizing genetic risk factors and to maintain a biospecimen repository from people who have experienced adverse events following immunization so that future studies can be done. Many of them are rare so CISA has begun a biobank for collecting specimens so studies can be done.

One of the goals is to serve as a vaccine safety resource for consultation and public for vaccine safety issues. They have monthly calls and they receive consultations from physicians and healthcare providers, different

from VAERS which receives reports from everybody, for CISA they issue, they discuss always from healthcare providers. So the other objective is to assist domestic and global vaccine programs in developing guidance for individuals who may be at risk of increased adverse events by developing evidence-based guidelines for evaluating adverse events and for revaccinating individuals who have adverse events.

So I won't bore you with details here but I wanted to share one of their publications. It's an algorithm for hypersensitivity by older models but this may help navigate to get how to manage hypersensitivity after receiving these vaccines and assist these patients. I've given you examples of what hypersensitivity reactions look like, such as hives and angioedema.

So we do also have international collaboration, we work with – closely with the World Health Organization, we work closely with the Brighton Collaboration that developed these definitions of adverse events following immunization, we work with a host of international organizations for medical science which together with WHO have a vaccine pharmacovigilance workgroup that we work with closely, and their reports will be completed later this year for their last five years of work.

And we work with foreign countries or agencies on vaccinated issues and recently we worked with Australia on their issue, which was associated with the CSL vaccine, it was associated with febrile seizures in children and ultimately it was published in this country.

MS. HOIBERG: And the CSL, I'm sorry, what is that?

DR. GIDUDU: The company that manufactures the drug.

MS. HOIBERG: Okay. Was it a flu – do we know, was that the flu vaccine?

DR. GIDUDU: Yes. So in terms of additional case scientific updates, we have recently completed our ISO agenda, scientific agenda that has been cleared early this week so it will be publicly available, I believe, in the next one or two weeks. So this agenda has taken a lot into accountability, the feasibility of the studies. Unlike the initial draft it has focused on what may be feasible, and also bearing in mind the resources available to our safety offices. We can't do everything we say we are going to do, and I wanted to first introduce you to what is involved in coordinating this very, very elaborate process to have this judgment.

So lastly, last week ISO provided safety updates from the February ACIP, last week. Our office was given a one-hour session to focus on vaccines and febrile seizures, and I'll just summarize for you that they discussed preliminary data from VSD using rapid cycle analyses. Rapid cycle analysis, which is one of the methodologies they use on the febrile seizures in PCV13, the Prevnar 13, the new vaccine licensed last year, as well as influenza vaccine.

So the VSD PCV13 study that was monitoring safety of Prevnar vaccine and influenza, was also looking at febrile seizures and other outcoems. They were looking at a longer window, day zero to day seven. But after the Australian issue with febrile seizures, we decided to break down the windows, the risk windows. So they looked at the window, zero to one day, and they found

a signal there. So this is the data that was presented. So the signal that was identified last year, most of the cases were six to 15 months, year old and they had received vaccine with seizures with Prevnar vaccine. But most of tthese children had also received some other vaccines. So other vaccines may play a role in also increasing these seizures, especially DTaP, which hasn't been evaluated.

So I've added a link in here in the slides for you so you can be able to upload the slides when they are posted. So in summary, vaccine safety monitoring is very important to detect potential adverse events after vaccination and so we can maintain confidence in the vaccination program. Thank you.

DR. HERR: A question. For the CISA, the Clinical Immunization Safety Assessment network, are they basically research facilities? How do they get patients referred to them?

DR. GIDUDU: Yes, that's a good question.

DR. HERR: And where do they get their patients?

DR. GIDUDU: Initially the mode of model for CISA was yes, to treat these people with adverse events, and the challenge of getting the patients there made the CISA group shift their priorities. But now they're based at – is there five, there's six of them, academic centers, so we have Boston, Johns Hopkins, we have Vanderbilt; there are many of them within the area. But also studies that have specific outcomes – for example, encephalitis or transverse myelitis, they are using the transverse myelitis center, which has all the cases,

most all the cases the U.S. has. Most referrals are sent there, and the studies have been taken (?) with those populations.

DR. HERR: I guess my question would be, how would anybody know to send somebody there?

DR. GIDUDU: They would have to – usually they use VAERS. VAERS is used as well. So when a case is plugged into VAERS, that's the easiest way. So when the case is into VAERS, there's definitely some simple (?) association with a vaccine.

DR. HERR: The VAERS context is --

DR. GIDUDU: They have specific outcomes they're interested in. Then VAERS sends the information to CISA, then CISA contacts the providers and they made up the (?) 00:25:55 distinctions.

DR. HERR: You know, as a simple guy in the field how would I know that I would want to send or think about contacting one of these particular centers?

DR. GIDUDU: It's driven by their statisticians. So I think it's difficult.

DR. HERR: I mean, it's hard enough to know when somebody's got something like – I hate to say - leukemia or whatever you have, a number of centers, and is one better than somebody else. Okay, you kind of toss that up and use your own experience of what you find out, but something like this -- .

DR. GIDUDU: It's a very early program, and as you may imagine (some of those patients aren't enrolled yet.

DR. HERR: Okay, thank you.

MS. CASTRO-LEWIS: I have a question. Other than the vaccine information statements where the virus information is included, what other efforts is CDC doing to let the public know about VAERS?

DR. GIDUDU: Yes, the channels we've been using are webinars with vaccine safety coordinators in each state. So those are the people we really work with and rely on them to take all that information down to their areas. So we have monthly webinars which coordinates and trains them and gives them information, then lets them know. But the VAERS website itself is where we post some of the information.

MS. CASTRO-LEWIS: It really doesn't go directly to the public? It goes to local immunization offices?

DR. GIDUDU: When we have meetings.

MS. CASTRO-LEWIS: Yes, so I was more curious to know how it goes to the public.

DR. GIDUDU: Directly on the website, but also we use the safety coordinators in various places.

MS. GALLAGHER: David, did you have a question for Dr. Gidudu, because earlier you had a question that you said you would defer?

MR. KING: Wasn't that a question to be deferred till tomorrow?

MS. GALLAGHER: Oh, sorry, okay.

MR. KING: But, I'm unsure on the – we have something called additional slides here. Is that part of the presentation or not?

DR. GIDUDU: These are the slides that were presented at ACIP. I just left you the papers so you can – you can check them out.

MR. KING: So are we allowed to ask any questions on them?

DR. GIDUDU: I elaborated the last one, on seizures. Yes, you can ask, yes.

MR. KING: So in the vaccine – so I'm looking at slide 37 on page 19 of our sheet.

MAN: Febrile seizures evaluation.

MR. KING: Right, and it's probably because I don't understand, but maybe someone can enlighten me. So when I look at the significant access, the second point, risk for febrile seizures, and it talks that there's an attributable risk of 61 per 100,000 doses, so what does – so the next bullet point says compare to an assessed risk of febrile seizures of 43 per 100,000 doses, and that's when we – so is it because it's a combined vaccine versus a vaccine that's given in two separate doses?

DR. GIDUDU: The risk was with a combined vaccine.

MR. KING: So, and is that the vaccine that we give?

DR. GIDUDU: That vaccine, I believe, is – I'll go to the first one.

DR. FISHER: Want me to get that one? So the MMRV is a combination of the measles, mumps, rubella and varicella vaccine, and that was manufactured as ProQuad for several years, and then there was a problem with having enough varicella vaccine. So in fact, right around the time that they were assembling this information they stopped making ProQuad. So when ProQuad is

supposed to be back on the market – and Tom you can tell us, it is back on the market this year, but because of this previous study it was found that if you used the combination for the first dose there's an excess of febrile seizures.

MR. KING: Sixty-one versus --

DR. FISHER: No, 43.

MR. KING: Forty-three versus the 61.

DR. FISHER: Yes, so I think what Jane was saying is giving us kind of comparative information. So as a result of that last study they actually changed the recommendations and suggested that for the first dose, you should give MMRV and varicella separately. So I think the implication would be, as we look at this information for influenza and PCV13 together, you might – I'm sure they will discuss this or maybe they did discuss it at ACIP, I'm sure we'll discuss it at the American Academy of Pediatrics – but the question would be, would you then make a recommendation not to give those two at the same time?

MR. KING: That's the question.

DR. FISHER: Exactly. But that would require a lot more than --

DR. GIDUDU: Sure.

MR. KING: Understood.

DR. GIDUDU: It's preliminary and they're going to do exactly as in the report.

MR. KING: And there would be additional research and studies done on it to – okay, all right. Thank you. You've answered my questions.

DR. EVANS: This is Geoff Evans. It took one to two years with a workgroup, a lot of effort on the part of ACIP to come up with the recommendation to go ahead and do the first and second dose differently. So this is preliminary data, no one was ready at this point to even suggest a recommendation change in terms of usage. It has to be studied further. But you've got to sort of put it in a context because it is a good example of the MMRV versus just separating them. That was a signal that came forward, VSD studies, and that took several years, one or two years, to make sense of it and confirm it and then the recommendation changed.

MR. KING: Based on this information. Okay.

DR. GRUBER: This is Marion Gruber. I just wanted to clarify, and you probably know that but I just feel the need to sort of talk to this a little bit. The MMRV vaccine ProQuad was actually a combination vaccine in which all these different vaccine antigens from the measles, mumps, rubella and varicella virus were in one formulation, so that was one shot, if you want, given. It's different with the TIV and PCV13, right? These are co-administered vaccines. So these are not combination vaccines like it was in the case of ProQuad versus MMRV. I just wanted to clarify that. These are two separate vaccines and not combined in one shot. But, you know, everything else of course was correctly portrayed here. I just wanted to clarify that.

MS. GALLAGHER: Any more questions? Thank you very much, Dr. Jane. And Dr. Mulach will be the next one on our agenda, update on the

National Institute of Allergy and Infectious Diseases, the National Institutes of Health vaccine activities.

Agenda Item: Update on the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) Vaccine Activities, Dr. Barbara Mulach, NIAID, NIH

DR. MULACH: Good afternoon. Good afternoon and thank you for giving me the opportunity to spend a little time talking about what the National Institutes of Health has been up to. I give very brief updates normally and so this is kind of an opportunity. Geoff had said, you know, maybe just spend a little bit more time, give a little bit more background on what it is we do and hopefully this will be useful. And if I go on too long just drag me off.

So just at the most basic level, to make sure everyone knows, the National Institutes of Health's overall mission is really science in pursuit of knowledge to improve health. So anything that involves human health really does sort of touch on us in some way, and we work with many other organizations and agencies in order to accomplish that.

But that's really at the bottom line sort of what we're about. A little bit of history, for those who are history buffs. Background from the NIH started as early as 1887 in the Laboratory of Hygiene, but really sort of one of the milestones for us was when President Roosevelt dedicated the buildings of NIH, and the Federal Funding Law for NIH came into effect in 1944. So that picture is of President Roosevelt on the steps of Building One.

So I apologize in advance for the alphabet soup, but I figure if you get bored you can quiz me on these later. I don't expect you to know what all of these are. The reason this is up here is for me to just explain that a lot of times people get lost when we say, you know, you're not talking to the right component of NIH or whatever. It is an alphabet soup. But one of the things I'm here for, the other agency reps are here for, is to kind of help you through that. If there are questions that you have about what's going on at NIH, you know, we can even bring people from other parts of NIH to come talk to you.

If you ask me about autism, I know some things about autism, but obviously there are many people at NIH who know a lot more than I do. So if there are specific items, certain vaccine studies or whatever that you're more interested in, I would be happy to kind of help be that bridge for you. So it's not about the alphabet soup; it's just about the fact that from the outside it does look like a really complex mixture. But everyone that I've dealt with at least at NIH – I don't know everyone, but everyone I've dealt with has been very friendly, very open and helpful, and they like to talk about their science. So it's really at the level at which you're interested in listening that we'd like to share that information with you.

MS. HOIBERG: Do you have a list of who these people are?

DR. MULACH: I don't on slides but I can get one for you. And if there are ones in particular you're interested in, I can share more information about those. And each one of these organizations has a separate website, so again, if there are particular diseases, for example, the National Cancer Institute

has information about cancer, or the National Institute on Mental Health has specific information there. So it is a little bit of an alphabet soup, but again, if there are particular things, the National Institute of Child Health and Human Development, NICHD, might be another one you're interested in, involved in many studies understanding health of children and adolescents and pregnant women as well. And there is some overlap between these, so again, a lot of interesting things going on. It's not just about my institute.

So I think I've already pretty much said this, but again, we're really looking at basic knowledge and how that can help us to understand how to make people live healthier and happier lives. So that's really what we're about. And the way we do this, we have laboratories on NIH campus and a few other locations throughout the United States, but the bulk of the money that we get at NIH goes out in the form of grants and contracts to academic institutions, industry, non-profits, small businesses.

So really NIH relies a lot on the scientists and behavioral researchers and MD's and economists and other people throughout the United States and actually throughout the world to bring their knowledge, propose a project that they think needs to be studied and then for us to fund it for them to do the work. So it's not just about what NIH wants. It's about the ideas that come from the research community and then that is reviewed by peers in that field, and then we fund a subset of the work, the applications that come in. It's also important that we're training researchers and building communities of investigators, and trying to communicate that medical information.

And this is just a point I made earlier. This is a slide of the United States, but it's really global. We fund people throughout. So it's not just about a group of scientists in Bethesda, Maryland. It's really about people connecting all over the world.

So now I'm going to talk just a little bit more about the National Institute of Allergy and Infectious Diseases, which is where I work. And the reason that I'm going to focus on that – partly because that's where I'm from, I know a little bit more about that, but also because really the bulk of the questions that are addressed here are related to vaccines. And so the vaccine research and development activity is really mostly occurring in the National Institute of Allergy and Infectious Diseases. There are other institutes, like the Child Health Institute, that is also very interested. There's cross-collaboration, but we do a lot of that work.

So a lot of the basic research kind of goes into better understanding vaccines, developing new and improved vaccines, as well as the development of therapies and diagnostics and other interventions. So this is just sort of another way of saying that same thing. The basic research really builds to develop the next generation of vaccines, therapeutics and diagnostics.

And particularly lately diagnostics has been very interesting, because a lot of people say if you don't know what it is you're trying to treat, how are you going to treat it well. So that's gained a lot of attention lately too, that if we could quickly understand what it is that person has, if it's a mixture of a

couple different diseases, do you know if it's flu or is it some other respiratory illness, you can better figure out how you can help them to get better quicker.

And just to remind people that in the United States we're very lucky that we don't have a lot of infectious diseases. We do still have some, but there are many more globally that we do not have to deal with in the United States but it's still an issue. And just some examples of some of the things that may or may not be on your radar, I always like to look at this, and for things chikungunya or tuberculosis, things that we don't have to deal with every day in the United States but globally there are a lot of infectious diseases that we worry about. And I think the recent activities in Haiti where cholera has really become an issue, it really highlights for us things that are going on in other countries as well as concerns that we might have if a disease is only a plane ride away or if you're traveling and you might be exposed.

And I hope the other agencies don't mind. I have them on this slide, but basically I just wanted to put in context what some of the different agencies are doing. This is really to say that NIH's focus is on the development of new and improved vaccines, the development of innovative vaccine technologies, basic understanding of the human immune response – and I'll talk a little more about that – as well as vaccine safety research. And you can see from the other agencies sort of what their roles are in surveillance distribution, regulatory activities, coordination. And of course it is not on my slide, but we all know you're very important in the Vaccine Injury Compensation Program.

And the other thing I want to reiterate is that a lot of times the things that you guys are looking at in terms of vaccines are vaccines once they've been licensed and are used in the public. But just to emphasize that there is a lot of safety that goes on before a vaccine ever makes it to the licensure stage. So there may be a lot of vaccines that never make the bar, if they're not safe enough to get to the licensure process. We really are testing from the very basic end of the spectrum all the way out to in vitro and animal testing to make sure that if it isn't something that we would consider for our community that we want to learn that early and often.

NIH is involved from the basic research end, all the way up to clinical evaluation, and then in the later stages other people sort of take on that role. Industry and FDA is involved in the regulatory process throughout the way, but safety is a huge factor in anything that we do in the early stages in pre-licensure.

So now I'm just going to talk about a few examples of things that I've brought to the ACCV in the past but just to kind of give you a flavor of some of the things that I've heard that you guys have been interested in hearing status updates on, and kind of let you know these are some of the things that are ongoing, and I might be bringing to you guys over the coming years.

Flu, I think everyone remembers 2009, and we were hit with sort of a strain of flu that was different. It started in April of 2009, and you can see just by this chart that by early 2010 it was really all over the globe and we called it a pandemic, and wow, how scary is that. And one of the things that it took many,

many different people to think about how to develop a vaccine, how to implement a vaccine for the H1N1. And in terms of implementing, it was very difficult as well because we're used to, every year we create, pick the three strains, we put it in a vaccine and then by the fall we have it and we give it to everyone. And this was a very, very different scenario.

So NIH was one of many, many players in this role, but I kind of wanted to talk about some of the things where we were involved. As you probably know, and FDA probably could say much more eloquently than I could, the timeline is normally that it takes nine months from – at least nine months to get to the stage where you create a vaccine. And for H1N1 we had a much shorter time period. So again, many people were involved in the process, but some of the things that NIAID was responsible for was looking at some very specific criteria for the vaccine once it was developed. We did this in addition to industry and FDA and other partners, but we were looking at the different dosages and what dosages would create an immune response.

You may remember that when we thought about a pandemic, we weren't sure it was going to be H1N1. A lot of people thought H5 was going to create a pandemic. So when we were looking at H5 influenza vaccines it was like 90 micrograms was going to be needed to create an immune response. So we really weren't sure with H1N1 were we going to be able to protect people with the vaccine, would we be able to make enough to protect people. So we really did look at how much vaccine was needed.

We looked at different age groups. We were looking at – starting with adults but once we found that the profile was similar to the standard flu vaccine, we looked in children and the elderly to make sure that there were no safety issues involved. And again, this is in the populations of the clinical trial size group. We also looked at special groups like pregnant women to see if it was safe to give that vaccine to those women and if it caused the appropriate immune response.

We looked at the ability to give the seasonal flu vaccine at the same time, or before or after the H1N1 vaccine. We had on our list to study adjuvants, but luckily that wasn't really necessary because we were able to get enough of an immune response without the adjuvant. We looked at specific populations like HIV-infected individuals and people with asthma.

And this just brings up how do we conduct these trials. We don't actually conduct these trials specifically on NIH campus. We have contracts for a series of vaccine and treatment evaluation units throughout the United States. We're very proud of the capabilities of these units because basically they're at the ready to help us when we need to do a particular study and as they were established in 1952, so we have sort of a longstanding network that we use. They've done a number of studies over the years but in particular for H1N1 they were able to help us with these studies. And you can see the sites there on the slide.

And so what did we gain? We gained information on the preliminary safety of the H1N1 vaccine, we learned about the immune response

to the vaccine, we learned the number of doses, and we began to look at adjuvants, and then we also looked at the special populations. In addition to H1N1 when we don't have pandemics in our wake, we're also looking at new strategies. I mean, wouldn't it be nice if we didn't have to give a vaccine every single year in the fall? Wouldn't it be nice if we could create a vaccine that had longer protection, like we do for some of our other diseases that we protect people against? So there are many strategies that are being used, and here are just a few examples.

If sort of the world of what is the future of flu vaccines is something of interest to you guys, I could bring someone in to sit down and talk to you a little bit about some of the strategies we're using. This is a very exciting field and I think ultimately you've probably heard the language "universal flu vaccine" which means it would work for everyone, you could give it, one or two doses and then just be done. You wouldn't have to worry about it for the rest of your life. And so that's the ultimate goal. But again, there are probably many steps between here and there, and many people are working on that.

I'll talk briefly about vaccine safety next. So one of the things that I think was developed in response to a lot of the feedback that we received and CDC received from people who are concerned about vaccine safety is that it's very difficult to do these studies and there's no one who's going to support funding these studies. And one of the things we did in 2008 is, NIH and CDC together put out a program announcement, which is basically a call to investigators to say, you know, there are some really important areas of vaccine

safety research that we think need more research conducted and we want to encourage you to submit applications in that area.

So in this particular case I've listed out the actual institutes at NIH that are involved in that. So in addition to the National Institute of Allergy and Infectious Diseases, the Institute of Mental Health, the National Institute of Nursing Research, the Child Health and Human Development Institute, the Environmental Health Sciences Institute, and CDC's Center for Chronic Disease Prevention and Health Promotion all came together and we solicited feedback from a lot of people and came up with – here it goes – several topic areas that we would encourage applications in. And you can see the list here.

DR. GIDUDU: Can I ask a question on a previous slide?

DR. MULACH: Yes, sure.

DR. GIDUDU: Was that different data and from where?

DR. MULACH: Oh, I think that's what we put on the program announcement. We probably need to update it. The name has changed.

DR. GIDUDU: That's a different center.

DR. MULACH: Okay, so we'll fix that. Again, there's a lot of movement around in NIH, but that's originally who we worked with. But basically what we're looking for in this announcement are better understanding of the components of vaccines and the vaccines and how people respond to those vaccines both immunologically and physiologically. Looking for genetic variations, looking for are there certain genetic components that might make you have a weaker immune response, a better immune response, some kind of

adverse event; are there particular risk factors or particular markers that we can look for to help us understand a possible link between a particular disorder and a licensed vaccine. I mean, these are very complicated questions to be asked, so it's a very difficult environment. But we really want to encourage investigators to apply in these areas.

And what I'll tell you so far is we've funded a few projects through this and they're in early stages. And again, if you're interested we could tell you sort of what the progress is as we move along. But one of the things I'd really like to encourage is, you know, to get the word out that this exists, and to have more people apply and really try to answer some of these questions because I think that's one of the limitations we face. If people don't apply there's no way for us to fund them to do the work. And again, it's very complicated work so it takes someone to really think about how to address some of these questions.

To date we have – just to give you an idea of some of the projects – we have one group that's looking at metabolic and immune responses to flu vaccines in people with mitochondrial disorders. It's again, a small study, but to try to identify if there are some factors, some – we call them biomarkers, but some thing that might be different or that might flag us that there's something different, so that we can try not to vaccinate people if they have some susceptibility that we can know in advance. And that's a really, really hard question, but that's sort of the ultimate goal.

One of the other studies is looking at varicella, or chicken pox zoster vaccines and how that changes the immune system response, and better

understanding it. I mean, one of the things is, we know that we're using it now for shingles, but what is the longevity of that and how does it really work, so better understanding that. But again, like I said, what we need are more people to apply and to get funded in this area.

MS. HOIBERG: Barbara, we wanted to check for the risk factors – how are you going about that? Is this just a goal that you have, or is this is a pipe dream that you have? Or are you doing it?

DR. MULACH: Okay, so what this program announcement means is that we tell researchers that these are specific questions we want answered. But what we have to rely on is someone at an academic institution or a non-profit or somewhere, to write up a proposal, it's 10 to 15 pages or a certain application process that says I want to study this disease, and I want to study this vaccine. And they come in with that proposal, and then that gets reviewed, and then a subset of those get funded.

And so the issue is, because it's a difficult question, I don't know if that's the only reason. There may be other reasons that people don't apply. They don't think there's set aside money for those, which there's not specific money set aside for this. But what I would say is, it's on our radar and if somebody comes up with the right kind of questions, we can do what we can to fund them but if they don't apply we can't fund them. So again, I think the vaccine safety community is saying there's nowhere to go, and what we're trying to do is giving them a place to go.

MS. HOIBERG: Because I know that if you had - if this went out and parents of, even of vaccine-injured children knew about this, they would say look at my child, look at my child that was not injured. This is something that I know that the vaccine injured community has been asking for for years. We want answers as to why it happened to one and not the other. I mean, it is incredibly rare, so why researchers aren't banging down our doors is --

DR. MULACH: You know what, I was really happy to hear when you said earlier that you would love for someone to better understand what happened to your child, because I guess in my mind I would have thought that would be a really hard thing to ask of a mother, to have them go through certain tests and things like that, because you've already got a lot going on. And I think that's fabulous and I don't know – I don't know if researchers, how well they know that. Because again, I think Jane had mentioned with the CISA network that they try to pull people from the VAERS reports and other things, but one of the things I think there's a – I think Dan mentioned there's a vaccine safety working group and Bonnie is on that working group, so she well represented the parent concerns.

MS. HOIBERG: She has asked the same question.

DR. MULACH: Yes, absolutely, absolutely. But one of the things I think we're starting to realize is, in talking to PDC and the vaccine safety working group, is that we probably need to pull scientists in. I think there are a lot of scientists who don't associate with the term vaccine safety, but they could be doing work that is very impactful for vaccine safety, and I think one of the things

we need to think about how to do is how to frame it in a way so that we draw more investigators. When I'm asking a question about children with certain diseases or certain genetic susceptibilities or something like that, to kind of broaden their mind to say, well as you're studying these things we want you to ask questions that might be related to immune response, that might be related to vaccines.

And I think we'll get a lot further. I think if we're just looking for vaccine safety scientists those people are a small group. But if you look at the field of researchers overall, that alphabet soup that I showed you, all those people that we fund research on, if we can help bridge the communication gap in a way, if we can kind of talk to them more so we can say, hey, when you're doing your study this is a really important area.

DR. HERR: I guess one of the questions then that comes up is are you expecting people from around the country to come up with ideas and studies that might answer some of these questions?

DR. MULACH: That's correct.

DR. HERR: Or, you have specific questions that you're looking for somebody to do the work? I think that's a different question, because you might find it easier to phrase the question and phrase the study that you want done and what you want to investigate, and then find people who are capable of doing it and ask them, as opposed to waiting for them to come up with the ideas and then you approve the idea.

DR. MULACH: So I understand what you're saying, and I can see that there would be a balance of both things that need to happen. Because I think in a way, sometimes when you give researchers sort of the opening to ask a question, they might ask it in a much better way than I would think to tell them to ask a question. So I'm telling you what I want, I'm not telling you how to get there maybe. What we're trying to tell the researchers is what we want, not what method they need to use to get there. And maybe in their creativity they can come up with a way of studying things in a way that, again, the limited number of people at NIH --

DR. HERR: Well it's all in how you want to modify that idea.

DR. MULACH: But I do understand what you're saying. I do understand what you're saying. And again, one of the things that maybe we could think about doing in the next iteration of this program announcement is thinking about putting more examples of exactly what specific things might be --

DR. HERR: If you want a widget, you've got to – you come up – you have somebody with an idea of the widget. And you're probably going to get it. If you say come up with an idea about widgets and talk to us and we'll see if we like it, it's a lot harder question.

MS. HOIBERG: And you would almost possibly, if you're wanting information on these children that are damaged by vaccines, what you could do is even put out an announcement on a blog on somebody's page that deals with a lot of vaccine injury, that says listen, we're looking for people that have experienced a vaccine injury, what kind of testing would it entail? I'm willing to,

say, offer up my daughter for it, as long as it doesn't mean that you're going to be cutting out a piece of her brain, or, you know, as long as it's not incredibly invasive.

But, you know, to be able to look at her medical records and along with her medical records, the records of, say, another child that had the same reaction, okay, why does Kate look like this and this other child looks like this, but they have the same diagnosis, same vaccine, what is the common denominator here. So I think that if you do that, you guys are going to come up with so many answers. I think you'll find answers. I think you'll realize, okay, well this child was allergic to a certain component.

You know, a lot of these children that I've – a lot of the parents that I've talked to that have vaccine-injured children, their children are highly allergic to a lot of things, lots of different foods, they're allergic to formaldehyde, formaldehyde causes seizures in them or whatever. So vaccines have a small trace amount of formaldehyde. So that could be a reason why they reacted to that. So I just think that – I'm excited to see this because this is a first in the whole – my whole time on the Commission, and we've been asking, I know Tania and myself both asked in different meetings, why don't you study our children, why, no one's knocked on our door.

And in the program you have a vast amount of information, all these medical records. And I know that I myself signed a confidentiality thing that said go ahead, use my child's name, you can have the information. So I think that if you have those records and you have such a vast amount of them

and it's just a wealth of knowledge, hat if somebody would take the time to actually look at them and compare, okay, these are the encephalopathy cases that pertain to DTaP, I think that someone could do that. But of course it's all a matter of money.

DR. MULACH: So I really appreciate that feedback, and I guess what my brain is going to right now is how do we connect those researchers with that capability. And I think that's going to take a little bit more brainstorming, but I think maybe see, see if you us(?)and, you know, maybe the Vaccine Safety Working Group can help as well, I don't know, but the --

DR. GIDUDU: I have just a comment, we had a CISA program review last December. They struggled with their basic objective of studying the basic pathophysiology of understanding safety. That goal, they can't move further with the representative from NIH. I think we need to do more collaboration because the basic is not known. So I think that it's really a lot of things that could be done. The cases can be identified but we need to collaborate more.

MS. HOIBERG: And I think it breaks down to that, is that there's so many cooks in the kitchen but no one's talking to each other. So if you could fix that communication gap, if you guys actually did speak to one another.

DR. MULACH: Well actually we do talk to each other; we might not talk to each other as much as we should or as often as we should, but we do talk to each other, so just to clarify a little bit.

MS. WILLIAMS: This is Michelle Williams. In our orientation yesterday the Chief Medical Officer that we're going to hear again tomorrow has physicians that reviews all these medical records. And I know that physicians like to talk to other physicians. It would seem to me you've got – you don't need to pour through the medical records, you don't need to talk to the children or their families. You have doctors, a whole panel of doctors that have already reviewed all these medical records, and it would be potentially a source of information.

MS. HOIBERG: You don't even have to use their names, the children's names. It could just be these are Jane Doe and had this and, you know --

MS. WILLIAMS: And those physicians don't seem to be plugged into any of this, and they're the ones that are on the front lines reviewing the medical records.

DR. GIDUDU: We do have the CISA consolidation network where the actual fact difficult cases get discussed. Maybe the only thing is they need inquiries from the doctors, if the doctors can have their log or send directly, they definitely can be discussed on the phone as a beginning.

MS. WILLIAMS: All right, but these are different doctors. These are the doctors now that are reviewing the medical records, that are going through the injury fund, and if I understand there's 20 of them.

MS. GALLAGHER: Maybe you can have a think about the suggestions that have been made, and perhaps get back to us at the next

meeting about any thoughts you've had on the matter. Does NIH consider funding centers outside of the United States if they send in a proposal?

DR. MULACH: Absolutely, absolutely. So right, as long as the application comes from - pretty much anybody is eligible to come in for an application. There are certain types of applications that only certain groups can apply for, but this particular announcement could be any type of organization.

So on to the rest of the story. I wanted to talk a little bit about some of the things we're doing in terms of the human immune system. So this is sort of backing up a step. In August of 2010 we awarded these human immune phenotyping centers. And I feel this is at the very early stages, also, trying to get at, again, what happens when a person is infected with a virus, or what happens when a person receives a vaccine. What happens to their immune response, and so what is sort of baseline immune response and then what is sort of, what happens when you get a vaccine.

And so this is just sort of a simple depiction, but really now we have a lot of tools, we can identify a lot of different cytokines and a lot of other different biomarkers, maybe, where we can look at sort of in the general population or in certain subsets of the population, what does the normal resting immune system look like, or the normal innate immune response, and then sort of if there are people who have certain susceptibilities how might that differ.

And so it's really quite interesting when you think of all that we know in this day and age, in 2011, and yet really a lot of the basic immunology studies have been done for years in animals and they're finding more and more

that, you know, what we learned in animals is nice but it's not necessarily always indicative of what's going on in humans. And so really more and more we're emphasizing let's understand the human immune response, let's understand what happens to a human when they, again, either get the infection, when you get flu naturally, or when you get the vaccine.

And the idea is, again, to better understand, you know, if this marker increases does that mean that you are protected against flu? If this marker decreases as you get later in life does that mean you're no longer immune, your immune response is no longer strong enough to combat the flu? Does it mean that certain people shouldn't be getting the vaccine, or have a much stronger reaction and that's why they have an adverse event, or just something altogether different?

So it's going to take awhile before we know all the answers, but I think we're finally getting at a point where we could really ask the questions, we have a lot of technology to utilize, and I'm really very hopeful. And on some of the examples that we're using, in addition to flu, pneumococcal disease and vaccination and something else we're looking at too and a couple other things, so stay tuned on that front. I think it'll be very exciting.

And then the last thing I wanted to talk about is the Human Microbiome Project, and that is an NIH-wide project and I think the last time or the time before we talked about, again, we're in 2011, we know so much, and yet we're finding out more and more every day. There are trillions of microbes in our body all the time, and for the most part that's normal, for the most part it doesn't

have any problems. But you get an imbalance in that situation and you start having problems go on, you get diarrheal diseases or other things.

You know, one of the questions you may have heard is helicobacter pylori, you know, they find it in people, they don't know if it's causing a problem or if it's fine. You know, what should we or shouldn't we have, and what are the implications of that? Does it mean if you take a certain drug and you have helicobacter pylori it works better or worse? You know, if you're taking antibiotics and you're killing out something that was causing you to be sick, are you also getting rid of some of your good microbes and that's why you have these other effects? You know, it takes you awhile to get back to your normal self because you're sort of cleaned out and starting all over again?

So anyway, it's just a very fascinating study, and we're learning about what healthy individuals have and don't have in their immune system. And so again, I think over the next couple of years we'll be getting some really interesting feedback on that.

And what is it going to tell us? It's going to help us hopefully understand things like Inflammatory Bowel Disease, asthma, allergies, Crohn's Disease. So hopefully, again, we'll have some really good things to tell you. And again, this all leads to sort of where we're going in the future, and just to kind of throw out some of the things that NIH is really looking at, we're now able to keep people – you know, people live to 100 years old. Well you know what? They come with a lot of baggage when that happens. You know, there are a lot of things you have to take into account. If someone has a chronic condition, does

that change the way you would treat them or the type of vaccines or therapies they might have? Health disparities is always an issue. Re-emerging infectious diseases, you never know when the next pandemic or something else might hit. And then other things like obesity.

And so I think we really are moving from treating things when they appear to really trying to understand before something happens and trying to prevent as much as possible. And everyone talks about personalized medicine. Well we're not there yet but we have a lot of really good tools that we're putting in our toolkit to move in that direction. So hopefully we really will move to the point where we'll be able to understand, for individual people, what is good for them and what we need to avoid. So moving in that direction.

And that's the end, and I'm happy to answer any other questions.

MS. HOIBERG: A very good report, thank you.

MS. GALLAGHER: Thank you very much for a very comprehensive report, and I'm sure that the new commissioners will look forward to reports in the future. Now we will turn to Dr. Gruber, who comes to us from the Center for Biologics, Evaluation and Research, which is part of the Food and Drug Administration, and she's going to report on vaccine activities there.

Agenda Item: Update on the Center for Biologics, Evaluation and Research (CBER), Food and Drug Administration (FDA) Vaccine Activities, Dr. Marion Gruber, CBER, FDA

DR. GRUBER: So I have to say I'm a little bit intimidated now, because that was such a beautiful presentation and now we're going into the

more bureaucratic part of, you know, vaccines and what they do to humankind. Yes, so I'm Marion Gruber. I'm within the Office of Vaccines. I'm Norman Baylor's Deputy Director. I was asked by Geoff, since it's my understanding there are some new members with ACCV, to get, provide a little bit of background about our organization, what the Office of Vaccine's role is in vaccines' chemical development, what is really an IND and what is a BLA, what does it stand for, and what are really sort of the critical parts in vaccine development, what is the role of our advisory committee, and then last but not least give you a little bit of an update on most recent vaccine approval activity.

So as was mentioned, the Office of Vaccines is part of the Center for Biologics Evaluation and Research, and that is the center within the Food and Drug Administration that regulates biological products under applicable laws and regulations. Biological products include blood products, cell and gene therapy products, and vaccine products.

And I think I have a slide here that shows how the Center for Biologics is organized. First is the Office of the Director. Our current CBER Director is Dr. Karen Midthun. And then we have eight offices – The Office of Vaccines Research & Review is one of the offices. We interact, of course, with other offices. One of the offices that we frequently do business with is the Office of Compliance and Biologics Quality, and I'll tell you a little bit more about this later on.

The Office of Biostatics & Epidemiology, we all work together. We form teams in terms of looking at vaccines' clinical development and approval.

And then there are the other offices, the Office of Cellular, Tissue and Gene Therapies, and the Office of Blood Research and Review. So we all sort of have different authority for regulating different biological products.

Here's another slide looking at the organization of the Office of Vaccines itself. We actually have three different divisions. There's the Applications Division, the Division of Vaccines and Related Products Applications. They're the folks that actually process incoming submissions and applications for vaccine review. That is the division that houses the clinical, the medical offices, the toxicologists.

And then we have two left-based divisions, the Division of Bacterial, Parasitic and Allergenic Products and the Division of Viral Products. Folks in those divisions really perform research, and they also do review, regulatory review. Their job is to look mainly at the chemistry, manufacturing and control information. So they take a look at how a vaccine is manufactured, and again, I'll talk to you about this in a little bit more detail.

So what is important to mention, that the Office of Vaccines really regulates preventive and therapeutic vaccines for infectious disease indications. We also regulate a couple of other products such as the allergenic products. We do not regulate other vaccine products such as cancer vaccines. These are regulated by the Office of Cellular and Gene Therapy.

Now as Jane was telling you, of course the unique consideration when it comes to preventive vaccines is that these products are administered to healthy individuals and that of course places special emphasis on the safety of

these products. Now I just put up this table a little bit to look at a little bit the difference in preventive vaccines and therapeutics. If you look at the people administered vaccines, these are usually healthy children and adults. Therapeutics usually are administered to people with disease or other underlying conditions.

Vaccines can have an effect on the overall population, even though not everybody is immunized. They may decrease disease transmission; they may thus benefit the unimmunized. Dosing, there's another big difference between a therapeutic and a vaccine. Vaccines are usually administered in episodic dosings. Therapeutics are usually administered continually. And the type of evaluations that are going on in pre-licensure clinical trials are also very different, and I will be focusing on vaccines today to explain a little bit the vaccine manufacture of the clinical development. But before I do so, I want to talk a little bit about the laws and regulations that form sort of the underpinning of the job that we are doing.

So the authority for regulating vaccines resides in a law that's called the Public Health Service Act, specifically Section 351, and then we also refer to specific sections of the Federal Food, Drug and Cosmetic Act. There are certain criteria for vaccine approval that the law prescribes. For instance, it is stated in the Public Health Service Act that data must show that a vaccine or a biological product in general is safe, pure and potent. And there are actually definitions in the law that speak to what safety is, what purity is, and what potency is. And I really don't want to go into detail.

I just wanted to make sure for everybody to understand is that safety can never be absolute. And this is what Jane had also pointed out in her presentation. Safety really is based on a risk/benefit evaluation. So when we approve a vaccine we want to make sure that the benefits of using the vaccine in a certain population for a certain indication will outweigh the risks. And so that's really what safety means. And another important consideration is that the facility in which the vaccine is manufactured is designed so that it can assure the safety, purity and potency of the product. And more later.

So what you don't find here is the word "efficacy" or "effectiveness." That is really contained in the term "potency." That term is prescribed in the law and it has been interpreted by the agency to include effectiveness. How do you demonstrate effectiveness? Well, you perform controlled clinical investigations to really demonstrate that a vaccine really, you know, has an effect, the desired effect. So only those vaccines, then, that are demonstrated to be safe and effective, and that can be manufactured in a consistent manner, will be licensed by the FDA.

And I apologize to the lawyers who probably get a kick out of my very simplistic view of the FDA legal framework here, but I just – this is how I understand it. So we have laws that are made by Congress and signed by the President, and then we have regulations. And regulations are really a standard or a requirement of content which is set by a government agency under the authority granted by Congress. Congress really leaves us, leaves it to the specific government agency to really implement, prescribe and interpret a

specific law. Now these regulations that we have are binding, so the FDA has to follow these, and the manufacturers who make a vaccine also have to follow these regulations. And I'll show you some examples.

And the other thing that we have are so-called guidance documents. We call it a document "in the trenches." Guidance documents reflect the FDA's current thinking on a particular issue. It could be a scientific issue, it can be an administrative issue, it can be a policy issue. So there are many different guidance documents that we have on our website that can interpret a law or a regulation, it can interpret what is meant by a specific methodology that the agency thinks you need to apply to collectivize a vaccine and support and so on.

So the regulations that are followed in vaccines' development are contained in Title 21 of the Code of Federal Regulations. And that is basically a set of basic approval criteria that apply to vaccines regardless of how they are made or manufactured. They are basically describing the methods and the standards that pertain to the manufacturing of this product to assure that these products are reasonably safe and that they have the quality characteristics that they plan to possess.

These regulations also describe the type of clinical trials that a sponsor should perform or conduct to demonstrate the safety and effectiveness of this product, and they're basically – and they contain many, many other regulations and provisions.

So what is then an IND? That stands for Investigation New Drug Application. And it is an important document to have because the law states that a product cannot be introduced into interstate commerce, that is, it cannot be shipped across state lines, unless an approval is in effect. And what the IND does, it really exempts a new drug or biological products from these requirements. So in other words, it would allow an investigational vaccine to be lawfully shipped across state lines for the purpose of conducting clinical trials and investigations.

And so a sponsor who now wants to conduct a clinical trial with a vaccine candidate – and Barbara described to you the type of research and effort that goes into identify valuable vaccine candidates, and it's only a very small percentage of products who really make it into an IND stage. And I should tell you that it's only a small percentages of IND's which make it to the next stage, which is your marketing application.

But a sponsor who wants to perform a clinical investigation with a candidate vaccine must submit an IND to the agency. So that is a document that describes how the vaccine is manufactured, that describes the manufacturing process. It would describe how the vaccine candidate was initially collectivized, what in vitro studies have been conducted, what safety studies have been conducted with that product in animal models, what proof of concept studies – that is, studies to really look at the initial immunogenicity of this product in animal models – has been conducted. And it also will then contain a proposed clinical protocol.

So the FDA then looks at the submission and determines by the pre-clinical data submitted, is it reasonably safe to proceed to clinical investigation of that product? And if the answer is yes, then what starts is the clinical investigation of this vaccine candidate. And that goes typically in three phases - phase one, two and three. And I will talk about what that means in a couple of minutes.

If the clinical development was successful – in other words, if it was demonstrated that the vaccine is safe and effective, the sponsor, then, or the vaccine manufacturer, will then submit to what we call a marketing application, or a Biologics License Application, short a BLA. And that's the document that contains all the data to support the approval of the product. When we review that document, there will be also in parallel an inspection of the facility in which the product was manufactured.

And as I will tell you in a couple of minutes, the safety monitoring of the vaccine doesn't stop, of course, with the license application or with the approval. Many times the sponsor will then conduct what we refer to as Phase 4, or post-marketing studies, to further evaluate the safety and even effectiveness of this product. And this says the same thing in other words.

I wanted to show the slides to give you sort of a flavor of what type of investigation new drug applications, or IND's, will receive. There is of course IND's for new products. There can be IND's for altered versions of an original product. The formulation may have changed, the product is given a different dosage, the rule of administration may have changed, or the vaccine antigen or

the vaccine is given with what we refer to an adjuvant, like an immune enhancer, simply put.

There could also be changes in indications for an already-approved product, so there is a new age group that is studied, as again, a new indication or a new schedule. Or, the product is now studied with other routine vaccinations that are given concomitantly. So for all these different scenarios, we have IND's under review.

The Biologics License Application – well, I was saying that is the document that has all the supporting data for the safety and effectiveness of the vaccine, and based on this submission the FDA makes a decision whether the vaccine can be approved. So there are two basic questions that we ask: Are the clinical data adequate to support the requested indication and use of the product; and are the chemistry, manufacturing and control, that is the CMC data, adequate to support the manufacturing process and ensure consistency of the manufacturer.

And to really address that, a vaccine manufacturer really has to look at five different areas. One of them, as I stated, are the pre-clinical data. Is the product sufficiently safe to support initiation of clinical trials? Then, what is the quality of the clinical data where the studies were designed and executed so that safety and effectiveness can be demonstrated? And what is the quality of the chemistry, manufacturing and control data? Is the manufacturing process of a caliber to ensure quality product and consistency of manufacturer? And also, there is information in these license applications on the facility itself, so the

building where the product is manufactured, and the equipment that are being used.

And again, what we always want is a so-called post-licensure pharmacovigilance plan to monitor, to further monitor the safety and effectiveness of the product once the product is licensed.

So manufacturing. I will not bother you with this slide. It's very complicated. It is very technical. But the point that I wanted to drive home is that biological products are very complex products. They're devised from living sources that cannot be simply collectivized by a chemical formula, and they're very sensitive to changes. So what we – our approach is really to say, the product is defined by its manufacturing process.

So it's very, very important that a vaccine manufacturer can develop a manufacturing process that by which the product can be made reproducibly and consistently. And these, the refinement and the development of this manufacturing process can go hand in hand with the clinical development, which is here depicted as Phase one, two, three chemical trials. But at the end, by the time the vaccine manufacturer submits the Biologics License Application, we have to have assurance that a robust manufacturing process has been in place that allows the manufacturing of a reproducible and consistently made vaccine.

DR. HERR: Now if something comes up where there's a contaminant, it's noticed in the production process, is that monitored at every major step of the production of the vaccine?

DR. GRUBER: Yes.

DR. HERR: So they can identify where this little spot is?

DR. GRUBER: Yes.

DR. HERR: And how often does something like that happen?

DR. GRUBER: Well, you know, that really varies. First of all, yes, the production process is really controlled and monitored at every step of manufacturing. And this is something that we call, that we have what is called in-process controls. So let's say the bacterium is fermented. So we have certain in-process controls at the fermentation step. Then it is purified, so we have in-process controls here. Then it is formulated and built. Again, in-process controls. And at the end we have what we call final release criteria, so there we look at the purity, at the identity, at these, you know, many, many other general safety that there's certain prescribed tests and other tests, and by which the vaccine then can be released.

The problem is that contaminations can happen. And there are very many different sources. It can be the media that is used. It could be certain raw materials that are employed in the manufacturing process, that say you always use, you know, a certain serum source because sera, that is something that has been used frequently in vaccine manufacturing, and you switch the vendor and all of a sudden there is a contamination problem. Or, it can be contaminated by the personnel that is performing the manufacturing. So this was something that, you know, it's tightly monitored and tightly controlled, and yet this can happen.

Does it happen very often? Well, you know, it happens occasionally. I think we have a pretty good process in place that really monitors that and assures that it doesn't happen often, and the way you do it is really, you go out and inspect these facilities, and you have our field inspectors go out and see how is that done. You're looking at the – what we call batch production records of these products to really make sure that everything is okay. But you know, it's not 100 percent. Things happen.

DR. HERR: It's monitored frequently in the industry?

DR. GRUBER: Yes. It is. So I really didn't want to get into that slide. Yes, no, that's okay. So we have the manufacturing process development, and then we have the clinical development of the vaccine. And I was telling you that before a vaccine candidate is allowed to be studied in human subjects there's a lot of evaluation going on in the pre-clinical data to assure that it's reasonably safe to proceed to a first time in human clinical trial, which is the so-called Phase One trial.

So the Phase One trial is really, the primary objective, the major purpose of a Phase One study for a vaccine is to assess the initial safety and tolerability of a vaccine candidate in human subjects. You therefore would limit the number of subjects that you enroll in the study. So you're not going right into thousands of subjects with a new vaccine. Usually these studies are very small, 20 to 80 subjects, sometimes only 10 to 20 subjects. It depends on the product.

The safety is investigated or evaluated in healthy adults 18 to 50 years of age. Before even if you're dealing with a childhood vaccine, you would

start the clinical investigation in healthy adults and then you sort of step down until you finally go into your target population. Only if you find that the safety as determined by the Phase One clinical study is assuring, you will allow further clinical development of this product. The safety of the human subjects is closely monitored. Usually there are diary cards in all studies, you know, any adverse events that a subject will experience is recorded – fever, local symptoms, other systemic symptoms. There are frequently clinical examinations, the subjects are asked to come back to the doctor a couple of days later, a week later, to really look at them. There are laboratory investigations.

And what we always have, we invoke stopping rules. That is, you go ahead and you do your clinical study, but if you see a certain adverse event – let's say fever in X amount of subjects exceeding a certain threshold – you stop the clinical trial and there will be an investigation to see if it's reasonably safe to continue with clinical development.

But if everything looks good, then it goes into what we call the clinical development Safety Phase Two Study. These are safety and immunogenicity studies. They enroll additional subjects, usually up to several hundred subjects per trial. They are randomized, they are controlled – usually you would use the vaccine and then you'd have what we call a placebo vote, where you're looking at the safety compared to nothing, or you look at the safety compared to another licensed product.

These trials can include subjects which include the private population – let's say toddlers or infants, when they're using it with a childhood

vaccine. They serve the purpose really to optimize what is the right dose to administer, what is the right schedule, do we have an optimal formulation, what is the route of administration. And, does the vaccine elicit an immune response.

So if data looks favorable, the vaccine then proceeds to what we call Phase Three clinical study. Now the objective of this study is to demonstrate the effectiveness of this product. So if you want, these are the pivotal studies. They can include safety assessment, and many times we would ask for separate safety trials in order to evaluate the safety of these vaccines. And since vaccines are given to healthy subjects, safety trials typically include thousands of subjects.

And in terms of demonstrating effectiveness of the product, the gold standard of a clinical trial is always looking at prevention of disease, so the clinical endpoint, if it's prevention of disease, that is the gold standard. And many times, especially in those days and ages, it is not always possible to really look at prevention of disease. And that can have several reasons. If you look into the United States, many times the disease incidence is so low that you can't really do the study. It would be prohibitively large, you know, the number of subjects that you would have to enroll in clinical trials. Other reasons could be that there are other licensed vaccines already in the United States and so it's ethically not feasible to just withhold that product and test a new product.

So then we would have different outcomes by which we – or different endpoints, we say, by which we measure effectiveness. Usually its immunogenicity, but I don't want to go into this. Then we have another provision that's effectiveness demonstrated based on animal studies. But that's only for a

very, very narrowly carved out product category, and that product, these products, how that you cannot do studies in humans. Small pox, anthrax, plague, right?

DR. HERR: You wouldn't want to be the control.

DR. GRUBER: You don't want to be the control population, that's right. So then with pre-licensure clinical development of these vaccines, if it was successful the vaccine manufacturer then would submit a Biologics License Application. And the purpose of this document is to provide adequate information to allow the FDA reviewers to reach a decision if the product is safe and effective for its proposed use; do the proposed benefits outweigh the risks; and is the prescribing information that accompanies the vaccine, is it adequate and does it have any false claims in it? And of course, very important, is the manufacturing process adequate and are the control methods adequate.

Now many times, almost in all cases, if we have a new vaccine product that is going for approval, we would seek the advice of our Vaccine and Related Biological Products Advisory Committee to really weigh in on the data that are before the FDA to make a decision is the product safe or effective. Of course, there are certain agency regulations that govern the procedures and rules of the advisory committee, but the purpose is really to get independent expert advice on a range of scientific, technical and policy issues.

So in other words, let's say you have a vaccine that is up for approval and we think the data is safe, the data show that the product is safe and effective. We would convene our advisory committee, we would give them a

document where we sort of – which we refer to as a briefing document, that shows or summarizes the most pivotal data, and then hear them discuss the safety and effectiveness of the product in an open forum that – where the public can basically participate, can listen.

So for these committees, or these advisory committee meetings really provide a forum for a public hearing also on important matters. And then of course we would like the recommendations of the committee to us; however, we actually make the final decision of whether a vaccine can be approved or not approved. So that is one of the functions of the advisory committee.

If you were to post-marketing studies – Jane gave a nice presentation on the post-marketing surveillance of the safety of the vaccine – many times what the FDA will do when we approve a product, we will say that the pre-licensure clinical trials, pre-licensure data were adequate to say that the product is safe and effective for approval. But many times pre-licensure studies are just too small to really determine the safety or the potential for more rare adverse effects. So many times we will ask the sponsor to continue to monitor the product's safety, and they have to submit protocols for post-marketing study that are also reviewed by the FDA before they approve it. And once the product is approved, the sponsor will then conduct these studies in the post-marketing arena. So they're conducted after the FDA has approved the product.

There are certain laws and provisions. Some studies are required, others are agreed upon. I don't want to really – I can't really go into this right now. But all these studies are described in the approval letter. They're up on the

FDA website, and basically the sponsor really commits to conduct these post-marketing studies, and there is another FDA website that sorts of lists the status of these studies and if the sponsor has not done it or is late or delayed, you can read about this on our website.

So that in a nutshell is the vaccine approval process.

DR. FISHER: Just one comment. It's marvelous, as always, but I think it's important for us to all remember that it's not an all or none phenomenon. So sometimes you might approve something for, maybe a company comes in and they want it approved for this age to that age, and you say no, we'll only give you the in-between age, or we'll only do it for men, not women, like the HPV. So it doesn't – just because the company gives you the information doesn't mean that you approve it as they've submitted it. And in addition to that, you'd do the post-marketing stuff. So I think it really is an incredibly robust system.

DR. GRUBER: That is correct. So if licensure for a product is – it's a data-driven process. So if the clinical data show, let's say, that's here for this meningococcal vaccine, it was studied in children two to 10 years of age. And we've seen that it was effective and safe. Then we can give the indication for this product. We cannot give the approval for children less than two years of age because the product was not studied in that age group. That is right. And that's why I mentioned before, part of the Biologics License Application review is the review of the prescribing information, the packages. Because sometimes sponsors make different claims, and then we'll have to say no, this has to come

out because you haven't studied the product for this use, in that population or for this indication. That's true.

DR. GIDUDU: Marion, I have a question. Who constitutes the committee, the approval committee?

DR. GRUBER: Yes, it's a multi-disciplinary team. So we can, on a Biologics License Application, the reviewers, they're usually between 20 and 30 reviewers. And they consist of medical licensures which will review the clinical trials together with the statisticians. Then we have epidemiologists who look at the post-marketing proposal. There will be the reviewers that look at the chemistry, manufacturing and control information. There are reviewers who will specifically look at the essays that were employed, for instance, to evaluate the immunogenicity of the product. So they're – you know, and the disciplines, there are microbiologists, biologists, mathematicians, statisticians, as I said clinical medical officers, there are regulatory project managers on there, and – who, I forget – I mean, there is just a multidisciplinary team.

And they all come together and we have many, many, many readings, hours long. And then we disagree and then we have to meet again. So it's just a – it's a very – we have something which is called the mandatory review process because we have to have reviewed a BLA, a Biologics License Application, within 10 months. So there's a lot of – by the time it's submitted there's a lot of steps that have to be met and followed, and that may be a subject for yet another presentation, Jane. So, but yes, many, many people who decide.

And it's class office wide. It's not only the Office of Vaccines. As I said, we work together with the Office of Statistics & Epidemiology, or the compliance people, of course, our inspectors, the facility inspectors, the people that review the documentation that comes for the facilities. They of course are also very important components of the review team. So I think I outsource my work from here.

DR. EVANS: There's a BLA and an ELA. I know you didn't want to get into that. Does that still exist but it's a separate documentation?

DR. GRUBER: That wasn't formalized - I think that – that stopped, was it '90, '95 or something. Yes, you're right, in the old days we had an Establishment License Application and a Product License Application, an ELA and a PLA. That has been put together, and it's now part of the Biologics License Application, and it contains the documentation of clinical trials, the manufacturing process and the facility, yes.

So in terms of – two more minutes – approval actions, we have since my last update, we gave MENVEO, that is a vaccine to prevent invasive meningococcal disease. That was already licensed for subjects 11 to 55 years of age. But based on the review of clinical data to support the safety and effectiveness in children two to 10 years of age, the indication was extended to now include children two through 10 years of age.

We also gave GARDASIL, which is the Human Papillomavirus quadrivalent vaccine, an additional indication. It's now also indicated for the prevention of anal cancer caused to HPV types 16 and 18 in both males and

females, nine through 26 years of age. So these were – and we have a number of additional approval actions that I didn't list, and mostly from concomitant administration of routinely recommended vaccine products.

What I thought it was important to mention – and that is my last slide – last week our advisory committee convened to consider which influenza virus strains should be included in vaccines for the next influenza season, the '11-'12 season. And basically the recommendation was that all the strains, vaccine strains that were in the last composition of 2010-2011 vaccine are going to be retained. So it includes the 2009 pandemic H1N1 virus, the H3N2 virus, and A, B virus. It was an interesting discussion, though, because – and maybe this is very important for the people on the Vaccine Injury Compensation making the vaccine injury table, because there was a lot of discussion. We actually – there are two Influenza B strains circulating, they're called Victoria and Yamagata strains. Right now, this thing here, Brisbane, is belonging to the Victoria lineage, but in China and Asia we have the other lineage, the Yamagata lineage circulating. So there's always a little bit of uncertainty, what is the right strain to put in the vaccine.

And so there was a lot of discussion of could we not just put the two B strains together in the vaccine, to really prevent a potential mismatch. And so in other worlds, you're going from a trivalent to a quadrivalent vaccine. And lo and behold – I should tell you, and that was publicly discussed at that meeting – is that vaccine manufacturers do have plans to make quadrivalent vaccines,

influenza vaccines that have two A and two B strains. None of this is licensed yet, but they have plans certainly there.

And the other discussion, and that was very interesting, is that people thought that since influenza B affects children in a different way, that one should consider licensure of so-called supplemental B (?) vaccines. So in other words, you have a different vaccine for children than you would have for adults.

So these are the discussions. And then an interesting point was made that well, you know, monovalents and quadrivalents are not really captured in the vaccine injury table. So there's a lot of stuff that has to be ironed out before that table - but there was certainly a lot of interest. And I thought that was a very interesting discussion. So we'll see where we're going with that.

MS. HOIBERG: This is Sarah Hoiberg. Are you also looking into the fact that since we introduced the influenza vaccine onto the table of accepted vaccines that we compensate, that we have gotten huge amounts of claims coming in for injuries? Now I do understand that it's one of the most widely distributed vaccinations and many, many, many people are getting them, but are you looking into making the vaccines safer than what it has been, seeing as we've seen so many – a lot of neurological disorders coming in. You know, like the correlation between Alzheimer's and the vaccine, and --

DR. GRUBER: Yes. This is again what I've tried to – in the pre-licensure, if you have a new product, a new manufacturer wants to make a new influenza vaccine, they certainly have to do safety studies as I referred to, before the product can be licensed. For the vaccines that are out there, we have six,

seven, I think, vaccine manufacturers now. When the vaccine strengths change from year to year they don't have to perform necessarily clinical trials. The strain changes and approvals are based on manufacturing data only because – and the reason for this is because there have been such experience of these vaccines.

Now you are absolutely right that it was expanding the recommendations. I mean, first it was adults and then it was children and then little children and now everybody can be immunized. I mean of course in its uptick- I think uptick of the vaccine has never been as high as in the last season - you probably would see more. I don't – I can't really speak to what the underlying causes for this is, and the reporting, and in terms of adverse events.

Making vaccines safer, we always strive to making vaccine safety. You had Barbara saying that we're trying to even make it more effective by really looking at antigens that do not require these yearly strain changes and changes in the composition of the vaccine. But in terms of requiring pre-licensure trials, to tell you the truth some of the events that I've seen and you referred to, maybe neurological events, they are rare. You can't have – you won't be able to really capture these type of adverse events in the pre-licensure scenario.

MS. HOIBERG: And my other question is,because the influenza vaccines are so widely distributed in so many different venues, does the FDA and CDC, do they encourage you to go to your doctor to get them? I mean how do they really feel about the CVS's and the airports and the malls?

DR. GRUBER: The FDA really doesn't have any regulatory authority in terms of how the vaccine is distributed. I mean, our job is to license it, but what comes after that, that's not really something that we are dealing with.

MS. HOIBERG: Because I would think that that would go to vaccine safety and how it was distributed, because you're having a lot of people that really are not – in some, like very many ways experienced enough to give these vaccines. And I know there were children, practically children, sitting behind the table at the malls giving these vaccines. They're not giving them, they're not administering them properly, they're possibly not being stored correctly. I think that that's something that really needs to be looked into because it's very important that we protect our children and ourselves against the flu. It's a yucky disease, you know, yucky illness. But I really feel that they're not given the respect that they deserve. They're just being handed out like candy, and they're not – you know, and people are getting hurt, but there's not a way really to track and to make sure that they're being given correctly, and handled carefully and whatnot.

DR. GRUBER: I acknowledge this concern. To me, I mean, I think it does, it really goes into the, what we refer to as practice of medicine almost. And the FDA does not regulate it. We don't have any control over that. But maybe some of our medical officers can look into that.

DR. FISHER: Yes, this is Meg Fisher. I think there's sort of – there's lots of things that go into your question, that if we restricted it to physicians' offices only a minuscule portion of the adult population would ever be

immunized because the fact of the matter is, people don't go to doctors. So if you really want to have a universal immunization you need to have sites other than doctors' offices. But I think your point about we don't know how, we don't have all the details of the storage in the other things, is – and the administration, is an excellent point.

I think the other major thing that we don't have – which makes this exceedingly difficult – is we don't have a number of how many doses were given. So we know how many are distributed, but we don't have the denominator to say how many were given. So you have 300 reports. If 180 million doses were administered that's an incredibly small number. On the other hand if only 90,000 were administered that's a – that becomes a much bigger number. And I think we're really in this kind of nowhere land where we don't have the ability at the moment, or we choose not to collect that information. And I don't know how – I mean, the FDA doesn't do that.

DR. GRUBER: Well, the Office of Biostatistics, I mean they have information as you say to how many lots are distributed. But we don't know – you're absolutely – we also don't have that information in terms of the number of doses administered. We don't.

DR. FISHER: And we don't require people to give back their vaccine that they don't use, which would be one way that you could actually then figure out presumably how many were given. But we don't even have that simple part.

MS. HOIBERG: You can't use the 2010-2011 for the 2011-2012. I mean, don't they expire?

DR. FISHER: No, it expires.

MS. HOIBERG: I mean, it doesn't need to be destroyed. And if we're not knowing that they're – I mean, how are you knowing that you're getting the good vaccine and not the one that was from last year. See, I'm just asking this, you know, just from a lay person, how – how is it being controlled. That's what I'm here for.

DR. FISHER: That's – yes, that's yet another issue.

DR. GIDUDU: The VSD has – it's geared to denominator data, the doses distributed. And like I mentioned, those that go to their CVS and other areas may be missed, but they pretty much have some estimate but it doesn't cover a large population of the U.S. unfortunately.

MS. GALLAGHER: Thank you very much, Dr. Gruber. That was excellent and it was a very good review for our new members.

And now, I asked Sarah Hoiberg to give us the update on the Communications and Outreach Subgroup. As everybody's noticed we're a bit behind and so I know the petition for adding injury to the vaccine table was scheduled at 3:00, but we're past that time, and we'll just go in order of the agenda right now and when we get to it, we'll get to it. So Sarah was scheduled to be earlier. But I think we've had some incredibly good presentations and I didn't want to rush anyone.

Agenda Item: ACCV Communication and Outreach Workgroup Update, Ms. Sarah Hoiberg, ACCV Member.

MS. HOIBERG: My name is Sarah Hoiberg and I am the Chair for the ACCV Communications and Outreach Workgroup. It has been my goal all along really, since coming onto the ACCV, to get the program more visible and get it into the hands of the community and those who are injured but may not know it, that they have an option for compensation.

What we ended up doing was, a few years ago we contracted with Banyan Communications to do some research for us to let us know how we could best reach our goal in getting the communication out there about the program. And they gave us a very extensive report – and you do have those in your folders – so if you would take time to read that for the next meeting. We don't expect you to sit here and read it right now. But what came from that was a whole bunch of ideas that we thought were wonderful, but we're now facing a budget crisis. So we're having to become very creative and do things that we can do that will not cost any money, or very little.

So Geoff came up with a wonderful slide presentation which you have in front of you. This is a draft. And what I would like to do is just take the time, instead of giving you an update because there really isn't much of one, this is what we're doing right now, I would like you all to look at these slides. We'll go through them one by one. And we did have a phone call, and that will be your draft minutes for January 12th, 2011. It was our last phone call that we had. And we went through this wonderful presentation that Geoff created for us.

It looks like this. It says “Draft National Vaccine Injury.” It was not in your blue folders. It was handed out yesterday. Where’s Annie? It looks like – yes, yes, it says “Draft National Vaccine Injury Compensation Program.” Got it? Does everybody have it? Now what we did was, we went through and made some suggestions to Geoff on how we thought would make the slides better, and that’s going to be found on page two, at the bottom half of your page. So what I would like to do is have those members who are not part of the workers, and of course our new members, to take a look at this as we go through it one by one and make your suggestions. Because I feel that as the Commission that has been on for more time, we’re I guess more knowledgeable about the program and so we see a lot of things as maybe repetitive and not necessary, but maybe in turn they actually are necessary.

So if we look at the first one, it’s just going to be like the introduction slide that says Vaccine Injury Compensation Program. The purpose of this presentation is going to be, we hope, to be able to put it on a website where people can go and use it for presentations in their hospitals or at things such as grand rounds (?) 00:04:14 or something that doctors can go to and download and then show them to their offices, just so that it could be used as an educational tool. It’s not meant to shock or anything, and we hope, we’re wanting to make it very user friendly and very informative but straight to the point, not too much meat. Just enough so that they know that they can call this number and get something started.

So we then come to the one where it says “National Vaccine Injury Compensation Program,” it’s like on your second slide. Media reports in 1982 alert public to the risk of DTP vaccines. We talked about this yesterday in orientation, where we gave you the history, and this is the background. What we had decided was the last bullet, “Congress passes National Childhood Vaccine Act,” we thought that we would add the year, 1986. Does anybody else have anything that they think needs to be added or taken out there?

MS. GALLAGHER: As some people are looking at it for the first time, please feel free to review it afterwards and e-mail any suggestions to Sarah and then the subcommittee will get them to here.

MS. HOIBERG: Okay, and then slide number three is headed “National Vaccine Injury Compensation Program, Legal Provisions.” On the first bullet where it says “federal no-fault compensation system” we had asked that it be added “for children and adults.” I think that was the only thing that we had added to that one.

MS. GALLAGHER: And that was because we thought there might be different interpretations --

MS. HOIBERG: Because it’s called Childhood Act. Yes, Tom?

DR. HERR: The question is, I’ve got a little note I don’t remember why. It’s on last bullet, it says “No age restrictions on who may file.” And I think the implication was, that it wasn’t children and adults. But if we have “for children and adults” in the first bullet, do we need that last bullet at all? The question is, I had a note I can’t read, about the last bullet that said “No age restrictions on who

may file" and I guess my question, since we're changing the first bullet, it says "for children adults." Do we actually need that bullet?

MS. HOIBERG: I don't think we need it. Take it out. All right, the next slide, "National Childhood Vaccine Injury Act, Vaccine Safety Provisions," that was slide number five?

DR. HERR: I think it's four, I think.

MS. HOIBERG: Four? Okay, we had made no changes to that one. Does anybody see anything now that may possibly -- ?

DR. FISHER: Do we want to add – if we have that last bullet is "instituted medicine reviews of vaccine adverse events," there are also – there's the current one.

MS. HOIBERG: That's true, there's the current ones. So do we want to say the 2000 -- .

MAN: It's not out yet.

DR. FISHER: It's in progress.

MS. HOIBERG: It's in progress. What should – do you want to add something there, too? Do you think that that's okay to say? Okay, so then let's make a note that they will add the new report?

MS. WILLIAMS: Do you want to add the links? Were there links in this report?

MS. HOIBERG: That is a good idea, to add the links to their report. Yes?

MS. PRON: This is Ann Pron. Under “mandatory record keeping” I may be missing something, but the patient’s name and date of birth is supposed to be recorded, or is this meant to be something else?

MS. HOIBERG: I think that when they do – this is like for the – well yes but in the VAERS they do – they do put the person’s name, don’t they, or is it just the --

DR. EVANS: It’s the mandate for record keeping requirement. Are you suggesting that we add exactly what they are?

MS. PRON: No. That healthcare providers must record the date of the vaccine, the manufacturer, and all that. That’s great. But what about the patient name and date of birth? Because I thought you’re also concerned about people that are giving the shots in other places and are they keeping records. Or am I just misreading that?

DR. EVANS: That’s not part of the act.

MS. PRON: Oh, that’s the Act, okay, sorry about that, okay, fine, got it.

MS. HOIBERG: Okay, so then moving on, we’d wanted to put Department of Justice – I think we had wanted to add the DOJ in parentheses because later on we talk about the DOJ, so we wanted people to know who we were talking about. And that was it on that. Does anybody – oh, and then we wanted to change, we wanted to say – on the U.S. Court of Federal Claims we wanted to move Special Masters down, where it said “eight court-appointed

attorneys" end parentheses, "Special Masters decide for and against compensation and the amount of the award if compensated."

I thought – here's a question, Geoff, when – with the Special Masters, I thought that they only decided the amount if it went to their decision, and if it's – oh, DOJ's not here any more. They stamp, they approve.

DR. EVANS: They still have to approve it.

MS. HOIBERG: They have to approve it, okay.

MS. GALLAGHER: But I think instead of "attorneys" they wanted to call them "judicial officers" to have people get a better sense of what a Special Master is.

DR. FISHER: Why don't you just say "eight court appointed Special Masters."

MS. DREW: Because we don't think that people will understand the term "Special Master." We think it would be clearer if we --

MS. GALLAGHER: We were going to say "Judicial Officer" parens, "called Special Master" end parens. Special Masters is a term that's used in other legal contexts for other kind of people than judicial officers and why they used it we're not really sure but it just has confused people over the years. So we're trying to be less confusing.

DR. FISHER: In most cases aren't – have the Special Masters been judges? Or is that not a requirement?

MS. HOIBERG: No, it's not a requirement.

MS. GALLAGHER: They Act more like an administrative judge but they're not called an administrative judges. They don't Act mostly like other Special Masters but that's what they're called. So that's a big conundrum that we have.

MS. HOIBERG: Anything else on that slide? On slide number six, we were – this is where I – we have "is there a better way to say it for?" and then --

MR. KING: So Sarah, when you say "a better way to say it" meaning a better way to transmit the information on this slide? Is that what we're talking about?

MS. HOIBERG: I think that's what we're trying to say. This is a long time ago.

MR. KING: So we've seen a number of slides today where people have given us one that was referred to as a wire chart, whatever, but we had charts that were listed, and it may be a process flow that we could just create so that it's pictorial and might be, with that graphical representation it might be a lot easier to understand.

MS. HOIBERG: Sometimes graphs are easy to understand and other times they're just – like if you're sitting in the back of the room, to see a chart, and to see the tiny little print, and then when they print it out – like a lot of times you say with the flow charts that we have here because a lot of times they're printed in color or made in color when they're photocopied it's black, you

can't see what it says. So that's an idea. We could think about doing a flow chart. But we're saying no flow charts.

MR. KING: We don't like flow charts.

MS. HOIBERG: We're not going to – it's easier to explain.

DR. EVANS: The flow chart that we have come up with before is two pages side by side. And you had Mr. Rogers' one this morning which was the flow chart from the DOJ side so it's a fairly complex thing. If we could have a flow chart that was a series of a small number of boxes that would be fine. But I don't know that you can do that very well.

MR. KING: I guess I'm looking at it, and then I see four bullet points here with a few subpoints underneath the recommendation. So I was thinking at a high end level, of four bullet points, just one, two, three, four, in a graphical representation. I understand, Sarah, that if it's photocopied it might be difficult in the back of the room so it might be that you add an additional slide of that so this is the slide in text format, the slide immediately after.

But I guess, as a new member I don't want to go crazy here on you guys because you spent so much work on it. But my understand is that the purpose of this is to make it clear for people. Pardon?

MS. HOIBERG: He said if we didn't do anything he did it.

MS. GALLAGHER: What my recollection of what our recommendation was, and that sub-sub bullet points, "parents, expert medical witnesses," we thought that could just go away because it didn't really add anything, who would testify if you had a hearing.

MS. HOIBERG: And then they were making the “court may compensate,” making that a bullet point.

MS. GALLAGHER: Yes, and the “court may compensate,” that should be a full bullet instead of --

MS. HOIBERG: Right, instead of a sub-bullet.

MS. GALLAGHER: -- a sub-bullet to the DOJ’s recommendation. And then we have one, two, three, four, five main bullets, and we lose the sub-sub bullet. And we thought that was clearer. But we’re asking everyone else to look at it and say whether they think that would be clearer.

MS. CASTRO-LEWIS: Sarah, how is this – I’m having difficulty between these – how are these going to be used? Somebody will get, a healthcare provider will get in the website and look at this to get information? Or this is a presentation that somebody’s going to use to give to others? How is this going to be used? Because depending how it’s going to be used, I’ll have totally different kinds of comments.

Because I see to begin with it’s extremely busy. And if we have bullets, they should be shorter, and then perhaps have some kind of explanation at the bottom for somebody else that wanted additional information or somebody else that is going to need information. But the bullets are not complete, nor they are really short to make a slide very clean and easy to understand. It’s not either one or the other, in my view.

MS. HOIBERG: What we had thought was that this would come accompanied by a script, that the person would then show the slides and have a script that they would read from in order to further explain the bullets.

MS. CASTRO-LEWIS: Okay, so that's great. If we have a script then my opinion is that these slides could be shortened, and make them a little bit – so the slides are not so heavy. It can be reduced a lot.

MS. WILLIAMS: Who's the person who's showing the slides?

MS. HOIBERG: It would be, say, for example, Tom would be at his office and he would have – poor Tom – he would have the script, and maybe that or his nurses, and so if you have other doctors in your office. We're going to pretend you have other doctors in your office. Anyway, at a luncheon meeting or whatnot you just come together and just show this as a continuing education.

MS. WILLIAMS: So it's for medical professionals?

MS. HOIBERG: It's for medical professionals, yes. Sorry if I didn't say that from the beginning.

DR. EVANS: Well Sarah, let me add, I think that the idea was that this could – and when I put this together, this had been kind of a skeletal presentation of many other variations I've put together over the years, the idea was that it could maybe be posted on the website and policymakers, nursing personnel, legal staff, whoever is interested in a quick look at the program and basically getting a basic understanding, would be the people that would be utilizing it.

MS. HOIBERG: And that's why my idea first, and some of the slides are a little bit heavier, because if someone was just going through them on the website, they would be able to get the gist of the program without even looking at the script. But to get a more in depth view you would have the script, and the script would then take and elaborate on certain points.

DR. FISHER: Getting back to David's point – this is Meg Fisher – I think we shouldn't dismiss the idea of a wire graph or whatever, because different learners learn better in one way or another. And I think for some people charts are really very useful, other people skip the charts all the time. So I think it would be nice to have a combo.

MS. HOIBERG: And that's fine, and that's why we're doing this, because different eyes see different things, and new people will give us an idea.

DR. FISHER: Even have it as an appendix and it wouldn't matter if it were two pages.

MS. GALLAGHER: So the VICP process, the second bullet point – should that relate to medical staff or scientific review? Because I'm looking at this and for all they know it's all the attorneys on your staff looking at it. And I know that it's really a scientific review, so I don't know how to give that idea.

MS. HOIBERG: Review the medical records? But it does not say – or department of – but it doesn't say that it's the medical examiners. Medical examiners aren't mentioned at all.

DR. HERR: It says "reviews medical records."

MS. HOIBERG: Right, but it doesn't say who.

MS. GALLAGHER: I'll just say that when I was in private practice of law defending doctors and hospitals I reviewed all the medical records too, but it wasn't really a scientific review, it was more like a legal review. I guess I'm wondering if there's some word we could put in there.

DR. EVANS: Medical staff.

MS. GALLAGHER: I think that gives a different flavor to the bullet.

MS. HOIBERG: Okay, yes, that works, because they're the ones that do it, as Rosemary has seen. Okay. So that was that for that slide. Is there anything else? We have a wire graph possibility, we've taken out "parents, experts, medical witnesses," we've created the "court may compensate claims" as a bullet not a sub-bullet, and we've added "medical staff" to bullet number two. Or the word "medical," sorry.

Okay, the next slide, VICP statutes limitation, filing deadlines. We had decided that we wanted OGC – what is that? That doesn't match the slide.

MS. GALLAGHER: Anyway, from the onset of first sign of a clinical manifestation after vaccination, and I guess what we're trying to say that the statute of limitations issue is floating right now. Maybe we should just leave it at – or should we take the language from the statute? That won't change.

DR. EVANS: But that is the statutory interpretation.

MS. GALLAGHER: That is? Well, I'm saying is that the statutory language?

MS. SAINDON: That isn't exactly the language, but I can provide that.

MS. GALLAGHER: I think maybe if we just stick to the statutory language the interpretation will come.

MS. SAINDON: I think for both injury and death claims.

MS. GALLAGHER: Okay, so and you'll help us with that.

MS. HOIBERG: Okay, so then this one's going to be changed. Then we have the VICP entitlement determination.

MS. GALLAGHER: I think it was very heavy slide, and so I think the subcommittee couldn't decide whether they thought it should say, or if it was too much. So I guess we're asking everybody else.

MR. KING: So here's my opinion. If you have a very heavy slide but that the information is most valuable and you need it, just create a second slide called "continued" and then it becomes a lot less on one slide and it's no longer as heavy.

MS. HOIBERG: Okay, so break it up?

MR. KING: Divide it in two. Maybe the second slide starts with "standard of proof, civil standard," and then you just have "continued." "Entitlement determination, continued" as the title of the slide.

MS. GALLAGHER: We're glad we brought you on board.

MS. HOIBERG: Like I said, when you've been on it for three years or more, you get so almost numb to it and it all seems like – we've all seen it before. Okay, the awards part. Remove "unlimited." You said "unlimited."

MS. GALLAGHER: "Unlimited awards for lost wages and attorney's fees or costs."

MS. HOIBERG: Right, you had said that because it's not unlimited at all, so we were --

MS. GALLAGHER: And we were going to add "hourly."

MS. HOIBERG: The "hourly" to the "attorney's rate." Attorneys fees --

MS. GALLAGHER: "Attorney's hourly fees."

MS. HOIBERG: Yes, "attorney's hourly fees."

DR. HERR: Why do you want to make it more busy?

MS. HOIBERG: Because we're trying to make it to where --

MS. GALLAGHER: It doesn't have to be in a sub-bullet if you just say "awards for lost wages and attorney hourly fees/costs."

DR. HERR: Why don't you just say – I mean, if there's going to be more extensive information provided later or elsewhere, why not keep the slide simple? And so it just says "fees." It doesn't say how but you figure it out later.

MS. DREW: Hi, this is Sherry. I actually would not use the word "unlimited" in lost wages, because there is a formula that's used for children's lost wages. So I would just take out "unlimited" and put in what the elements of damages are. Keep it as simple and as possible.

MS. GALLAGHER: Just put "lost wages" and "attorney's fees/costs"?

MS. DREW: Yes.

MS. GALLAGHER: Okay.

MS. DREW: Just put "awards for."

MS. HOIBERG: Yes awards. But you know what I think, I don't think you need to say "awards for." You just say "lost wages and attorney's fees." So take out "unlimited awards for" and then we just make "lost wages and attorney's fees" not a sub.

MS. GALLAGHER: It was somebody else who had suggested "hourly." I don't remember who it was.

MS. DREW: I think I suggested the word " hourly" because it makes it sound as if you can get $1 million for the lawyer when clearly that's not true. But I think we would say attorney's hourly fees paid if the claim is brought in good faith and on a reasonable basis.

MS. GALLAGHER: So in that bottom --

MS. DREW: Right.

MS. HOIBERG: Yes.

DR. FISHER: I would actually leave it – don't put "hourly" in there because honestly that would make me a little annoyed that we're paying you guys by the hour and that you can spend the hours as long as you want. But I think it's kinder, gentler to forget that you're on the hour.

MS. GALLAGHER: Okay, so we'll leave that.

MS. HOIBERG: Well do we want to say "attorney's fees and costs?"

DR. FISHER: Yes.

MS. HOIBERG: "Attorney's fees and costs" because they get paid for their costs. All right. So we added "costs" and took out "hourly."

MS. GALLAGHER: So then we don't need them up here. Okay. So up here --

MS. HOIBERG: No, no, this is down here. This is --

MS. GALLAGHER: I know, but up here all we need is "lost wages" as part of the injury claim because then we also have "attorney's fees" down here, so we don't need it twice.

MS. HOIBERG: They want to make sure they get paid, okay? Put it in there as many times as you possibly can. Okay, anything else on that slide? Okay. Next slide, VICP Appeal. This is how we appeal our cases. The first level is a judge, the U.S. Court of Federal Claims, second level is the Federal Circuit Court of Appeals and the third level is the U.S. Supreme Court. I think we didn't have any changes.

MS. GALLAGHER: The question was, at level three, about how you can appeal it if you don't like it, if necessary, so a presentation by a healthcare professional. Or is that too much information?

DR. FISHER: No, I think it's fine.

MS. HOIBERG: You want to leave it in there? Okay.

MS. GALLAGHER: You need a period after "U."

MR. KING: Oh, for "U.S." Right. Just a note on it, so we talk about the compensation and then appeals, but I guess people will make the connection immediately to appeals, but maybe to be – you know, what if you lose or what if you don't get an award, and then it just says "appeals process," first, second and

third level? I might be over-thinking here. The later in the day it gets the more I think. You want to stop me.

MS. GALLAGHER: It can be appealed even if you get an award.

MR. KING: That's right.

MS. GALLAGHER: Occasionally the DOJ appeals. So there's always a nuance to everything.

DR. FISHER: So I guess the only question might be, do we want to make it clear that if a person doesn't like the outcome of the Vaccine Injury Compensation Program they can go outside the system? They haven't given up their right totally.

MR. KING: So maybe just put "if outcome unacceptable" or something along those lines, "process for redress" or whatever.

DR. FISHER: You might add a fourth bullet that says you can go outside the program.

MS. HOIBERG: That's true, we don't have about going outside the program.

MS. GALLAGHER: Well it's actually still in the program.

MS. HOIBERG: No, but people can opt out at 180 (?) days, we don't have that in here at all.

MS. GALLAGHER: Oh, okay. I meant the appeals in the program.

MS. HOIBERG: I didn't think about that.

DR. EVANS: I did, and it's a matter of if I thought about all the things that I generally cover in my talk, we're talking 20, 23 slides. So I tried to

cut back. But no, there's a value of the collective group, if you think there's a certain point that needs to be made, we create a slide that's made, and that's just understanding that the longer it is, the chance that it becomes less compelling.

MS. HOIBERG: And what people are going to turn up.

DR. EVANS: Right.

MS. HOIBERG: Yes, okay. Do you want to revisit that? You don't want it in there? Okay. All right, the next slide, this is the VICP vaccinated – vaccines covered. I don't think we need to add anything to that. They didn't have any changes on that one. Adding new vaccines, there's two sets. Regulation – here we had – it's very wordy.

MS. WILLIAMS: Do you even need that slide, if the idea is to get --

MS. HOIBERG: Yes, I don't think we need to put that in there.

DR. FISHER: Which one?

MS. HOIBERG: The "adding new vaccines." I don't think that that needs to be --

DR. FISHER: May I also make a suggestion that you take out all the stuff in parentheses, because there's all kinds of combination vaccines that are covered. I would just put the – I wouldn't put the details because you don't have them all. There's like 20 different combination vaccines. Kinrix isn't on here, you know, but it's covered.

MS. HOIBERG: So you just want – do you just want to have a series of tetanus and pertussis, and then take out DTaP, DTP.

DR. FISHER: Yes.

MS. GALLAGHER: Yes, MMRV isn't listed and that's covered.

MS. DREW: This is Sherry again. Maybe we actually do want to use some of the statutory language and just put "any vaccine routinely recommended for use in children, including -- " and then just list these without the acronyms.

MS. HOIBERG: Okay, that's a great suggestion. Any vaccine --

DR. EVANS: What I was going to say is – I think it's much too complicated, but the fact is it's important practitioners know that vaccines that are recommended by CDC for routine administration in children are covered. Then people like Elizabeth have trouble sleeping if you don't, then add the second point which is it's not actually covered until there's an excise tax. Now whether we include that on a slide or not, I don't know, but that is in point important. Now there's no vaccine around the corner now that's ready to come onto the program that I'm aware of, that's going to be coming up for ACIP, but in the future it's going to – the tax is going to be an issue, but it's really an issue in the background.

MS. SAINDON: But the point of this document is to give an overview of the program as it exists, and I don't think this is a necessary slide in the sense that people in Tom's office won't really much care about the ins and outs of adding immunovaccine potentially sometime in the future maybe.

MS. HOIBERG: Well that's what we're saying. That doesn't need to be in there.

MS. GALLAGHER: But I disagree with that.

MS. HOIBERG: We're taking out "adding new vaccines."

MS. GALLAGHER: Put it on the slide above: "any vaccine routinely recommended by CDC for routine administration to children including -- " Is that -- ?

DR. FISHER: That's okay, except now the implication is that it's all time covered. You see what I'm saying? It now becomes a childhood only, and since most of the claims are for adults.

MS. GALLAGHER: Right, but if it's only recommended for adults it doesn't come into the program.

MS. HOIBERG: It doesn't come into the program. It has to be routinely scheduled for children.

DR. EVANS: In terms of routinely, the rheumavax vaccine is not recommended, is not covered by the program, only the pneumococcal conjugate vaccines are.

DR. FISHER: Oh, because it's not routinely used.

DR. EVANS: Exactly.

DR. FISHER: Okay, then you have to say – I don't have a problem with then routine -- . So that should be "routinely recommended in children even when used in adults." Or "especially when used in adults" or whatever. But somehow you have to get in there that adults are okay.

MS. HOIBERG: Well we were just using the language that was in the statute.

MS. DREW: Actually, based on what Geoff said, I withdraw that suggestion and think that we leave it just the way it is but take out the acronyms after GPC.

MS. HOIBERG: Okay, sounds good to me. All right. So we're taking out the second slide, the slide about adding new vaccines. I really – you know, Geoff, I really don't think that we need to have the VICP outcome either, because you are just talking, but you're introducing a program and they don't need to be weighed down with this information. So I'd say strike that. And then but definitely, of course leave the VICP contact information so that they know where to reach us. Yes, call Geoff Evans.

DR. EVANS: I was actually suggesting Sarah's name.

DR. FISHER: I should have done this already but I haven't. So if you go to that website or if you call that number and you say, okay, I want to file a claim, can you give me the name of a lawyer – I mean, how do you get the name of the person to help you file a claim?

MS. HOIBERG: Kay, do you want to speak to that?

KAY: The court's website has a list of attorneys.

DR. FISHER: Can we spell that out, because I honestly think that is something that physicians should know. I guarantee you, other than the two that are sitting on this thing there is nobody that knows that.

MS. HOIBERG: Okay, because what happens is, when you file a VAERS report, they then send you a VICP packet, and then in that VICP packet there's actually information about lawyers whom you can call.

DR. FISHER: Right, but this is geared for doctors.

MS. HOIBERG: It's geared for doctors, that's correct.

DR. FISHER: And who never get the VICP packet.

MS. HOIBERG: Okay, so then do you want us to put --

DR. FISHER: It should be like, I don't know where but somewhere.

MS. GALLAGHER: A third bullet, petitioner attorney list available.

DR. HERR: Put it on another slide.

MS. HOIBERG: Do you want another slide?

DR. FISHER: Or another slide.

MS. HOIBERG: I could always do another slide.

MS. GALLAGHER: I was just saying, this is contact information so it has it differently.

MS. HOIBERG: Okay, so do we just put that attorney information is made available?

MS. GALLAGHER: But you want to make sure that they understand, it's attorneys willing to represent petitioners listed on the court website. Something like that, that they understand it's petitioners' attorneys, somebody that would help them.

DR. EVANS: And our office is not able to provide that information. This is a reminder to the new members, that we are not in a position, since we are respondent we are not in the position of being able to supply that information.

MS. HOIBERG: So the petitioners' attorney information, it is made available on the court website, right? That's something we want to put in?

MS. GALLAGHER: Can be found?

MS. HOIBERG: Can be – is made – can be found.

DR. FISHER: Do you want to say a list of attorneys to represent petitioners can be found on --

MS. WILLIAMS: Well is that an ethical bar that would prohibit the information from being put on – just when your lawyer walks out the door.

DR. EVANS: I know.

MS. WILLIAMS: You know, I'd put a question mark. If we personally couldn't as respondent make that offer can we do it in our PowerPoint, make that? No.

DR. EVANS: We can direct people to where the information is available, but when individuals call our program or the HRSA hotline and ask us for that, we direct them over to the court.

MS. WILLIAMS: You can direct them to the --

DR. EVANS: To court, yes.

MS. WILLIAMS: Okay. Thank you.

MS. PRON: Is that what they say, that's on here already, the internet, USCFC court?

MS. HOIBERG: Yes. The U.S. Court of Federal Claims.

DR. EVANS: And they have done this for many years.

MS. HOIBERG: Well that really concludes my presentation. I appreciate everybody's input. Also, if you would like to join my wonderful --

MR. KING: I have one question.

MS. HOIBERG: Yes.

MR. KING: I'm trying to – I know that we go into the four letter – what do we call it?

MS. HOIBERG: Acronym?

MR. KING: Acronym on the VICP, but I'm trying to figure out where people know that we're going to start using that, when I start looking at this.

MS. HOIBERG: Okay, well that's a very good point. We can actually go ahead and said the National Vaccine Injury Compensation Program and underneath, VICP.

MR. KING: Perfect.

MS. HOIBERG: For the first, very first slide. Thank you, David. Anybody – any other suggestions? Linda?

MS. WILLIAMS: Michelle. I would put, right on the very first slide I would also put the website, on the very first slide.

MS. HOIBERG: The www.HRSA.gov/vaccinecompensation. That one?

MS. WILLIAMS: Uh-hmm.

MS. HOIBERG: Okay.

MS. WILLIAMS: Sometimes people don't want to hear somebody else's words. They want to go straight to the website.

MS. PRON: Can I ask another question about this? Will this have the ACCV somehow on here?

MS. HOIBERG: No.

MS. PRON: It will not? And will it be a .pdf or will it be just PowerPoint? And the reason I ask that is because doing presentations and things, people will take it and just do it and they'll modify it and they'll whatever, and that's why.

DR. EVANS: If it's on the website I would imagine it's a .pdf.

MS. PRON: So then it can't be used as a presentation. It would be --

DR. EVANS: No, it can be used as a presentation as a .pdf. Oh, all the time, yes. At least in my world I get presentations that way. This is open for modification in terms of its source, and we can certainly give credit, deserved credit to the ACCV, depending on where it's being distributed, if there's other special audiences, so that's certainly an open question, if that's what you're suggesting.

MS. PRON: Right. That's where the information came from. But when you present it people should know – it's like CDC, all their slides are --

MS. HOIBERG: This is really, it's – you know, HRSA put it together, you see, so we wouldn't be taking credit. And we are simply an advisory commission, so we're not – I would not want to get into that.

DR. EVANS: It will have the logos. This will be cleared. It will have the HHS and HRSA logo at the bottom, just like CDC has on theirs. But I'm open to the idea that at some point there should be information about the HCCV too. Now whether – again, it gets to the point, does the average person looking at this program wanting information, are they going to really care that much, but

yet there's a way we might be able to give credit to the ACCV too. We'll work on it.

MR. KING: So I go back to Magdelena, when we say the average person versus is it going to professionals, I don't see them as the same. So who is this geared to? Again.

MS. HOIBERG: Medical professionals. Right?

DR. EVANS: This is geared to professionals to begin with. I mean, the healthcare providers, people who want the – immunization program managers, the whole gamut of people that are interested in understanding more about the compensation program, but it certainly can be shared with legal staff, paralegal staff, policymakers, whatever, as an entry point for understanding the program.

MR. KING: Right, so if it was for patients or the general public it would be something entirely different.

MS. HOIBERG: It wouldn't have to be entirely different. It could be very similar, but you would want to simplify it even further, or maybe even give more information for a parent.

MS. GALLAGHER: It would be a whole different --

MS. CASTRO-LEWIS: It would be a whole different approach.

DR. EVANS: And there is a two-page fact sheet that we're also – I'd like comments on also. But the point is that once, as we discussed yesterday at the orientation session, and Sarah articulated, providers are the first point of

the stop, and so we can get them, access that group, then of course they can utilize it also, too.

MS. HOIBERG: Right. My main concern was getting information out to the doctors, and having that, and healthcare professionals, because they are the first line really. If a petitioner comes, or if a patient comes to them and says I believe my child has been injured by a vaccine, they're going to go "What?" You know, they're not going to know what to do. This is actually, it would be something to kind of spark their – and I say from personal experience, you take your child to the Emergency Room, and I do it all the time, and they're like "vaccine what?"

So it's very near and dear to my heart, and so this is something that I feel very strongly about and I'm so thankful to Geoff that he was able to put this together and willing to put it together. So if any of the commissioners would like to join the workgroup I would love to have you, because we are losing two very important people, so I can take too more. Right? Can I take too more? Maybe three people even, because you were on it too.

DR. EVANS: You can take up to how many?

MS. HOIBERG: Six.

DR. EVANS: Well eight, eight altogether.

MS. HOIBERG: Eight. All right, I just can't have nine of you.

MS. GALLAGHER: I think what we need to do maybe is have anybody who's interested e-mail Sarah, because there are other commissioners who are going to be sworn in for the June meeting, and so they certainly could

also join the outreach communications subcommittee. And I want to also remind everyone, again, if they think of anything after the meeting about the slides or they get the bright idea while driving home or taking the train, please e-mail Sarah and say, “You know what we forgot to say – blah blah blah.”

MS. HOIBERG: I do find that some of my best ideas come after the meeting. As I’m sitting on the plane I’m like, “Oh, I should have said that.” So yes, keep these close to you and drop me any notes, and I’d be happy to hear them and then I’ll pass them on to Geoff.

MS. GALLAGHER: This is really our first attempt to put anything out there.

MS. HOIBERG: Thank you very much. Thank you, Geoff.

MS. GALLAGHER: And we have more ideas coming up when it comes to the outreach and communications subcommittee, but we’re taking one step at a time, particularly as everyone knows that the federal government budget is completely up in the air right now. We have to wait and hear how that shakes out before we send you concrete plans having to do with a contract. We’re doing the best we can without having authority to go forward with a contract this moment.

Agenda Item: Petition for Adding Injury to the Vaccine Injury Table, Ms. Charlene Gallagher, Chair; Dr. Geoffrey Evans, Director, DVIC

MS. GALLAGHER: Okay, so now the next thing on the agenda is the petition for adding entries to the Vaccine Injury Table, and I would direct

everyone to tab seven in your book. On August 27, 2010 a member of the general public wrote to Chief Special Master Lord at the United States Court of Federal Claims and described her mother's illness following influenza vaccination, and requested that Guillaume-Barre Syndrome, commonly referred to as GBS, be added as an injury or a condition on the Vaccine Injury Table. Her letter, or what we're going to refer to as a Petition to Change the Table, was then referred on to the Advisory Commission on Childhood Vaccines on October 28, 2010, and that is what we're now discussing.

The National Childhood Vaccine Injury Act of 1986, as amended, authorizes the Secretary, after consultation with ACCV, to create and modify a list of injury, disability, illnesses, conditions and deaths and their associated timeframes, associated with each category of vaccine included on the table. In addition, Section 2114(c)(2) of the Public Health Service Act, 42 U.S.C. 300aa-14(c)(2) provides that any person, including the Advisory Commission on Childhood Vaccines, may petition the Secretary to propose regulations to amend the Vaccine Injury Table. So unless clearly frivolous or initiated by the Commission, any such petitions shall be referred to the Commission for its recommendations.

And then following a receipt of any recommendation of the Commission, or 180 days after the date of the referral to the Commission, whichever occurs first, the Secretary shall conduct a rule-making proceeding on the matters proposed in the petition or published in the federal register a

statement of reasons for not conducting such a proceeding. So I'm just giving everybody the background in case they haven't memorized the statute.

And now Dr. Evans, who's the Director of DVIC, will represent the Secretary's views on this petition.

DR. EVANS: Thank you, Charlene. As the Executive Secretary and representative secretary, I will state the following. The department takes seriously this petition to change the table, and it actually is the first petition that's been submitted in the programs 22-plus year history. The Secretary seeks the ACCV's recommendations on this petition.

Before you make that recommendation, I will remind you that in the past the Secretary has utilized the Institute of Medicine reviews of the medical and scientific literature of adverse events following vaccination in proposing modifications to the Vaccine Injury Table, and the IOM is expected to release a new consensus report in early summer updating findings on the possible causal relationship between influenza vaccine and GBS as well as many other VICP covered vaccines and injuries and medical conditions.

We believe the best course of action this time is to await the release of the IOM report, and at that point the Secretary will review the IOM findings and may develop proposed changes to the table. Following release, the Secretary will consult with the ACCV as is its statutory charge before going forward with any rule-making proposals to modify the table. So because of its prescribed role – proscribed role – in advising the Secretary on changes to the table, the ACCV must vote on the department's proposal, proposed response to

the general member of the public's petition. A Federal Register notice will be published later this year reflecting the outcome of the vote, and the department's decision in this matter.

MS. GALLAGHER: And I will first invite everybody's attention to the guiding principles for recommending changes to the Vaccine Injury Table that was prepared by the Advisory Commission on Childhood Vaccines in March of 2006, and that's also under tab seven. And there's a long list of considerations that we should take when considering changes, including review of the Institute of Medicine's recommendations when there has been a study of the specific adverse event. And they have already undertaken the study of this adverse event and the report is due out soon. It was delayed and I'm sorry that it isn't already available. But as of today we don't have it.

So I will make a motion, and we'll see if it's seconded. I move that the ACCV defer a recommendation on this particular petition until such time as we've had an opportunity to review the IOM report. And do I hear anybody second it?

MS. PRON: I'll second it.

MS. GALLAGHER: So now we can have discussion on my recommendation.

DR. FISHER: So Geoff, can we do that?

DR. EVANS: Well let me just clarify with legal counsel. The Secretary's proposal at this point is to not go forward with rulemaking pending

publication of the IOM report. It's that decision making, that position that we would like concurrence or --

MS. GALLAGHER: I amend my motion, that we – give me the words again.

DR. EVANS: That you concur if indeed you do.

MS. GALLAGHER: We concur.

DR. EVANS: You concur with the Secretary's --

MS. GALLAGHER: Secretary's --

DR. EVANS: -- proposed response to the Petition that's been submitted by a general member of the public regarding the addition of GBS to the Vaccine Injury Table.

MS. GALLAGHER: Okay, so my motion is so amended.

MS. SAINDON: Can I just clarify? This is Elizabeth Saindon from the Office of the General Counsel. The statute gives us two options. We can proceed with rulemaking or we can publish a notice in the Federal Register indicating our reasons for not proceeding with rulemaking. So those are really the only options that I see as available on the table. So the question is, do we go forward with rulemaking now or do we publish a notice in the Federal Register indicating our reasons for not doing that at this time?

MS. GALLAGHER: Okay, so then I move that we --

DR. FISHER: You have a motion to second. You can withdraw your second. Withdraw your second.

MS. GALLAGHER: So is it properly amended? Do you need the qualifications?

DR. FISHER: Why don't we withdraw it and start again.

MS. GALLAGHER: I withdraw my motion.

MS. PRON: I withdraw the second.

MS. GALLAGHER: Tom, why don't you make a motion?

DR. HERR: I propose that we publish in the Federal Registry that we are deferring a decision on this rulemaking until the IOM report, Institute of Medicine report is published.

DR. FISHER: So actually I think what we're doing is, we're agreeing with the Secretary to forego the change pending the IOM report.

MS. GALLAGHER: And I second that motion.

MR. KING: And now we have discussion on the motion. So just so that we understand, and for clarification, what we're saying is that we agree with the Secretary, we want to defer decision on this until after the IOM publishes it and then we'll review it then. Is that what we're really saying? No, we're saying no, we're never going to review this? Is that – no. All right, so tell me what we're doing here.

DR. EVANS: There's a 180-day window in which to either go forward with rulemaking or publish in the Federal Register the reasons, your decision not to go forward with rulemaking, explaining that. And it is the Secretary's decision not to go forward with rulemaking and is asking for advise and consent by the ACCV regarding that decision.

MR. KING: Just so that I understand.

DR. EVANS: Not to go forward with rulemaking at this time.

MR. KING: I guess that's so they may choose to then review this at another time?

DR. FISHER: Absolutely.

DR. EVANS: Right, what you – now this is extremely unlikely, but if the Institute of Medicine report were to come out and there were no proposed changes as a result of that, then there would be – there would not be clear, a need for you to consult and advise on that, but there's nothing to prevent you as a group coming forward with your own ideas about changes to the table. The point is, we do not have the benefit of the review of the Institute of Medicine at this point, but we do have the statutory clock ticking in terms of responding to this particular petition.

MS. SAINDON: And further to that, we don't need another petition in order to propose changes to the Table at some date later. So the petition comes in, we have a mandate to respond to it within a time certain, and then that petition is off the table. But the world is our oyster when the IOM report comes out. Maybe another petition would come in, maybe the ACCV itself would make recommendations, most likely the Secretary will bring recommendations to the ACCV.

DR. FISHER: So do we have a motion and a second?

MS. PRON: Can I ask another question? So is the only way this woman is going to get an answer is through the Register? Is someone going to -

- MS. HOIBERG: Yes, this is Sarah Hoiberg. She received a letter in response to her petition from the Chief Special Master but that's all I --

MS. PRON: She received a response to her e-mail and then she wrote this letter. We don't have a response.

DR. EVANS: The program has sent her by U.S. mail a letter notifying her that this was an agenda item for discussion. There has been actually a personal communication with the individual as well as the e-mail follow-up. It could very well be that she is listening to this discussion at this moment.

MS. GALLAGHER: Okay. I'd like to say here that even though the correspondence was not addressed to the proper party it was communicated to the right people and we received it as a petition, notwithstanding that it was done in good faith to the court but it wasn't the court's job to do that. So I think that things are working well in that it was treated with great respect and we felt that it was an important piece of correspondence to address, notwithstanding the form of it and to whom it was directed.

MS. PRON: Thank you.

MS. GALLAGHER: So do we have an appropriate motion on the table? We have a motion that's on the table, and --

MR. KING: So before we go, just so we – I want to make sure that we know what we're voting on here. So what we're voting on here is a resolution – I guess that's what it's called, right? – for – to say that we agree, support the Secretary's decision, is that correct? And that we are not going to make any

recommendation one way or the other, we're simply not doing it. And that's basically what we're saying.

DR. EVANS: You're supporting the Secretary's position not to go forward with rulemaking in response to the proposed change to the Vaccine Injury Table from this – in this petition.

MR. KING: From this petition?

DR. EVANS: Right. And after that --

MS. HOIBERG: We're waiting for the IOM report to come out, the Institute of Medicine report to come out. We'll review it and then see what they have to say, whether or not they're recommending or making – right? They recommend things, right, Geoff? And I know I use the wrong word all the time. What is it? They make suggestions?

DR. EVANS: I'm glad you brought that up again. Let me be clear. The Institute of Medicine will be evaluating the medical and scientific literature on adverse events following a variety of vaccines, medical conditions, and will be characterizing the biological mechanisms, some of the theories that have been put forward, and will be publishing as they've done in the past – and no reason to think they'll be doing differently this time – a table with five categories that weighs the various levels of evidence having to do with causation. The Secretary will receive the report, evaluate it, and then come forward with proposed modifications to the table that you will review based on the evidence categories that the Institute of Medicine puts forward in their report. But they do not make recommendations for changes to the Vaccine Injury Table.

MS. HOIBERG: So we're waiting to see what they have to say, what the evidence – we're waiting for the science.

MR. KING: There's a 180-day window.

MS. HOIBERG: Right, so we're responding right now to it, correct, Geoff?

DR. EVANS: We're responding because of the 180-day (?) 00:59:32 within the Statute. And what we're proposing is a – what we need from the Advisory Commission on Childhood Vaccines is a motion to support the Secretary's decision not to engage in rulemaking to amend the Vaccine Injury Table in response to this petition.

MS. HOIBERG: At this time.

MR. KING: I don't think it's at this time. I think that's not part of it. This is it.

MS. GALLAGHER: This is it. This petition?

MR. KING: Yes, this petition.

MS. HOIBERG: So we're not ever going to look at it again?

MS. GALLAGHER: Right.

SPEAKER: Not this petition.

MS. HOIBERG: But then we can turn around and say, oh I really think that GBS should be added to the Injury Table?

DR. EVANS: Exactly. This is this particular – this is this specific circumstances has arisen. Now if I were to guess what would be one of the top five or 10 questions that will be surrounding release of this report, I would think

that one of them would be the possible relationship between GBS and influenza vaccine, which is what this petition is directed to.

MR. KING: So what we're saying is – just to make sure because I want to make sure we know what we're doing here – what we're saying is that we're not going – that we're going to support the decision of the Secretary to not make changes as a – from – as a result of this petition. And that's it?

DR. EVANS: And that's it.

MR. KING: And that's it. So we can discuss this motion, right?

DR. FISHER: Right.

MR. KING: So my question on the motion is, what happens if we choose not to approve this motion? What are the ramifications of that?

MS. GALLAGHER: We need to publish the reason in the Federal Register that we did not go forward with rulemaking for this --

DR. FISHER: No, no, that's not his question. Suppose we vote down this motion.

MR. KING: Right. What happens? What are the ramifications there?

DR. EVANS: The Secretary will receive – the secretary will – you're the advisory bodies of the Secretary of Health and Human Services, she will receive your advice, take it into consideration and publish a response in the Federal Register.

MR. KING: So she could choose to ignore our advice, is that correct?

MS. SAINDON: Absolutely.

MR. KING: That's okay, that's all right. I just want to know what we're doing here.

MS. GALLAGHER: We are the advisory commission.

MR. KING: Nothing wrong with that. It's okay.

DR. FISHER: So we have the motion and the second?

MS. GALLAGHER: Yes, and I don't know – you were asking me how they read. Should I read into the record what I think it is even if the words were slightly different before? The motion is to support the Secretary's decision not to go forward with rulemaking to amend the Vaccine Injury Table in response to this petition. Okay, so now – is there any more discussion or is it time for me to call a vote?

MS. HOIBERG: I second the motion.

MS. GALLAGHER: Okay. Any more discussion? I don't want to cut anyone short.

MR. KING: I guess the only discussion, the discussion has to be pertinent to the motion. So if the motion – but we're chartered here. We can – we don't – the IOM, we don't have to always look at their results. We can choose to look – is there any other medical basis that this person brought to the table? Or was it just all the anecdotal evidence that they provided? Is that what happened?

MS. GALLAGHER: It's just this letter.

MS. HOIBERG: My question is, or I guess my feeling behind it is that if we were to make – if we were to advise the Secretary to add GBS to the Table of Injury and then the IOM report were to come out and there were to be no scientific evidence towards that, then we would really have no leg to stand on. If we wait for the IOM report to come out, and there is scientific evidence, then we can make the recommendation and we have something to stand on. I think that we would have more of a pool in a way – I know we don't have a pool, but we would have evidence to state that GBS is not caused but can be caused by, can be brought on by --

DR. FISHER: And we would be following our own recommendation.

DR. EVANS: Just as a point, I did not recall this but the petition does not indicate which vaccine GBS should be added for as an injury. Just as a point of clarification. Nor any timeframe for that matter.

MS. GALLAGHER: Yes, different vaccines including influenza. So everybody in favor of supporting the Secretary's decision please raise your hand. (All in favor.) All right. And anybody opposed? (None opposed.) The motion is carried and we will support the Secretary's decision not to go forward with rulemaking to amend the Vaccine Injury Table in response to this petition. Thank you very much.

DR. EVANS: Let the record reflect it was a unanimous vote.

MS. GALLAGHER: It was a unanimous vote, for anyone just listening on the phone. And thank you very much.

MS. WILLIAMS: Can we send our appreciations to the public for bringing this matter to our attention?

MS. GALLAGHER: Yes, absolutely, and as I said, I think it was important for the member of the public to write to the judge and to bring this matter forward, and this is what we encourage people to do, and I don't think that this is the last time that this Commission will be talking about GBS or adverse events. But the Institute of Medicine has been putting a lot of time and effort in, and it really has done and I think that we should at least have a look at what they have to say.

MS. WILLIAMS: This is Michelle Williams. I think we should commend Chief Master, Chief Special Master Lord for handling it the way she did.

Agenda Item: Public Comment

MS. GALLAGHER: So at this point it is time for public comment. And Operator, could you please make the announcement that we are taking public comment, and then when you're ready I will poll the audience here in the room first and then we will go to the telephone.

OPERATOR: At this time if you would like to make a comment, please press "star 1."

MS. GALLAGHER: Are there any members of the audience present who wish to make a public comment?

OPERATOR: At this time no one has queued up.

MS. GALLAGHER: All right, and we have no members here, or no members of the audience here who wish to make a public comment. So I hereby adjourn the meeting until tomorrow morning at 9:00 a.m., when we will finish with any unfinished business. Thank you.

(The meeting was adjourned at 4:36 p.m.)