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P R O C E E D I N G S (9:00 AM.)

MS. GALLAGHER: Good morning everybody and welcome to second day of our meeting. I believe that we finished all the business from yesterday so we are going to start with our very first agenda item for this morning and that would be the clinical update from DVIC. Dr. Rosemary Johann-Liang will be presenting that for us. So she is coming to the speaker right now and we will begin with that. Good morning. Thank you.

Agenda Item: DVIC Medical Analysis, Dr. Rosemary Johann-Liang, Medical Officer, DVIC

DR. LIANG: Good morning. I am Rosemary Johann-Liang and with me are Dr. Barbara Shoback, who is an adult rheumatologist with our group, and Dr. Tom Ryan, who is a family practitioner within our group as well. I am going to go over the quarterly update of what has been reviewed in the last -- let's see, the first quarter of the fiscal year 2011. It starts in October, our fiscal year. Then I will ask Drs. Shoback and Ryan to review with you our current experience with HPV claims and meningococcal claims and I will explain why -- we just cannot tackle everything within these sessions, but we thought it would be nice to tackle that young adult, adolescent age group. You will see why based upon the slides prepared for you.

So this is the outline we will first talk about and I am going to concentrate today on the non-autism medical reviews. If you would like, we could do a whole session. There is so much information about the autism from the clinical and medical perspective. We have so many of these cases

being submitted but today really we would like to focus on the non-autism medical reviews.

Then I was asked by Dr. Evans to give a quick update on the rotavirus vaccines on an intussuception issue and basically what I have prepared for you is one slide. It is really not a slide. It is just for your reference that summarizes the current post-market experience for both Rotarix and RotaTeq, side by side, so that that would give you a good reference moving into the future as hopefully some of these studies are ongoing, finalize their information and we can get some more data.

Then as you heard and discussed yesterday, we are gearing up to receive the comprehensive review of adverse events from the Institute of Medicine this year. In preparation, our group has tried to look at in a systematic way, which really has not been done for many, many years in group information's of looking at, for example, adverse events. So if you have anaphylaxis, what kind of claims do we have and tried to have an understanding of what our claims experiences are.

Or, we will look at it from the perspective of the vaccine. If we are looking at HPV, what is experienced that way? Hoping that looking at our own claims database information will help us as we move towards updating the table. That goes to kind of what you guys were discussing yesterday and we can talk more about that.

Keep in mind though our database is a medical legal claims database and there are confidentiality issues so we really are cognizant of that -- of the folks who are applying to the program and we really try to be careful to look at groups of information rather than one case at a time.

We cannot obviously share everything today and we would hope that these different sessions moving to the future we can discuss different projects but I wanted to follow up on the SIRVA, which was presented by Dr. Atanasoff in our last session -- that it has been published. I also wanted to talk about anaphylaxis case series, which is in press and it will be published shortly and also our syncope is something that we just are looking at that Dr. Ryan will actually discuss in a little bit.

Okay, so that is sort of what we will talk about this morning. He was kind enough to make a special, give you guys pretty slides today. I am a pediatrician. I believe in primary colors.

So as you can see, a picture tells a thousand words, right? We have lots of these claims coming in in the last three years. The curve is just straight up so we have been very busy trying to grapple with the changing landscape of the claims coming in -- the numbers, the pure numbers that are coming in.

Most of these non-autism cases you really cannot really template it either. So every case really needs a pretty substantial medical analysis. It is a lot of work. Just reviewing the case and the generating a report is not the end of the story. The case has a lifecycle of its own and the managing of the case through its lifecycle in collaboration with our Department of Justice colleagues that is a lot of time for our reviewers as well.

So this is the last three years: number of claims and these are non-autism claims and they are increasing. I just thought well how can we explain why the increase? It really works out nicely. This is the hard data. I

mean this is -- what I did was I asked how many of these increasing claims in the last three years were due to allocations of flu vaccine and HPV because that is what we are reviewing a lot. As it turns out, if you look at the numbers, the purple is the total number of the claims increasing. This is on the left side. And the yellow is the flu claims that are going up over the last three years and the HPV in the blue. So everybody see that on the left side, right? But that is really just the number of claims.

The last couple of times we did the clinical update, one of the Commission members had a really good suggestion. I really try to go back and incorporate that information, which was is there any way for us to look at more of a broad denominator data, which is information we do not have in-house. Obviously, this is something that we would have to go to find, which is the how many of the vaccines were actually given and is that is what is reflected in the number of claims coming in? In fact it is but we didn't have the data last time to show you.

I have that today and this is the CDC biological surveillance data from 2005 to 2007 that was supplied by CDC. Basically, what this shows is when our claims come in almost all datasets are kind of bell-shaped curve but the majority of claims, if we get to review a submission that came in in 2010 and we look back, usually the vaccination that is alleged happened in 2007. Do you guys understand that?

There is a three year lag to the claim coming in because of the statute of limitations for a non-fatal event. I mean if it was a death claim they really need to file within two years but for the majority of our cases it is filed within three years. So we do have some claims that are actually the

immunization, I mean the vaccination, the alleged injury happened two years ago or what not, but the majority of the really falls within that three year timeframe.

So this is a good way to compare the three years. Three years of claims going up, but then if you look at sort of the broad denominator what is the distribution of the flu vaccine and the HPV vaccine looking three years back? So that would be 2005, 6 and 7 and in fact you will see that in 2005, flu distribution -- now is the net dose distribution data from CDC, which is how much they gave out, how much they collected back so subtracting what they have remaining.

This is the data from 2005 and you can see the substantial rise of flu vaccine dose distribution over those years and I believe the preliminary distribution data for seasonal flu for 2010 is now in the order of 160 million plus. So it is really the amount of flu vaccine that people are receiving really driving the number of claims that are coming into our program. I think the data speaks for itself.

Any questions right there?

DR. HERR: That is really nice to see that you are showing a denominator.

DR. LIANG: I listen to you guys and I try to present it so that it makes sense. It does make sense if you think about the claim, the three years and you actually plot the graph it just comes out very nicely. So that kind of explains we actually have an answer sometimes in medicine, which is nice.

So going back to now our analysis for the fiscal year 2011, the

first quarter, so that would be October to December, three months timeframe. I want to tell you that the numbers change now so don't get confused. This is not now the claims filed during that time. This is actually what our reviewers were assigned and reviewed and generated a report.

Even if a claim was filed if there are not all of the records available to actually doing analysis, we cannot really analyze at that time. So that would be assigned sometime later on. The numbers do not correlate in that way. These are the number of new cases that a medical reviewer has reviewed and generated an initial report with an initial recommendation. Of these 122 were non-autism reviews. There were a couple of actual new autism claims and the rest of it are what we call the activated autism claims. We are still doing the trail end of activated autism claims, which are pretty much on hold right now because of what is happening with the Omnibus Autism Proceedings. So 122 were non-autism reviews.

Surprisingly -- I worked for many years at the FDA in the drugs part and in the adverse event drug reporting system we always had kind of more females reporting in than males, but surprising for this group the gender was pretty equally split. It was like 50 percent males and 50 percent females.

This is looking at age bands with all of the primary colors here. I thought this was really instructive, especially since we have a lot of new folks in the Commission. The green bar is actually fiscal year 1998 so like twelve years ago. The red bar is ten years later. If you compare the green bar to the red bar you will see the dramatic change in the age bands distribution of the claims coming into this program.

In 1998 almost 70 percent of the claims are in little babies,

babies less than two years of age. Whereas in 2008, the red bar, you will see that it is now more distributed equally over all of these age bands with the shift to the dotted line coming down in the middle separates out for you what we usually call pediatrics. You know people less than eighteen are considered pediatrics that we see in the clinic and the older ones, eighteen and above, are adults.

You can see actually the adult claims, if you total them up more than Peds now starting with 2008 and then 2009 is the yellow bar and then 2010 that is where we are most closest to where we are now. In 2010, you can really see that the real adult, 50 and above, that blue bar, that is really where the distribution of the age bands are going.

Again, the next slide really this is the data I will talk to you about for the first quarter of the fiscal year. This is the actual ages of the folks that our reviewers, our doctors reviewed in the first quarter of the fiscal year 2011. The age distribution is similar to what you are starting to see for 2008, 2009, 2010 except that now it appears that we are actually getting that two to seventeen year olds -- so this would be the adolescents -- and the eighteen to 29 year olds -- so adolescent, young adult claims. It is primarily driven by HPV. That is also a lot of the new cases that I am assigning.

We will talk about the two to seventeen year old in the context of Dr. Shoback's HPV presentation. For this adult age group I thought -- I was trying to look into CDC website. They have so much information in there, in case you were interested and had nothing to do you can kind of -- but one of the things I thought of regarding another way of looking at vaccine distribution from the perspective of age groups was -- this is actually flu coverage trends

for the same period we talked about, 2005 to 2008, which would translate to the claims that we are reviewing right now three years later.

You will see for those three adult age bands, their age bands are a little bit different. They actually break out the 50 and above to two age bands. You can see that there is a gradual trend up for adults being covered with influenza. This is really just the National Health Interview Survey. This is just asking people if they get the flu vaccine or not.

DR. HERR: Okay, Tom Herr again. Interestingly, we see the rise in the more mature adults, but why is there a decrease in that middle age group if you are looking at the 30 to 49.

SPEAKER: Which slide are you on?

DR. HERR: I am still looking at this one way back.

DR. LIANG: I am sorry. I just stopped.

DR. HERR: Under the 30 to 49 age range. Interesting why has that going down?

DR. LIANG: You know I am not sure.

SPEAKER: What has gone down?

DR. HERR: The number of claims; the percentage of claims.

DR. LIANG: From 2008, 2009, 2010 -- why is it more of adult? It is hard to explain. Maybe we will have to look at those trends over time because you are looking at 30, 29 to 15 percent here. That is hard to explain, actually, because if you go to here -- although let me see. Thirty-nine, nineteen percent, we will see how it pans out this year 2011, okay Tom. They are kind of within the range of -- there are no confidence levels here or anything. They are just absolute number of claims coming in.

If you look at it over here, all of those age bands are increasing as far as if you ask them a health interview did you get a flu shot or not that is also an age group that is increasing. So I am not sure. That is a good question. We will keep an eye on it to see why those folks are not putting in more claims than the older age group.

MS. HOIBERG: This is Sarah Hoiberg. To me it just shows like when you compare these two charts, it is the older age group of course that is getting the flu vaccines. That is a pretty high rate of injury claims in comparison to how much is -- that is a lot of injury being claimed for that age group.

DR. LIANG: Which slide are you looking at?

MS. HOIBERG: I am looking at if you compare the two together like in 2010 you can see the blue on this one and it is up at, what is that 40, almost 40 percent, 33. This is who got the shot, right? This is not injuries. This is who received the vaccination.

DR. LIANG: This is just asking -- so if we look at the slide that I have up right now, this is asking people in those age bands did you receive, by interview, you know CDC staff is asking them did you receive the influenza vaccine? They are looking at these are calendar years in 2005, 6, and 7. What this is saying is that for older than 65 years folks in 2007, over 60 percent said they received the influenza vaccine.

If you remember in 2007, if we go there, what was the distribution of that? That was about over a hundred million doses. We are talking about a lot -- that is in millions. We are talking about a lot of doses. That is percent of people saying that they represent reporting so you cannot

really compare. This is saying 60 something percent of adults greater than 65 years actually receive the influenza vaccine.

MS. HOIBERG: And then 30 in 2010, there is like 33 percent in that age group that is claiming injury, right?

DR. LIANG: Okay, yes I see what you mean.

MS. HOIBERG: That is half.

DR. LIANG: No, so let me explain to you. If we look at this slide, this is showing by age band what percent, how much percent proportionally were in this age bracket. That really doesn't account for -- that is not talking about the number of vaccines. It is the proportion in our database, what proportion were that age bracket that were claiming. Do you understand? That is different than actual doses.

In other words, if 100 people file to the VICP in 1998, 70 percent of them were in little babies. Now 33 percent of them, or 32 percent of them are in people, mature adults, 50 and above. So we are just looking at proportion of people filing claims by age band. That is different than --

MS. HOIBERG: That is different so these two right here you cannot really compare these slides.

DR. LIANG: Right.

MS. HOIBERG: Okay.

DR. LIANG: The only thing you can really compare and look at is the one that I gave you between the distribution and the absolute number of claims being filed and the explanation that the claims are actually flu and HPV. That is a distributions data and that kind of -- the curves look similar. That is really, the other ones you cannot really compare.

MR. KING: Could you stay on the last three years of comparison slide for a second just so that I understand it. On the dose distribution, which is the net, meaning that we have tracked what has come back, so the HPV, what is the actual number there? I noticed -- is that is that a ten?

DR. LIANG: It is in millions.

MR. KING: So I have a little over a hundred million of flu. Is that correct? Then I only have ten million or so of the HPV?

DR. LIANG: In 2005 there was no HPV. I believe in 2006 when it first, where it was starting to be distributed.

MR. KING: You know what it is? I am looking at the chart and comparing it to the other one. I am saying wouldn't it be nice if you had it in the same format both of them to compare each other. Then it would be easy. So I don't have a total on my vaccine dose distribution, unless I calculate it in my head versus. You see on the left side of the screen where you have three?

DR. LIANG: The number, they are not the same scales.

MR. KING: I have no problem with the difference of the scale.

DR. LIANG: The number of the vaccines. This is the total distribution in millions.

MS. HOIBERG: So there is a hundred and ten million HPV or is it just ten?

MR. KING: I want to interpret the chart correctly and because you have it plopped on top of the bar, I do not have the clarity that I want.

DR. LIANG: Got it, got it. It would have been better if we did it like the other ones.

MR. KING: Exactly. Could you just tell me what it is so that I know that I am reading it correctly or understanding it?

DR. LIANG: I think it was like four million in the 2006 and something like I don't know, seventeen million. Do you know what I could do? Let me see.

MR. KING: That is good enough and the next time we can separate it out so that it is easier to read it. Thank you.

MS. HOIBERG: It looks to us, I mean at least to me it looks like there was like we are close to over 110 million distributed because it is kind of sitting on top.

DR. LIANG: Right, so there was a hundred and then about sixteen, seventeen with the blue on top; fifteen, sixteen million. I have the actual numbers behind the graph because that is how you make the graph but then we would have to get out of this slide set and all of that.

MR. KING: And you don't need to do that.

DR. LIANG: I got you. You want it to be done like that.

MR. KING: Yes, so the real value of the slide when we have it and when we look at it is it tells us that on the left side that there were roughly a hundred eighty or so flu vaccine claims in fiscal year 2010 and that it was driven by slightly over a hundred million actual dosages given and therefore you can then calculate what the actual percentage is. Perfect, thank you.

DR. LIANG: I just want to put a little caveat, too. I am sure CDC would agree. The dose distribution is actually not the actual dose given. It is not like one to one. It is what is distributed to people. Pediatricians may have some things on the shelf and then it gets sort of chucked at the end of the

season. So it is probably a little bit of an over estimate -- probably not an under estimate -- an over estimate of how much was actually given, the distribution. Does that make sense?

MR. KING: That makes a lot of sense. So the question is there any way to pin a number of what that estimate is on the over estimate.

DR. LIANG: That is the difficulty. We talked yesterday about the registry and things like that, but not all states do it. I don't think there is a national registry per se and one of the ways CDC tries to do it, especially to identify subgroups to make sure that people are receiving vaccinations is do things like this National Health Interview and then nationally they ask, they pick random samples and ask for people who smoke. How many people who are in renal failure? How many people actually take this vaccine and that is how they kind of do it.

Not everybody in the country is registered to a database that tells you what kind of risk factors you have, which vaccines you receive. Unfortunately, we don't have the exact data, but this is probably the best we can do, the net distribution of dose.

MR. KING: And this is valuable. I just was wondering if we had a variance that we kind of knew that we would be able to estimate and say we are missing it usually by ten percent or we are missing it by eight percent. Is there a scientific guess out there where people have an estimate of what we don't actually get back because it might be sitting on shelves or things like that. There is no estimate? There is no guess that people make on that?

DR. LIANG: I think the best that is done is that CDC would give that a bunch of vaccines and then they will try to bring back as many that

have not been used. This is the net data. So that is probably the closest that we can get but I am just trying to explain that is not really one on one. I couldn't present this data and just say this is the number of vaccine doses received. It is really just the net distribution, hoping that we captured all of those things back that really actually were left there. Does that make sense?

MR. KING: It does make sense and what it sounds like is that we are not making a guesstimate -- if we can call it that -- on the number that does not come back.

DR. LIANG: Actually, if you are interested I do have that aggregate number for other vaccines. I think for flu, I only receive from CDC the aggregate total, but for like tetanus and HPV they actually present the data out in the total number of vaccine doses distributed and the number that were actually received back and then they report out the net. So they do try as much as possible from the CDC's perspective to capture that information but I don't know of anything else more granular than that at this point in time.

MS. PRON: I have a question related. This is Ann Pron. Does all flu vaccine now need to be purchased from the CDC or do people still purchase it from private companies? Then how would you even track that?

DR. LIANG: You know what they do purchase it through private means and not all through CDC. I think that is also tracked by CDC as much as possible by requesting information from manufacturers. Everything is not exact. There is no -- so it hard to say one on one.

MS. PRON: The best guess.

DR. LIANG: It is like that in drugs, too. The way you figure out how someone actually got the drug, even if the manufacturer said that we

sold this many drugs, that may not be exactly how many doses people actually received. Then you go to the database that is looking at how many were actually prescribed. So there are many ways to capture that information nationally.

As we go more and more electronic for all of this kind of information, we are hoping that kind of information will become more and more tighter and more precise as we develop data networks. But there really is no exact way to know one for one.

MS. PRON: I have another question. Does the flu data reflect all types of flu vaccines -- the live virus and --

DR. LIANG: Yes. All I have is really -- I am unable to get the aggregate total dose distribution data. Starting in 2009 I think they are, I am sure, capturing H1N1 monovalent distribution separately from the seasonal but as you know in 2010 and 11 now H1N1 strain is now folded into the trivalent so that is something that comes to us now and again for review for seasonal flu vaccines. As this data moves forward and we look at it, you will see some of the breakdown from the H1N1 and hopefully we will be able to get that kind information as we move forward. Okay?

MS. PRON: Thank you.

DR. BERNSTEIN: This is Jessica Bernstein. I have a question about the graph with the primary color bars. What I am wondering is when you see the claims for 50 to 85 year olds increasing from ’09 to 10, is that actually an increase in the numbers or is that reflecting that some of the younger age groups like if all of the blue bars have to add up to a hundred and some of the other age groups have decreased then you are not

necessarily seeing an increase in the absolute numbers of claims. Correct?

DR. LIANG: Right. This is really by proportion in age bands for that year captured.

DR. BERNSTEIN: Right so just by the fact that other age groups have declined it looks like there is an increase but that doesn't mean there is an absolute increase in the numbers.

DR. LIANG: Right, I mean it is proportional to the other ones are decreasing then -- right.

MR. KING: Although, it could. It could be because of a real increase in numbers, but you are saying it doesn't have to be.

DR. BERNSTEIN: Right so I guess I am asking was there a real increase in numbers?

DR. LIANG: Yes, but you are right. This is really to show the trends over the years, the fiscal years, taking a whole year and saying how did the age bands proportionally work out by the proportion? I mean we can report out the actual numbers but then it is hard to do the comparison over the different years.

It is just one way to present the data but I am glad you are asking the questions so we can all understand what these things mean. Anything else? We have a lot to cover. We are going to be here all day at this rate.

Now for the first quarter, so let's just focus now on that because I usually try to do quarterly updates because otherwise it is just too overwhelming. So this is the three month period, all of the medical reviews and what vaccines were alleged for those medical reviews that folks did.

Again, by far look at this. This is a different way to look at the data again. It is flu and HPV that is really the bulk of the allegations for vaccines and we do have tetanus is up there, ten percent. We have infant series and this is really you know the babies getting the two month, four month, six month but you can see how proportionally again looking at if we look at all of these vaccines and all of the claims, the denominators total number of claims that was reviewed during that three month period proportionally which were the alleged vaccines in that cohort. Okay, so that is kind of how it pans out right now. Every time I present this table it will changed because depending on that quarter we may have some claims that are like Rotavirus may be more or MMR may be more, et cetera. I don't believe we had any MMRV during this three month capture which I did have I believe the last time we had this talk. So it varies over but this is what we have reviewed during that quarter.

This is just for your reference. We have a lot of acronyms going because many of these things we just cannot get straight ourselves so this is just to give you a reference. I wanted to say the severe myoclonic epilepsy at infancy that is really more. Do you know how in medicine people keep changing terminologies too? This was characterized clinically by a physician named Charlotte Dravet, in 1978, and so as people and there is a lot of information now being characterized and I know people have asked about encephalopathy yesterday and the underpinning of genetic factors for in seizures. This is really more, should be more in vogue termed for Dravet Syndrome and not as MEI anymore. So we have to keep up with that too.

The Complex Regional Pain Syndromes also have a whole host of different names: causalgia and reflex sympathetic dystrophy, RSD but for

now these are some of the terminologies that you may be seeing when some of the slides go up from the Department of Justice in their settlement claims as well as when we present our medical information.

Now this is really after the medical officers have reviewed the reports, what were their final sort of diagnosis of what the patients had, not what was sort of alleged coming in. For example, there were more GBS claims being alleged but actually when you review the information it is not GBS. It turns out to be CIDP or some other none specific neuropathy. Some of these people may have diabetic neuropathy that is sort of, that disease in itself has sort of waxing and waning picture so it happens that when they had the vaccine their glycemic index was up. When you actually do the reviews some of the alleged diagnoses may not actually hold after review.

Of interest in this quarter anyway was as compared to last time we reviewed, we had a lot of genetic and underlying disorder cases and we actually I think had three mitochondrial cases during this cohort. We had three I believe Dravet variants and that is also because these genetic tests were not available and now they are becoming more available. There are sodium channel mutations and there are different variants. There were several chromosomal syndromes within this cohort as I spoke about diabetes and diabetic neuropathy, people with underlying disorders, renal failure and a whole host. Thirteen percent of our actual that three month cohort actually had some sort of genetic or underlying disorder which I thought was very interesting and something that we really need to keep our eyes on because we are always looking for possible underlying populations that may be at increased risk of vaccine injury as well.

Anything else? Any questions on the last several slides?

I apologize right up front. This is for your review or reference benefit and this is not to go over any more Rotavirus talk because I saw the slides from Dr. Gruber. Dr. Gruber gave you a long beautiful Rotavirus talk last time, the same time that Barbara and I were at ACIP actually. The information that she presented is pretty much in line with the information that we heard at ACIP at the same time. That was the latest information. There really has not been anything further. I know that during this most recent ACIP there really wasn't any Rotavirus update.

The reason why I put it side by side is because it is a nice way to sort of think about them moving forward. You all know that Rotarix is really from human and the other one, RotaTeq is really an assortment. You remember the RotaShield, the one that got withdrawn. That was a monkey driven and so there are differences in where the actual virus strains come from. The Rotarix really is distributed more Ex-US and RotaTeq is really is used in U.S. and this is part of the problems is how we are having trouble tracking the safety because there just isn't enough information in the U.S. of RotaTeq is as the denominator to really hone in on is there an excess risk or not. If there is it is a very small excess risk of intussuception but it is hard to say right now. In pre-licensure there really wasn't anything based upon that number and you have the numbers. It is something in the order of 30,000 for each of the vaccines versus a similar number in placebo and there really didn't see any increase in intussuception for both vaccines but then going into post marketing you have one which has Ex-US information and that is the one that went into most recent labeling, the Rotarix.

We actually, Barb and I actually met the woman who is the Director of the Mexico Health Services, whatever and you know we asked why they used Rotarix instead of RotaTeq. They only sold Rotarix in Mexico and it really just comes down to they compete, I guess, for how much that the government is willing to buy and I guess Rotarix won out as far as how much the government was willing to contract with GSK versus Merck and that is the only reason why Rotarix is given in Mexico.

This is the information that we have thus far. I am not going to go over it because guys already heard this from the last talk but if you have any questions that I will be glad to answer based up on information in front of you. I hope this will be helpful to you to have as like a cheat sheet of anything that is sort of ongoing right now and then we can add to moving forward. Okay?

You heard this before a couple of times and you are going to probably hear a lot of this year about IOM and adversary event review. It is just to let you know that we have asked them. We have charged them not only just to look at the clinical anatomy experience but also to look at biological mechanisms as well. So it will be interesting to see what comes in but they are reviewing eight vaccines, twelve antigens and it is due in.

Our charge and with your help moving forward is going to be to take the vaccine injury table that we have because remember to compensate someone if it is a presumption of causation that is on the table, it makes everything go so much faster because we at the clinical folks can actually make an initial recommendation to concede based upon table. It is really important that we update the table with the most current science and keeping

in mind what the whole philosophy of the program is all about so that is going to be happening this year.

Let me just go right into any questions on this slide

This is the one that is published that Dr. Atanasoff gave you a nice presentation about our observation of the adults and we felt that this is something that really is real. We do see cases that we think presents this way and we are able to characterize it. We were able to characterize it in a more detail minor by grouping this information together and seeing what are the characteristics of these folks who present with a shoulder injury related to vaccine administration.

Then I want to briefly go over the analysis of anaphylaxis.

MS. CASTRO: Just a question. Now that you have the paper and the results, are you going to present that at the NVAC?

DR. LIANG: Well since it is presented now, what should we do about presenting to NVAC? Did somebody present this information to NVAC or give an update?

DR. EVANS: We are not able to. We are not able to circulate the paper yet.

MS. CASTRO: We talk about the fact that the paper will be coming out with some of the preliminary that you talk about without any details as to who was not published but I think it would be of great interest in terms of preventing injury given the findings that you have in that research.

DR. LIANG: Right, you are absolutely right. We would like to disseminate the information to the public in a variety of channels, right Sarah, the outreach group.

DR. EVANS: I just learned from the office that we have now official permission to distribute the paper electronically. We have the copyright. We have permission to distribute the preprint version on our listserv so it will be getting wide distribution.

DR. LIANG: There are copyright issues but we are the government so it shouldn't be too hard. It's never easy.

MS. GALLAGHER: Excuse me for one moment. Can you just for the benefit of the new Commissioners describe briefly the findings? We are all aware of it because you presented it to us. They do not know what the paper is about.

DR. LIANG: I would be glad to brief you. Should I put Sarah on the spot to explain? She doesn't mind being put on the spot.

MS. GALLAGHER: Just a thumbnail sketch so they are following the discussion.

DR. ATANASOFF: Over the course of our reviews of cases we started noticing several cases that kind of stuck out where we thought that it looked like, based on what patients were reporting in the medical records where they would say that the vaccine was administered too high or it hit something hard and there were about thirteen of those that we identified. Not all of them mentioned that the vaccine administration factor but a number of them did. So we tapped into our database looking for shoulder injuries and other claims that match that have been from the vaccine administration rather than neurological injuries and we found thirteen total. It didn't seem to matter what the vaccination was. Basically the features of these patients were that the onset of pain was immediate and that they developed usually painful

limited range of motion and many of them went on to require injections or surgeries. One particular case actually required a removal of a small section of bone that was necrotic. From those thirteen cases we have sort of a set of a kind of internal criteria to help us identify future cases where these patients never had a problem with their shoulder in the past. The onset of pain was immediate and then they go on to have sort of a set of symptoms that seem to be characteristic of the injury.

I am not sure what else you want.

DR. LIANG: The reason for that is if you could just talk about why that is, Sarah.

DR. ATANASOFF: What we think and when we reviewed the literature there was only, there was one case report of two cases where they had looked into sort of similar findings that we saw in our cases and they did ultrasound studies and they felt that hypothetically that the needle could actually penetrate into the subdeltoid bursa and it is connected to the subacromial bursa and you could set up a very robust immune response leading to damage of the tissues within the joints basic cells and limiting the range of motion eventually leading to things like adhesive capsulitis, et cetera. So that is kind of our hypothesis and we worked alongside of a rheumatologist, who is on our panel, who helped us kind of flush out that idea. We cannot exactly prove it but that is what we think is happening.

MS. GALLAGHER: So would you say you characterize this as an inadvertent misadministration and you were saying that you did not seem to see a difference among or between the vaccines but merely where the needle ended up?

DR. ATANASOFF: Right, it is a factor of where the vaccine is actually being administered versus the actual antigen that is being administered.

DR. HERR: Technique? Is it a technique?

DR. ATANASOFF: Some of it may be technique but some of it also has to do with in some people the bursa can actually be lower and so it may be the right area, but maybe the needle length is too long. A lot of things could contribute -- using an inappropriate needle length or if the patient is seated and the provider is standing so it is better to have them both at the same level. We prefer seating for both because there is the risk of syncope too. Sometimes you can actually pinch the tissue, as well. I think that was in our article but there are a lot of things that can help prevent the injury from happening.

MS. HOIBERG: This is Sarah Hoiberg. Have you actually made it widely known that the way to properly administer the vaccine is both seated?

DR. ATANASOFF: We made it basically our suggestions, but I do not think we are in a position to make the recommendation, as far as I think that is more CDC.

MS. HOIBERG: Well is there any way that CDC could do that, Dr. Gidudu?

DR. GIDUDU: Probably they would review this and then have that study going.

MS. CASTRO: Yes, I think the importance of this is that it gets to the right hands to make the right decisions and recommendations on

vaccine application or whatever. I think it is a good study and it would help prevent more injury.

DR. EVANS: This is a real win-win as far as we are concerned. It has come up with a unique medical condition from our records as something and if you were to publish it. General recommendations or work group for ACIP is always revising the general recommendations. Certainly they are going to be made aware of the paper and they are another immunization technique video tapes and pamphlets that have produced that they have been utilizing for this part of that. So we are going to make sure that this gets to wide distribution and we will incorporate it with other information about suggestions for sound administration technique.

DR. ATANASOFF: I can't remember if somebody on the panel last time asked if there was a geographic distribution. If it depended on what state they were in. Was that you? Oh, there was not. Basically there were all different states. I think two came from one state but other than that there did not seem to be any pattern with regard to that.

MS. PRON: Will this Commission get copies of that link or whatever you are going to send out wide distribution of the article?

DR. EVANS: We will be certain you will get copies of the article.

MS. PRON: Great.

MS. GALLAGHER: Thank you very much for just doing that on the spot but I think that was very helpful to the new Commissioners.

DR. LIANG: As you spoke about the issues that it is not on the table right now but one of the things that we would like to tackle was the table revises, just general administration issues. A start off would be one of the

issues. It seems like these are also not vaccine specific. It is just certain populations faint when they get needled and it could be from a blood draw as well but it is something that we are also seeing in our claims as well as published regarding the various data and other information. There is enough published about that but that is also administration problem.

DR. GIDUDU: Rosemary, would you be willing to present this paper to the General Recommendations Working Group?

DR. LIANG: Yes sure, absolutely.

DR. GIDUDU: Probably I can link you with.

DR. LIANG: I know the General Recommendation just came up with some of the recommendations about patients sitting and lying down because of syncope signals so I think that this would also shed a light about it is important to sit but the person who is actually injecting, there is nothing about the position of the administrator so that would be something that we can actually add to that information so okay that would be great.

So let's go on to anaphylaxis. This is another case series that we wanted to look from our database and particularly I was interested in, and this was a charge that was given to IOM and I don't know what they are going to come back with because they are going to be looking at all of the medical literature anaphylaxis related to vaccines. We currently have in our tables year to four hours right?

It is really interesting to see is that the correct interval that we should have and that is how this thing started. We wanted to know well what have we had in our database over the years and what has been our experience. So we kind of grouped that information together. Work with an

adult and a pediatric allergist to put this together and we looked for cases that we clearly our database for anaphylaxes or anaphylactic shock over a ten year period from January 2000 to December 2009, comprehensive review of medical records. We actually re-did the review not based upon what was reviewed in the past and abstracted clinical and demographic data of interest. We used a pre-specified data retrieval form. Everything was identified.

Yesterday you guys talked about well shouldn't the governments' agencies talk to each other in vaccine safety and all of that. I would like to think one of the, this is an example where for the Brighton Collaboration which is really not a government agency per se but their mission is to really focus in on vaccine and vaccine safety and I think Jane you are a part of that group, right? They came up with a paper in 2007 really laying out the case definition for anaphylaxis and the levels of certainty because clinically sometimes we are not quite sure. If you have this, this, this and they laid all out, the clinical symptomology with some of the laboratories and major and minor criteria so it is really nicely done. What their purpose in having that working group and publishing that paper is to say other folks who may have database of anaphylaxis cases, let's all try to use common definitions that we can actually look at this information in aggregate. It is not the basic science research that the presenters from NIH talked about yesterday about mechanisms per se but this is really looking at clinical information and trying to have a common ground of sharing vaccine safety information. So we took that Brighton Collaboration published case definitions for anaphylaxis and applied it and in reviewing these records in de novo.

Then we categorize our cases to which were really anaphylaxis based upon meeting the Brighton Collaboration definitions in diagnostic certainty there is level one, two and three and what is possible allergic. Meaning they have had some signs of allergies but they did not meet the diagnostic criteria for what is published and then what is really not anaphylaxis and allergic that means there were other alternative reasons as to why the patient actually based upon medical review, what the diagnosis arrives at.

The numbers come out that we actually out of those ten years there were a total of 1,819 non-autism claims during that same timeframe. Three percent were alleging anaphylaxis and there were 53 unique cases identified. Of those, after all of the reviews were done, nine or seventeen percent of 53 were really true anaphylaxis cases and there were five males, four females; five adults, four kids and the interval as it turns out were of those nine cases were within seconds to three hours. Five of nine actually were within thirty minutes so it happens very fast when it happens. So our table, zero to four hours that captures the true anaphylaxis cases following the vaccine injection. If five of nine has a previous history interesting of asthma or allergies and of the allergies that they mentioned, three of the five had history allergies to antimicrobial dosing, antibiotics, things like that.

What were the vaccines that were okay so cases, there were one, two, three, four, five, six cases that actually had single vaccines and anaphylaxis. You see the list over there and then there were three that actually had multiple vaccines. The outcome interestingly and I don't think this is published really anywhere else following vaccines that I could find.

Five of these nine of our cases actually were death cases and that is pretty remarkable because the majority of vaccine in a big database looking for vaccine related anaphylaxis, the numbers are very small and actually that is coming next and very few of them actually die.

But five of our nine were actually death cases and that really does may sense because our claims really are people who are alleging sequela from the injury that they received. So it is an enriched population that we have that we reviewed. The possible allergic not anaphylaxis were four and the not anaphylaxis allergic there were 36 and that was very interesting itself too. The majority of those cases really were sudden death and they really had a majority of them also had an autopsy which showed that it was due to something else so that was an instructive in itself.

What do we get out of that? Well the not anaphylaxis case represented eight different vaccines so it is not like one vaccine over and over and that had eleven different antigens.

MS. HOIBERG: I am sorry. I was just looking here. It says under here nine anaphylaxis slash non-allergic one of them was a homicide? What does that mean?

DR. LIANG: So a baby was basically murdered.

MS. HOIBERG: Murdered by the vaccine or murdered by the doctor? I don't understand.

DR. LIANG: We do have cases that we receive in the program that allege vaccine related injury but in fact upon case review it is cases of homicide of usually family members and they still even though and some of them may be actually in criminal courts or what not but they still want to

blame the vaccine instead of the fact that they are in court.

MS. HOIBERG: They actually killed their own child.

DR. LIANG: It is just some of these cases are really awful to review.

DR. HERR: Rosemary, Tom Herr. In your non-allergic again, here was your use of the Brighton Collaboration criteria that helped to differentiate sudden infant death since that is pretty much a diagnosis of exclusion?

DR. LIANG: Right. Sudden infant death is diagnosis of exclusion but it was really determined based upon pathology when the autopsy was done and there really wasn't anything to point to an anaphylaxis related cardiovascular collapse and things like that that it was really determined to be a SID death. We did look at it. It would be really interesting for us to look at some of our death claims as a group and see what turns others many ways to look at things. This is really looking at it from the perspective of channeled anaphylaxis because we really need to tackle that to update the patients.

Some of the conclusions that we reached and this would be also published in the near future and you will get a copy is these cases represented the different vaccines so I do think that there are some vaccines at least we are going to add as an injury to the table for anaphylaxis, basically. So think that that was helpful. The interval is okay from this review anyway.

This is just our program experience. Remember our program experience is enriched. It is people claiming that they were injured from

vaccines. We do not have a denominator. We have a lot of limitations to our database to do safety studies. We really need to put it in the context of all of the other information that are out there and that is why we need an independent literature review from IOM to put things in context but I do think as you guys have pointed out that we do have incredible case information in our repository and we need to make use of that clinical information to help us be part of vaccine safety research.

We talked about the five of nine. I thought it would be interesting for you to just get a blurb about this study that was presented, that was published in Pediatrics in 2003 and this is a study from the vaccine safety data link that you heard about from Dr. Gidudu, from Jane. None of the episodes at that time and that study resulted in death. They were looking at big health care, HMO databases. They actually identified only five cases out of 7.6 million doses of vaccine given for true anaphylaxis with the risk of .65 cases per million doses so that is kind of gives you a baseline of how many of these anaphylaxis cases out there but again they were all patients who did fine, did not result in death. We do seem to get those really devastating claims coming into our program. Remember because they need to meet the six months sequela and death would meet that.

Anyway this was our first attempt at systematically analyzing our claims database utilizing the Brighton Criteria with all of the CDC folks involved which really laid out the case definition for anaphylaxis. I thought that was a really nice way for us to sort of move forward in how we can look at our claims database.

You have seen this already and I just circled this because we

wanted to explain this sort of proportional rise in the young adult adolescents which is really new to the program. We have little babies in the past and then we started to get adult claims. Now we are really starting to ratchet up our adolescence as well.

This is again the information of the three month that we reviewed. Again, that is what we are seeing and I think I have talked enough so I am going to turn it over to Dr. Shoback.

MR. KING: Let's not go away yet. Yesterday I had a question and I think it was to be deferred to today and I think it was deferred specifically to you so I do not want you to run away yet.

DR. LIANG: How about we do this. If it is something that is related to the discussion that you guys were having yesterday and I was listening in. How about if we have Dr. Shoback and Dr. Ryan present and I am going to come back at the end and then we can talk. What do you think?

MR. KING: That is fine as long as we have, yes.

DR. LIANG: I will be here. I am looking forward to our discussion after.

Agenda Item: Human Papillomavirus Virus Vaccine Claims Update, Dr. Barbara Shoback, DVIC Medical Officer

DR. SHOBACK: Good morning. I am Barbara Shoback. I am the Medical Officer with HRSA. Can people hear me? Is this better? My topic is human papillomavirus which us also known as HPV and that is probably how I probably will be referring to it throughout this presentation.

The human papillomavirus, HPV, is only a human virus. The

infection is the most prevalent sexually transmitted infection. There are more than 100 different types and certain types are associated with cervical and anal genital cancers. Type sixteen and eighteen are responsible for about 70 percent of cervical, anal, and genital cancer including those cancers of the penis, vagina and vulva. Types six and eleven are responsible for 90 percent of genital warts. Most infections are asymptomatic and transient. Cervical cancer is the eleventh most common cancer among women in the U.S. In contract in developing countries cervical cancer is the second most common cancer and a leading cause of cancer related death.

Gardasil, which is a Merck product, is a quadra valiant HPV vaccine for men and women. Gardasil is designed to protect against types sixteen, eighteen, six and eleven. The reason for HPV vaccination for men is to prevent transmission of HPV to women or to other men. Scheduled administration for the HPV vaccine is thee equal doses within six months. That is there is a first dose, followed in two months by the second and then the third dose at six months. Gardasil was licensed in the U.S. by the FDA for females ages 9 through 26 years on June 8, 2006. The only contraindication to its use are pregnancy and allergy to a previous does of Gardasil and to severe allergy to yeast. In June 2009 the FDA issued a warning and precaution for syncope which is fainting or passing out just after administration of the vaccine. It is usually transient. Gardasil was licensed in the U.S. by the FDA in October 2009 for males ages 9 through 26 for prevention of genital warts.

The other product, Cervarix, is a product of GlaxoSmithKline and that was licensed in the U.S. by the FDA also in October 2009 for

females ages 10 through 25. It is a bi-valiant vaccine covering types sixteen and eighteen.

The HPV vaccines were added to the vaccine injury table on February 1, 2007. There are no listed injuries for the HPV vaccines at this time.

In 2008 to 2010, the Vaccine Injury Compensation Program had 117 claims for this vaccine in total. All of those claims were from adolescent girls or young women except for one middle aged man. A majority of claims, that is 61 of the 117 involved neurological injuries. Of those 61 claims twenty percent were Guillain-Barre' Syndrome or GBS. Another twenty percent were other demyelinating conditions such as transverse myelitis or TM or acute disseminated encephalomyelitis also ADEM. The remaining approximately 60 percent of neurological clams included seizures, headache and neuritis.

The second largest category of injury was rheumatologic. That was approximately 25 percent once again of the 117 claims. This group included a wide variety of conditions: juvenile arthritis; rheumatoid arthritis; systemic lupus erythematosus or Lupus, fibromyalgia also known as fibrocytis and undifferentiated connective tissue disease. Other categories were gastrointestinal, hematologic and endocrinologic condition. Syncope with secondary trauma to head and teeth was claimed in five cases and we had one claim for SIRVA shoulder injury related to vaccine administration. You just heard a little more about that from Sarah.

More than twenty percent of the claims had mental health issues that contributed significantly to the injury and continued illness. Affected disorder that would include depression, anxiety or bi-polar disorder

was the most common mental health condition. There were eight alleged vaccine related death claims. All were female age ranged 13 through 21 years. All had autopsies. Seven were performed by medical examiners and there were underlying genetic conditions or acquired conditions that were linked to sudden death or were potential causes of death in six of those cases.

MS. HOIBERG: So in other words they were not caused by the vaccine. Is that what you were saying or was the vaccine actually possibly, aggravate the condition?

DR. SHOBACK: I have personally reviewed many of them, probably four, and I have reviewed the reviews of the others and they did not aggravate the condition. They did not aggregate them for that.

DR. GIDUDU: The hematological conditions, were any of them from thrombolic events?

DR. SHOBACK: No.

DR. GIDUDU: Because we see many of those in CDC.

DR. SHOBACK: I didn't handle that part.

DR. GIDUDU: No, we have seen a couple of those cases in our databases in CDC so I was wondering whether you saw any of those.

DR. SHOBACK: You are talking about death.

DR. GIDUDU: Deaths on hematological. I don't know whether you.

DR. SHOBACK: Well hematologic, yes but I thought you were talking about death. But hematologic conditions there were thrombolic events, yes.

DR. LIANG: And that is being requested as a review for an aide for the IOM. The CDC suggested it. For young women, thrombo embolic events are being seen in our claims as well as it has been seen in the literature and CDC suggested putting that adverse event as one of the HPV adverse events for review by the IOM so it is one of them.

DR. SHOBACK: Are there any other questions? Thank you for your attention.

MS. GALLAGHER: Thank you very much for your presentation.

Agenda Item: Meningococcal Vaccine Claims & Syncope Update, Dr. Tom Ryan, Medical Officer, DVIC

DR. RYAN: All right, cooking with gas here. I am Tom Ryan, and before I start I would really like to thank Rosemary because I would much rather think of myself as a real adult than older adult. Today I am going to be talking about meningococcal vaccines talking a little about meningococcal disease first which I am sure many of you realize is just a devastating although fortunate not common infection, little bit about the vaccines that are available, some new information that has come out on them and finally on our program's experience with the vaccine.

Meningococcal disease is caused by a bacteria called Neisseria Meningitidis. It is a human pathogen so we are the host for this. It does not circulate through the animal world as far as we know. Surprisingly, worrisomely, this bacteria is found in the back of our noses and throat in about five to ten percent of the population at any given time. The vast majority of those individuals have no symptoms related to that. It is there. It is transient. During that time it is spread to other close contacts and rarely it

will invade the body and lead to disease either blood born infection called meningococcemia or meningococcal meningitis.

There are several different Serogroups as you can see on the slide that cause disease with B, C of Y causing a majority of the cases in the U.S. If you read the literature, most of the literature these days says that there is about one case per hundred thousand but in some recent conversations with the CDC they tell us that the case rate has actually dropped down to about .3 cases per hundred thousand translates to about 900 to 1,200 cases of infection of meningococcal disease per year.

Susceptibility is related to various lifestyle factors things like hanging at the bar, sharing eating and drinking utensils, living in crowded environments like college dorms or military recruits in basic training. Genetics seems to play a part in it and then finally competency of the immune system. Protective factors against the disease include the meningococcal vaccine and then otherwise some lifestyle factors which basically incorporate not doing the things that are risk factors for the disease.

It is one of the leading of meningitis in the U.S. Like I mentioned, five to ten percent of individuals carry this bacteria asymptomatically and without any harm in their nasopharynx at any given time. It is interesting that in college freshman who have been identified as a possible risk group for this infection, the carrier rates can go up to around thirty percent in some studies. One of the concerns with this is that it does affect healthy young individuals. Probably the highest frequency in infection actually occurs in children under age two and as you will see as I go along, there are no vaccines that are approved for use in children under age two.

There seems to be another peak at around in the late teenage years around the time that kids go to college and about a third of the cases occur in real adults. Thank you.

It has a ten to fifteen percent mortality rate even despite the start of antibiotics rapidly. This as I mentioned is a devastating illness. It can really go from onset to death sometimes within a matter of hours and for those who do survive the infection, a significant percentage of them are left with some severe sequela as a result.

With regard to the meningococcal vaccine the available vaccines and I will be talking a little bit about those more later cover four different serogroups: A, C, Y and W135. So they cover about 70 percent of the Serogroups that cause disease in the U.S., but as you can see from the slide there is no coverage for serogroup B, about 30 percent. So we have no way at this point of protecting individuals against that particular serogroup nationwide around 30 percent. In some locations for instance Oregon I know this only because I moved here from Oregon, the prevalence of group B or serogroup B disease is 50 percent. So in some places it is more common. Among the covered serogroups, the vaccine is not a hundred percent effective. No vaccine is but it will protect about 75 to 85 percent so that is 75 to 85 percent of infections. Of the vaccines that are currently available, the first one was the polysaccharide vaccine. That immune came out in 1981. At that time there were frequently outbreaks of the meningococcal vaccine among U.S. military recruits and they started giving this vaccine to those recruits. It was highly effective. We don't see epidemics of meningitis among recruits any longer.

The polysaccharide vaccine has really been replaced by the conjugate vaccines. There are two of those. There is Menactra, which came out in 2005, and then Menveo, which was just approved last year. The shift has been to conjugate vaccines for a couple of reasons. One, it was hoped to provide a longer lasting period of immunity. This is all foreshadowing. I will be talking a little bit more about that also.

Secondly, it was felt to provoke an improved immune response and immune memory that if a vaccinated person were exposed to meningitis in the future or infected with the Neisseria Meningitidis, that their immune system would be able to more rapidly respond to that exposure.

We talked a little bit about the vaccine injury table that lists the covered vaccines and for some of those vaccines lists the adverse events that are presumed to have been caused by the vaccine. The meningococcal vaccines, all of them, just like the HPV vaccine were added in February of 2007, and at this point there are no adverse affects that are listed for the meningococcal vaccine. That is true for several vaccines and it is simply that at least from the scientific evidence there is no evidence of any particular condition or adverse affect being causally related to the vaccine at this point.

MS. HOIBERG: Can I stop you real quick? Rosemary can you tell us if there have been ones that have come, you know like claims that have come in claiming that a particular injury was caused by meningococcal disease?

DR. RYAN: Oh yes and I will be getting to that.

MS. HOIBERG: Okay, sorry.

DR. RYAN: This is some new information on the vaccines and

they came about as a result of ACIP meetings some of our alphabet soup of acronyms. One was the recommendation for a vaccine booster and I have mentioned earlier that one of the benefits of the conjugate vaccine was thought to be that it would provide longer lasting immunity and it does seem to provide longer lasting immunity than the Menomune and polysaccharide vaccines. But it also appears that it immunity begins to wane about five years after it is given. This is a vaccine that is recommended for administration during that eleven to twelve year old well child visit. So just about the time that kids were getting ready to go to college at which time freshmen living in dorms are considered to be a risk group for meningococcal disease, at about that time their immunity was waning and recognizing that the ACIP has now recommended that a booster dose be given at age sixteen.

The other thing that they recommended was a two dose series for anyone who was at higher risk of meningococcal disease between the ages of 2 and 54. That group includes individuals with complement deficiencies, individuals who have a non-functioning spleen or have their spleen removed for any reason, adolescents with HIV disease and probably workers in laboratories that are doing research on Neisseria Meningitidis where the options would be vaccination or maybe finding another line of work for research.

The second had to do with GBS risk, another one of our acronyms, Guillain-Barre' Syndrome. In 2006 the CDC reported on about seventeen individuals who had developed GDS within six weeks after receiving the meningococcal vaccine. Again referring back to the Brighton Collaboration, they have also given us case definitions for Guillain-Barre' and

relationship to vaccine and so that six week, 42 day period is a reasonable temporal association between the two. So they investigated that when those cases were identified through VAERS. As a result of their analysis they felt that it suggested a small increase risk of GBS after MenACWY vaccination. As a result they recommended in the 2006 ACIP General Vaccine Recommendations that the vaccine Menactra vaccine specifically should not be given to individuals with a past history of GBS.

MR. KING: Question? So if that is the case, so on the slide that says that there are no adverse events, are they in sync those two comments?

DR. RYAN: Well, I cannot speak. It was a suspicion of an increased risk but not proved. I cannot speak to how changes are made in the vaccine table. I think Rosemary might be talking more about that, but that is certainly one of the things that we will be looking at as the IOM comes out with their new report. We look to them to sort of guide us in terms of what maybe is considered to be vaccine causation.

DR. LIANG: So yesterday you heard a presentation that was explaining what their passive surveillance system is about. It is business that is illustrative so when you have a new vaccine coming in there is post marketing studies here moving forward. VAERS is a passive surveillance meaning people record in to you know people state I got this following a vaccination. So it is not really an actual; it is a signal generator as this says. But you tend to take that as something is really real. We really need to sort of verify that or do further sort of analysis and studies. Initially when the meningococcal vaccine first came out, there were some reports coming in around the time that that vaccine was received so sort of a clustering of

reports. When they receive something like that, they really need to go and further investigate. That is what they did.

The vaccine during table change, the vaccine was added upon its approval but it does take, it may take us time. Remember there is a three year lag of claims coming in so we are actually seeing those claims now and we are going to be going to changes if we think there actually is something that should be a presumption of causation of vaccine. That is a table. That is for our program. This is a surveillance system that is trying to look for signals of statement. Does that make sense?

MR. KING: It does but it is really more of a nuance then. In other words, there is a signal that there may be some issues and it has not yet caught up to being put on a table.

DR. LIANG: Right, the studies were done to try to answer the question of the signal. That is what Dr. Ryan said it presented.

MR. KING: So is my statement what I just said?

DR. LIANG: The table really we want to put something on the table after an independent review by the IOM which means it is going to include those kinds of adverse events that we really think there is enough evidence to say there is vaccine relationship. There is information along, although it really needs supplementary evidence to supplement that to say something that the signal is a real thing. You don't want to have a signal that goes down in the fight. We are, everyone is on heightened alert if you think something is happening to try to investigate that further and that is the story that is going to continue.

MR. KING: And that is why we have a recommendation out for

people who may be with a past history of GBS should not be taking the vaccine. Got it, okay.

DR. LIANG: That is different. That is a label. That is not the table. That is the drug labeling.

MR. KING: Thank you.

DR. RYAN: Thank you for that question and as Rosemary was saying more recently and perhaps as there is a reason for why it is not rapidly added to the table. More recently there have been a couple of studies. They are not published at this point. They were presented to the ACIP during their June 2010 meeting and the first of those studies were from Harvard Pilgrim Health study. It involved 1.4 million recipients of the Menactra vaccine.

It also involved a larger cohort age matching cohort of individuals who did not receive the vaccine. There were 99 total cases of GBS that were seen during that study but among the larger cohort but none of those cases occurred in vaccine recipients within that six week window following vaccination. So the take home message from that study was that it did not appear to be a risk of GBS with Menactra vaccination.

The second study was actually a VSD study. They studied individuals, 890,000 doses of Menatra and again they found no nuance of cases with GBS following vaccination with Menatra. So, neither of these studies supported the findings of that analysis of seventeen earlier cases that there may be a risk. As a result of that the ACIP at that point felt that the information was strong enough to remove that precaution against the giving the Menatra vaccine to individuals with a past history of GBS. They considered a variety of options and this was sort of the middle road in terms

of decisions that they made and again just as Rosemary said, the real purpose is to be cautious. They do not want to draw more from the information than is actually there and so what they recommended is that that precaution be dropped. The newest recommendations that have come out General Vaccine Recommendations, they have dropped that precaution for administering Menactra vaccine to individuals with past history of GBS.

MS. HOIBERG: But was are not going to know for the next three years whether or not giving it to people who had GBS if it actually flared up again.

DR. RYAN: Well I think that what we can say from that and what is really occurring is that there is ongoing analysis. VAERS is still there. VSD they are a variety and we heard about all of those yesterday, the different surveillance Vaccine Safety Surveillance programs that are in operation and all of those are going to be continuing to go on. This is not the last word. So again they will be looking for signals and if those signals occur than all of that will be visited.

DR. GIDUDU: I wanted to mention that there are several ongoing studies including one on genetics so some of them will take aware that there are a lot of studies going on on BGS.

DR. HERR: I have a question and this probably goes to you Jane, a little bit more in the sense that meningococcal disease is a reportable disease. Do we look at and part of the questions of those particular cases, have they been immunized? Have they refused the immunization? Have they not been immunized for a particular reason prior to their getting the disease?

DR. GIDUDU: I think that is a broader question for us. The cases we get in my group have already gotten the vaccine. So that question may be to the bigger meningococcal group, I think.

DR. HERR: That would certainly also be helpful in at least looking at the information because if we are recommending a group not to get the vaccine, okay what does that mean? What are the implications of that?

DR. RYAN: Unfortunately one that those of us here cannot answer but I think that it would be wonderful information to have.

DR. LIANG: The actual illness of GBS isn't their illness, and in fact start to go to your question. We have so many GBS claims but I think that we maybe have one or two cases where it is a GBS claim on top of a person's points of a previous history of GBS. It is very uncommon even without the meningococcal scenario just even looking at all of the other claims that have come in. It is one of those things that would be very hard to answer even going to the future about a subset of population who has had a GBS in the past receiving vaccine of meningococcal in particular and what is their risk that is different than the general population receiving.

Much of that will really have to be answered I think on a genetic basis at the laboratory more than really an epi type of picture because we just don't have, not going to have the numbers to be able to really do well controlled studies to answer things like that.

DR. GIDUDU: CISA is doing in its own way the association study so there are some efforts in that direction.

DR. RYAN: I am going to move on to our claims experience that we have had for the meningococcal vaccines. Since they were added to the

table there have been 32 total claims and nine of those claims only in the meningococcal vaccines was ministered and the other twenty-three it was administered along with other covered vaccines and they were all claimed to have caused the injury.

The most common injuries you can see that of really a little over 60 percent of the injuries are neurological in nature. GBS was the most common. Multiple sclerosis, transverse myelitis, CIVP, and then a couple of cases where it was really difficult to define. It did not fit into any particular diagnostic category. Then there were a number, about a third of the cases, where other things and they did not fall into any specific group. They ran the gamut of different types of conditions. Among those claims where only the meningococcal vaccine was administered, GBS was still the more common. TM, MS, other neurological injuries, fibromyalgia, autism and death have one claim each.

I put this slide in just so you would get some sense of what the other co-administered vaccines were. Not surprisingly, HPV vaccine, Gardasil vaccine shows up on all of these and I think that is just simply a manifestation.

DR. HERR: Good luck on getting single doses in the future.

DR. RYAN: Then finally the age of that vaccination. It averaged seventeen years. We talked about the fact it was recommended for eleven, twelve year old age group. The reason that it is higher is that when this first came out it was really marketed heavily to children that were heading for college. So we were vaccinating an older age group initially. The range from 11 to 49 for all conditions following vaccination, the average lag time between

vaccination and onset of that condition is 24 days. The range fell all the way up to 105. Questions?

DR. WILLIAMS: I have one question. On the MCV4 only administered, the medical claims analysis there is an autism case?

DR. RYAN: There is an autism case.

DR. WILLIAMS: But the age range for the vaccine is eleven, starting in around eleven?

DR. RYAN: Yes, it is not given to younger and I have not looked at that case specifically but my suspicion would be that it is an aggravation of an existing autism rather than causation that was claimed but that is supposition on my part. I can't say that with certainty.

MS. HOIBERG: If the child possibly had an underlying mitochondrial disorder, it could have, maybe that is what they are saying that a lot of the mitochondrial disorders are aggravated by vaccination and could possibly then roll into autism.

DR. RYAN: It is still in process so I can't really say how it has turned out, but yes.

MS. GALLAGHER: Thank you very much for your presentation.

DR. RYAN: Unfortunately I am not done but this one will be much quicker.

MS. GALLAGHER: Probably much more interesting, right?

DR. RYAN: Oh, ouch.

MS. GALLAGHER: No, I meant that in a positive way. Sorry about the way it came out. I have been so engrossed in this one I am sorry I must cut it off.

DR. RYAN: This is just a short talk on vaccine related syncope. We sort of mentioned that in passing with our other presentations. Syncope is medical jargon for fainting, usually caused by decreased blood flow to the brain. The most common variant or most common cause, the neurally mediated syncope, that is considered a benign disease and by that they mean that the condition itself does not lead to chronic illness or to death but any fainting has the risk for serious injury; the person who has fallen to the ground unprotected. We have already talked about the cause. It can be triggered by stress or pain and there is no question that vaccination can cause both of those in most of us.

Neurally mediated syncope is very common in adolescents and Devart screening, they have reported that there has been an increase in reports of syncope after vaccination since the release of three newer vaccines: the Gardisil vaccine the HPV vaccine; Menactra; and Tdap.

Gardisil is the only one of those vaccines that has a packaged recommendation, a warning and precaution for syncope. They do recommend that individuals who receive Gardasil be observed for fifteen minutes after they receive the vaccine. They are the only vaccine as far as I know that has any sort of recommendation like that. However, the ACIP in their newest recommendations and I think this goes back to Magdalena's question as to whether this is not related to SIRVA and sitting down and receiving vaccine but it is related to syncope and they have recommended that everyone who is being vaccinated either receive that vaccine while they are sitting or lying down. They go a little bit further and I think correctly so in terms of observation after vaccination, a little bit further than the Gardasil

package insert by saying don't just observe them but have them sit down or lie down while you are observing them, because if they are standing up then they are at a higher risk of injury anyway. I think that our experience, the claims that we have seen, I would take that a little bit further and I would say that sitting on top of an exam table does not count. That is quite a drop from there.

DR. LIANG: Those were actually our cases.

DR. RYAN: Those are our cases. We have had seven claims for syncope. Of course syncope occurs much more often. It is just that most people are not seriously injured. We are seeing those cases that have had sequela for at least six months afterwards. So these people had significant injury and several of them, I can't recall right off hand how many were left in the exam room after getting the vaccine and were left there or the nurse turned their back and they were sitting up on that tall exam table and just sort toppled.

More of them occurred after Gardasil, a couple after Gardasil plus Menactra, and one following the flu shot, which probably I shouldn't say this, but makes me think that when I received my flu shot here this year, we just sort of walked through and then plop and you walked out the door and were gone.

DR. HERR: I would be interested on those kids under 18 who got the vaccine and fainted. Who signed the consent and where were they?

DR. RYAN: And speaking from personal experience in older teenagers, they usually want even if the parents sign the consent, the teen is going to go in there by themselves. They don't want mom or dad thinking

back to my child, she liked to walk at least 10 feet in front or 10 feet behind so that she pretend that she is not with a real adult.

In our series, in the claims we have seen, the average age was 16 to 19. The reason there is a range for the average age, the patients were older – I think one was 25 and one was 29, so if you include them the age is 19 years and if you take them out it was 16 years. In terms of the injuries, there were lacerations, head injuries, concussions, skull fractures and then more serious injury, referring to one specific case where the individual received the vaccine, got into her automobile and started driving, had a horrible crash, had multiple severe injuries and was in the hospital for months.

I think the take home message from all of this is that this is a generally preventable complication. It is really not an indication of the vaccine -- having worked in clinics where we had a fairly active vaccine administration clinics, we knew that somebody could faint with any of these. So it is preventable. I think there is information out there for health care providers. In fact we did a literature search. There are probably eighteen or twenty articles on vaccine related syncope that are out there in the medical literature but I think it is really important that those offices and individual providers and clinics that are providing the vaccines really read and follow those recommendations if that is the only way we are going to really prevent from occurring in the future.

MR. KING: Just a quick question here. We recommend that people read the recommendations and things of that nature so on the product from Merck I believe it was, the Gardasil was that correct? So they have a warning and precaution in their package insert. The other drug, I do not know

who manufactures that one, GlaxoSmithKline? They don't have a warning in theirs?

DR. RYAN: They do not have a warning.

MR. KING: So was the Merck warning voluntary put in?

DR. RYAN: I can't say with certainty but there was an article published relatively recently in JAMA which was a review of VAERS reports related to Gardasil vaccination. One of the two signals from that review was syncope and I believe that is what led to Gardasil putting it in their packaging.

DR. LIANG: In other words, the second vaccine is a newer vaccine so because we don't have post marketing experience so things that take time to go into label. However we really do think that syncope is like something that crosses -- it is a cross vaccine issue. It really has to do with the population more of the young adults and the teenagers.

It may be something that FDA or CDC will take up and in fact I know the General Recommendations Group has said this is the way you should vaccinate in regards to syncope so I am sure it will be something that they will take a look at. It is not something that we deal with here. It is something that FDA will work with a company to get on with.

In fact, that is probably what it is. That is a newer vaccination. You need some post-marketing reports that come in before there is some ammunition to say here we have got to.

DR. GIDUDU: Just a brief comment on syncope because CDC jointly with FDA -- I presented with a colleague from FDA on syncope on clinician outreach call to clinicians about syncope and a lot of effort has been done to try and send out to providers information about syncope. It is true, it

may be across more vaccines than Gardasil.

DR. SHOBACK: I think that it may have been picked up easier because when Gardasil was first licensed or approved, it was essentially in this country for women. So everybody who got it was a female and everybody who fainted was a female so it was just I guess perfect storm sort of thing.

DR. PRON: Yes, I am just thinking about how it lines up being a recommendation for providers in that it becomes a logistical nightmare is that you have to have a patient seated in the chair, give them the shot and make sure they can stay in that same chair because then if they get up from that chair and go sit in your waiting room that in itself leaves them liable. It is going to be an interesting recommendation to implement.

DR. LIANG: Practically speaking, that is probably a lot of issues as to why it is still happening because those logistics are hard. Now think about how much we are talking about our occupation of health care but how about those like CVS shots and the mall flu shots. To have all of these people actually follow sitting down, have the administrator also sit down and have them wait there for fifteen minutes and then discharge them.

That is logistically very difficult and you are competing against vaccinate people as much as you can. Right? So this is resources and so, but I do think, particularly for the teenagers and the young adults, we should be more mindful. That is the group. That is all we have here and I think that is the overall data shows that that is the risk population that has a higher rate of fainting. So these things really do help and we can hone in on the subpopulations that are the highest risk of these adverse events.

We are discussing among ourselves whether we should put together a case series of syncope, as well from our experience because we certainly have seen all of this other literature out there. But our experience certainly shows in a graphic nature of some of the sequela that can happen. It is a very rare probably population. The subset again of all the people who faint, most people who faint are fine, but we certainly have reviewed cases where there was pretty severe sequela in young people: wired jaws and being in the hospital post for a vehicle accident. There was even a parent sitting with one particular patient where she just kind of fell over. There happened to be a little cabinet and got a head injury. So there are many different scenarios. So anyway our little case series show the very extreme circumstances of things that could go really wrong.

DR. GIDUDU: In VAERS we have seen a death from a skull fracture. So there has been a death associated with syncope.

MS. GALLAGHER: I would like to thank you very much for both of your extremely interesting presentations.

MS. HOIBERG: Dave, didn't you have a question for Rosemary? Your question for Rosemary?

MR. KING: Does anyone else have one first?

SPEAKER: You have to remember it.

MR. KING: That is an excellent observation which is why I wrote it down. Since I asked that question, I believe it was Mark Rogers yesterday, a lot more information has come so I don't know if it is. I will ask it but maybe part of it has been answered and if not we will kind of work our way through it.

On the cases that have been determined where there is awards

that have been paid out based upon claims for a vaccine injury, let's call it that, that there has been a roughly 2,500 of those. Of those 2,500 I am not sure of the number that has been conceited which means that there is absolutely considered no dispute. This clearly was a vaccine injury. Is that safe by the way, understanding what I mean on that?

DR. LIANG: Yes, so just to clarify one thing. The 2,500 I believe that that accounts for all those cases pre right, '88. So there was a whole school of claims that were compensated when the program first began and that had to do with the whole cell pertussis vaccination. So putting those claims aside and if we are talking about like currently, and you have heard from this from the Special Master.

MR. KING: Can we define currently for a moment? If we are talking pre 1988, then is currently post 1988?

DR. LIANG: Post 1998 and the next day.

MR. KING: 1998?

DR. LIANG: '88, next day the current.

MR. KING: I am sorry. I am unclear still. I heard '98 and '88 and so I want to make sure that I understand which number is accurate.

DR. EVANS: Let me start out. What has been asked throughout the years is that we have the reservoir of cases from the pre-'88, 4,000 bolus cases and many of them were DTP claims injuries and deaths and many of them were seizure disorders, encephalopathy and a lot of, a significant percentage of those were tabled compensations.

They were tabled compensations because of the initial table criteria residual seizure disorder. Now the question, that is one of the

questions that has been asked over the years and I think that was part of the questions that you and Sarah were asking is can we go back and look at those cases and see if there can be things that can be gleaned from those cases.

MR. KING: That was not my question because you just mentioned 4,000 and I was referring to 2,500 which would be a different I think.

DR. EVANS: But those pre ’88 cases make a significant portion of the 2,500 number that is now the number of families and individuals, children and individuals who have been compensated over the twenty-two year history of the program.

MR. KING: So I am confused because of the 2,500 because I have heard the number 4,000 in the past 90 seconds and 2,500. I need a delineation.

DR. EVANS: Let’s go to that sheet, if you have that table that was talked about at the orientation.

MR. KING: That big book that we did not have to bring today.

DR. EVANS: No, this was that little one pager that tried to make sense of that big toy. When the program opened its doors on October 1, 1988, there were two classes of claims: one is for vaccines given to that opening date; one is for vaccines given afterwards. We called the ones before pre ’88. There was no time limit how far back those claims could go and in fact we had one back to 1918. When the final deadline for filing the older pre ’88 claims expired 4,260 claims were filed.

It took fourteen years for those 4,200 and some odd claims to

be adjudicated. They were all tried under the initial table which had residual seizure disorder, shock/collapse, so on. This is very confusing. I know that this has to be brought up again and again to just keep things straight.

I am saying that a significant portion of the now 2,500 plus families and individuals who have been compensated over the entire course of the program, a significant portion of that 2,500 are from the 4,000 pre '88 claims that were adjudicated.

MR. KING: Right, do we know what that portion is?

DR. EVANS: We could determine that very easily. I don't have the number offhand, but that is something that we can get for you.

MR. KING: Do you think it is 50 percent? Thirty percent? Eighty percent?

DR. EVANS: If Mr. Sorenson was here he could tell us but I don't see Ward Sorenson here. Carol Marks? It is not just statistics. It is overall. It is not broken down pre-'88 or post-'88. We can get that for you very quickly and I would think something on the order of 50 percent.

MR. KING: Did you say 50?

DR. EVANS: I would think about half, maybe a little bit more than half. Because of the tabled presumptions a significant portion of residual seizure disorder cases were compensated along with some NMR, encephalopathy and some OPV polio cases and so on.

So that is a reservoir of cases and from time to time I have been asked over the years well isn't that in a group of cases that you can glean some information about, some of the clinical aspects of vaccines. So that has been a question for that staff.

MR. KING: What has been the answer to that question?

DR. EVANS: Well, we have tried -- I mean these are children with epilepsy with no known cause. A lot of them are thought to be genetic disorders that have yet to be proven through technology, modern technology to be able to be identified specifically. It could be migrational brain abnormalities, meaning that portions of the brain at a cellular level didn't form exactly correctly. They tend to cause seizures and so on.

This is the thinking of neurologists as to why children didn't start out looking normal neurologically, but sometime in the first year of life or second year of life began to have seizure disorders and began to have other kinds of neurological malaise and so on.

MS. HOIBERG: Geoff, in my daughter's case, they actually, we have brain scans showing a perfectly normal brain and then a brain that was definitely there was a chemical assault. So in that case, those are the cases that I want to have looked at not the old cases. I want the cases that where you have things such as brain scans where you have the MRIs and the cat scans and the pet scans, whatever.

You guys have such a wealth of knowledge and I am just very surprised that at this point there has not been a work group put together to study those children that have the same types of you know kind of like you did with the GBS cases. Why haven't you don't that with encephalopathy cases?

DR. LIANG: Actually we are doing that with encephalopathy cases in conjunction with Children's Hospital. We are looking at encephalopathy in particular. We can't tackle them all so we have to it is a lot of work to go back and look at case reviews. There are several levels here.

We at the program have a repository of all of the medical records and we can even go back and try to retrieve the medical records and do a systematic analysis of the records. But that would only really go to kind of what we presented to you about the SIRVA and the anaphylaxis. It analyzes the clinical information available and tries to kind of put some sort of an organization what characteristics are similar? What kind of laboratories were there? What did the scans look like and we look at and try to make

Dan talked about the viral repository that is in Columbia that is part of the clinical immunization safety assessment at work. That is something that is going to require a lot more work and we certainly should have a work group. I totally agree with you -- I think that there is a lot that we can contribute but we are enriched cases. We don't have the denominator. We really need to work within a collaborative group in order to really make broad sweeping statements about how this falls within the vaccine safety information.

What you are talking about is if I have a child and this is what has happened, how can you study that information further in the context of a clinical vaccine safety network.

MS. HOIBERG: Yes, it is like why did it happen. You know what I mean? Like was there maybe a way that the vaccine was administered in such a way that it passed the blood brain barrier. I mean why is it that seizures occur? And why is it that there are so many neurological defects after vaccines?

DR. LIANG: In order for a specific children that make claims to our program to become a study subject for part of the CISA network, we have

-- I really actually looked into this because this is very important and we have a number of hurtles to go through. This then becomes more of a case-specific study, instead of a de-identified retrospective looking at our data repository of clinical information.

There is something we have to go through institutional review boards. There is human subject considerations. What has to happen is we have to get something, probably that is in the act, actually, to say if we have a patient that makes a claim to our program and it is probably best if there is actually an adjudication that happens. So if we think there actually was vaccine injury that has happened, then we ask the parents to sign up for a study as part of the CISA network. That is the best way to go.

The problem that we have is because this has never been done before, and our legal and maybe they will be able to speak to this and we talked to OGC this is how do we? We can't, as people in the program, we do not directly talk to the parents. We go through our DOJ attorneys. They then go through the petitioner's attorneys. We then go through to the parents. In this road to kind of get to the parents there is barriers, legal barriers. That is mainly the most. In order to do we need permission from the parents.

There was a fascinating case and I can't tell you, one case and I wanted to try to actually do a case report because those kinds of information should be shared. We wrote out, we went to OGC wrote up this long email and explained why laws this is really part of vaccine safety. Could we please get parent permission to write up this case and put it in the literature? It went to our DOJ attorney who then presented all of that information to the petitioner's attorney. We never heard back. There is nothing we can do. It

stuck at the petitioner's attorney. There is no desire to, this is a case that was settled.

DR. EVANS: After everything. There is a theory to change the decision.

DR. LIANG: But then there have been some cases that have actually conceded because the legals have a case but there are cases where we really are not sure and it is important to get that information out there and we may settle that case because we are not sure but that medical information. We don't want to do anything with the legal part, but we want to present the medical information so people can have this information out there. But we are running into legal barriers.

So if there is a way to put something that is a statute or something that says when a case has been adjudicated we would like the parents would like to get it and full consent we would like to refer that to a clinical immunization safety network site, an academic site or we would like if it is a case report we would like permission. We can't really publish a case report. We have to wait until we have a group of reports to pull it together. But if there is an interesting, a sentinel case we would like to publish that. Can we get permission? There has to be some sort of a legal thing that has to be in place. Our hands are tied.

DR. EVANS: I would also add that their base project that Rosemary is doing is really getting a lot of what you are talking about because here we are taking a group. This has now gone on for a couple of years. We are trying to identify potential seizure cases that might have a genetic change, a sodium channel defect and taking advantage of this

reservoir of cases that we have and we are working with NIH. That is the most promising project drawing upon the experience of cases that we have but.

DR. LIANG: But I have to tell you we don't have the resources to go through those.

DR. EVANS: We don't have the resources to do it and we haven't crossed to the next big legal pressure as to what is going to happen when we identify the cases and we go and try as best to contact and get the permission.

MS. HOIBERG: It would be amazing if you were to go through and you were to find out that there is this particular issue and that a particular defect that could actually possibly be corrected. Do you know what I mean or anticipated?

DR. LIANG: I think with your base cases there are treatments that are coming down the line for these different kinds of seizure disorders and if a family was to know earlier than later that they have such a genetic defect, it would be very helpful for that family to seek help where they can get at least an overview of what treatments are available. These are all moving targets in time. Every day we are getting newer mutations identified. It is not only the sodium channeling anymore. There are potassium channel mutation defects now so this is really cutting edge of science but we do have a huge reservoir of cases that are available, clinical information available.

Our rate limiting steps are that we need bright medical people to go through those records and we are trying to deal with this rising rate of claims. We don't have the resources or the epidemiologist or the clinical

reviewers to go through those cases. We are trying all we can to do little projects amongst everything else so we can really help further the entry table that is coming down the pike and the other issues really are legal barriers. We don't have anything in the statute to say this medical legal claim once the determination has happened really should be identified as a case to be studied in the realms of vaccine safety work. But that is something that would be nice to get a work group together and try to tackle this moving forward.

MS. WILLIAMS: I second that. I hate it when lawyers and the law are looked as being barriers and so maybe we could cut short this discussion which I think is very excellent but move it because essentially what you are asking. It would be very useful I think because what we heard yesterday I think from the Committee members is there is this database of information which as it grows is becoming more important and so you all are not human subject researchers. That is not your purpose and so you are using the database in response to questions from us which is very helpful and very useful but that is not your core mission but it might be someone's mission, someone else, who could one make if the database could be available to researchers out there who we don't even know about who might be able to use the information and then make clinical recommendations and discussions. That is one way.

Then the second way that that information could be used is then focused for when there are clinical recommendations that need to come from or around associated with this Committee. I think the larger thing is you all can't be PIs. That is not your job, but is there a way to get that information out. I think if we were to maybe talk to the people that monitor the Common

Rule and talk to NIH.

DR. LIANG: We have no issues collaborating. We are doing that already like the studies that we are doing we are doing with Children's Hospital, with John's Hopkins. We are doing the collaborations of looking at the clinical information. That is not the issue. The issue is when what Sarah was talking about. If a parent actually wants their child to be involved as part of a study, we cannot take a patient in our program and study them.

MS. WILLIAMS: I understand that. That is what I am saying and it shouldn't be, that is not your job. It shouldn't be your job. So my question is, is there a way that the database. We don't know how the database can be used.

MS. HOIBERG: It is being able to get to the parent.

DR. LIANG: It is being able to get to the parent. As we use it is lawyers that are speaking to the parents. We need some sort of a way where when a claim is actually adjudicated there is an information that is sent out even automatically to the parents saying these are the people you should get in contact with to get your child involved in studies. These are the studies that are open and please do this or for us to say your child in cases it is very important to go out into medical literature. We would like permission to publish the analysis that we have done and it is just that I think if we can break through that with some sort of a well defined legal process that would be a first step in moving that forward.

MS. GALLAGHER: I would like to propose a subcommittee and would you like to chair that subcommittee, Michele?

MS. WILLIAMS: Do I have an option?

MS. GALLAGHER: I thought that perhaps your background lends itself to that.

MS. WILLIAMS: Yes, I would be happy to.

MS. GALLAGHER: Okay, and is there anybody else?

MS. HOIBERG: I will be on it.

MS. GALLAGHER: Okay, Sarah will be on it and David?

MR. KING: Yes, certainly.

MS. GALLAGHER: And Sherry? Now I think you would have to work collaboratively with both Rosemary and your office. I am not sure it would be you. Would it be you in particular? Okay. So we will get together through Annie's help, a subcommittee meeting just to have an initial discussion on how you want to go forward and what should we call this subcommittee? Does anybody have a suggestion for the name of the subcommittee?

MS. WILLIAMS: Proper use of the database.

MS. GALLAGHER: Okay, use of clinical data.

MS. WILLIAMS: The potential for using clinical data from the database.

MS. GALLAGHER: Potential for using clinical data.

MS. WILLIAMS: In a permissible way.

DR. EVANS: Database has a different meaning. It is the use of clinical information after the claims reviews. We will come up with it.

DR. PRON: This is Anne Pron. I said I will be on that.

MS. GALLAGHER: So we have Anne, Dave, Melissa, Shirley, Sarah, okay.

DR. FISHER: Charlene I just want to let you know I am back on the line. I had to leave there for a short period but I am back. It is Meg Fisher.

MS. GALLAGHER: Hi, Meg. You dodged getting on a subcommittee.

DR. FISHER: Well, I think this time since I am on my way out, that is probably a reasonable thing.

MS. GALLAGHER: I just thought I would say that as joke because I know that since you are leaving you wouldn't be on it.

MS. WILLIAMS: But our subcommittee could certainly solicit past members experiences.

DR. FISHER: Oh sure.

MS. GALLAGHER: Okay so we will go forward with the new subcommittee to explore this issue and see what can be done. I think according to the way we are doing things, Sherry will be chairing the next meeting because I will have left the Committee and at that time there will be selection of the new Chair and Vice Chair and so they can sort out the Committee going forward but I thought this was an excellent time yes let's have a subcommittee. So I didn't mean to cut anybody off. Have we finished this discussion? Did you ever get your question asked?

MR. KING: I think it will be answered in committee.

Agenda Item: Future Agenda Items, Ms. Charlene Gallagher, Chair

MS. GALLAGHER: I think now we just look for future agenda items and what I usually do is pick an agenda subcommittee. Could the

people who are remaining pick somebody? Tom, would you like to be on the agenda subcommittee?

DR. HERR: Sure.

MS. GALLAGHER: Okay.

DR. HERR: I would love to. I couldn't wait until you asked.

MS. HOIBERG: I haven't been on one in a while.

MS. GALLAGHER: Okay, Sarah and Tom will be on the agenda subcommittee. Is that enough?

MS. HOIBERG: And the Chair, so Sherry.

MS. DREW: I will be on it.

MS. GALLAGHER: Yes.

MS. DREW: If anyone else wants to be on it please let me know.

MS. GALLAGHER: What we can do, let me kind of explain, what we do is the agenda committee gets together by teleconference and they set up a proposed draft agenda. We then circulate it to all of the Commissioners and so you have an opportunity to what is proposed and add any new items and you have the opportunity if you leave today and think of one to send it anybody who is on the agenda subcommittee to be acted upon. So we need somebody to sort of put it together and do the administrative stuff but everybody certainly can contribute and the one item I have so far is that Tom had suggested that we have a presentation on annuity ratings and the increasing costs of some of these structured settlements. So that is the one item I have so far. We have all of our normal reports from the ex officio members so we don't have to ask the subcommittee for those but any extra

reports, special reports.

It may be too early to have a report from your subcommittee by June.

MS. WILLIAMS: I have a suggestion for an item if it is okay.

MS. GALLAGHER: Yes, absolutely.

MS. WILLIAMS: I thought we heard some really fantastic presentations yesterday of all of the research that the government is doing on vaccine and vaccine safety and all of the speakers should be commended on great presentations. I would like to know what is the vaccine industry doing in research and I am not suggesting anybody do a twenty hour literature search but the research that the government does is only a fraction of all of the research that gets down on vaccines in the country. I would just be interested to know certainly not proprietary information or ongoing or even what they doing currently but maybe in the past twelve months has there been vaccine research published by outside of the government.

DR. LIANG: Will the Institute of Medicine would be including some of that.

MS. WILLIAMS: I don't know. I don't know the answer to that.

DR. LIANG: Just published in journals, yes. The Institute of Medicine is doing a comprehensive review of anything that is published.

MS. WILLIAMS: So it may be covered by that?

DR. LIANG: Your suggestion is good. If there is an industry person who sits on one of those what do you call it to go over what is new in the industry world.

MS. GALLAGHER: I think the way that it is publicly available is

clinical trials dot gov (www.clinicaltrials.gov) if that is what you had in mind.

MS. WILLIAMS: I think www.clinicaltrials.gov are going to be government funded.

MS. GALLAGHER: No, the industries are required to post the clinical trials that they are doing there. Get the timeframes. I used to know them by heart when I had to deal with that every day. So that will include everything. I am not sure you can get one person from the industry to come in and say what is the whole industry doing because they are each doing their own thing and as you said there is some proprietary.

MS. WILLIAMS: Right and I assume we are not getting proprietary information.

MS. GALLAGHER: Somebody could look at www.clinicaltrials.gov and look for just vaccine research. Lots of companies have post approval commitment trials going on as Marion Gruber said and they would be published there. Now that does not have the results because it just says these are ongoing.

MS. WILLIAMS: I am not even really looking for results. I am looking for subject matters.

MS. CASTRO: I think that we actually did something similar to what you are requesting when this group first started. We had industry representative at the time and it was focused on vaccine safety. I think we need to know down, to request what is the issue that you would like to hear from the different sectors: the private sector, the public, et cetera. We did that on vaccine safety and it was very helpful to understand what is everybody doing related to that. We heard from the CDC and all of our regulars the

specific presentations and then we had a couple of guests also from the industry. The request is reasonable.

MS. GALLAGHER: Are you interested in efficacy studies, because I think Magda makes a great point. Is it safety you are after?

MS. WILLIAMS: I think it would be something to, it is just it is similar to what the presentations were about the research that is going on now relative to vaccines and vaccine safety. What is the private sector doing? We know what the government is doing. What is the private sector.

MS. HOIBERG: I think that is a good suggestion. It would be interesting to see like what affect does the vaccine injury table have on the vaccine manufacturers. What are they doing to eliminate the adverse events. What do they do when they find out that a particular shot is causing quite a few cases of GBS or encephalopathy. Do they do anything? Is it just considered oh well that is just what happens we have side effects but are they working to make the vaccines safer?

MS. WILLIAMS: I believe that all of that is going on and they are not absolutely. All I am suggesting is that we haven't heard yet.

MS. GALLAGHER: If you want to say what is industry doing that is one thing but privately there are academic institutions that are not government and are not industry and they are doing research as well so that is just so much out there.

MS. WILLIAMS: I guess I was just thinking more non-governmental. I just don't know.

DR. PRON: Might you need to limit it to certain vaccines because the field is huge.

MS. WILLIAMS: Maybe the way to ask the question is, is there a segment of the entire industry that we should hear from that we haven't at some point. Maybe it is not an agenda item. Maybe it is something to think about. So I will take it off the suggestion for an agenda item.

MS. GALLAGHER: Maybe the agenda committee can discuss it and see if they can narrow it to something that we can handle in one meeting or maybe in several meetings and so it may be that in June you have one presentation and then September you have another one and there may be a way because I know Christen does a lot of research down at CHOP so some of it might be industry response but then certainly some of it isn't and there is other huge academic centers that do really good research if you are interested.

MS. WILLIAMS: On the patient advocacy groups I am sure are sponsoring research as well. We are using industry too broadly probably.

MS. GALLAGHER: Right I was thinking of manufacturers of vaccines.

MS. WILLIAMS: What I am more thinking about is just non-governmental since we had all of the governmental.

MS. GALLAGHER: Okay so maybe on the agenda committee you can have a discussion of how to tackle that suggestion.

Agenda Item: Public Comment, Ms. Charlene Gallagher, Chair

MS. GALLAGHER: Now so we have the agenda committee set up and now we have to go to or we should go to public comments. Operator,

could you please call the audience that is on the phone and see if you have anybody who wishes to make a public comment. In the meantime I will ask anyone in the audience here in the building if there is any public comment to be made.

Is there anyone in this room that would like to make a public comment? If so, just come up to the mike. All right, we don't seem to have anyone in the room who wishes to make a public comment. Is there anyone on line.

OPERATOR: We have no one on line who would like to make a comment at this time.

MS. GALLAGHER: All right well thank you very much.

DR. FISHER: Thanks you guys.

PARTICIPANTS: Bye, Meg.

DR. FISHER: Take care.

MS. GALLAGHER: So I will do my last official duty and I will adjourn this meeting today. Thank you everyone.

(Whereupon, the meeting adjourned at 11:30 a.m.)