DEPARTMENT OF HEALTH AND HUMAN SERVICES

ADVISORY COMMISSION ON CHILDHOOD VACCINES

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TABLE OF CONTENTS

P R O C E E D I N G S (8:06 a.m.)

Agenda Item: Welcome and Unfinished Business from Day 1

OPERATOR: This conference is being recorded. If you have any objections, you may disconnect at this time.

Welcome to the 80th quarterly meeting of the Advisory Commission on Childhood Vaccines. I would now like to turn the meeting over to the ACCV vice chair, Ms. Sherry Drew.

MS. DREW: Good morning. This is the second portion of our September 2011 meeting. We have Michelle Williams on the telephone, as I understand. All of the other commissioners are present here. We did not identify ourselves yesterday. It might not be a bad idea for everybody to state their name, all the commissioners.

MR. SMITH: This is Jason Smith. I'm the industry representative.

MR. KING: David King. I am a parent.

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

MS. HOIBERG: Sarah Hoiberg, parent.

MS. LEVINE: Emily Levine. I'm with the HHS Office of the General Counsel.

DR. EVANS: Geoffrey Evans, director of the Division of Vaccine Injury Compensation and executive

secretary to the ACCV.

MS. DREW: Sherry Drew, acting chair and petitioner attorney representative.

DR. FEEMSTER: Kristen Feemster. I'm a pediatric infectious diseases physician.

MS. PRON: Ann Linguiti Pron. I'm a pediatric nurse practitioner. I'm a provider.

DR. DOUGLAS: Charlene Douglas, representing the public.

MS. WILLIAMS: This is Michelle Williams. I'm unaffiliated. I'm an attorney.

MS. DREW: Thank you.

Is there any unfinished business from yesterday?

(No response)

Apparently not.

The first item on our agenda is the review of the vaccine information statements that appear in our workbooks. Jennifer Hamborsky from the CDC is going to lead this discussion. Is she present? Is Ms. Hamborsky on the telephone?

(No response)

She was supposed to be by phone.

OPERATOR: Ms. Hamborsky has not joined yet.

MS. DREW: Okay. How about Skip Wolfe?

OPERATOR: Skip Wolfe has not joined yet.

MS. DREW: Until we are joined by Ms. Hamborsky, we're going to move to Dan Salmon, who is going to give us an update from the National Vaccine Program Office. Dr. Salmon?

Agenda Item: Update from the National Vaccine Program Office

DR. SALMON: (via telephone) Thank you very much. This is Dan Salmon from NVPO.

The update I'm going to give is really just a continuation of an ongoing topic which I have discussed with the Commission, which is the NVAC white paper on the vaccine safety system. We have discussed this at multiple meetings. Essentially, the NVAC was charged with looking at the vaccine safety system and developing a white paper to help us take advantage of new technology and new science and make the safety system as robust as possible. At the last NVAC meeting, there was a draft, of course, that was discussed at the NVAC. In the September meeting that report will have been revised and will be voted upon. This is really the ending of a process that has gone on for more than 2 years. If you want to see a copy of the last draft, it's available on our website, and the new revision will be available before the meeting.

That's really the only update I have. I'm happy to answer any questions you might have.

MS. DREW: Are there any questions from the Commission for Dr. Salmon?

(No response)

DR. SALMON: Thank you.

MS. DREW: Thank you.

Is Dr. Gidudu here?

(No response)

DR. GRUBER: (via telephone) This is Marion Gruber.

MS. DREW: Dr. Gruber, would you be prepared to go ahead now?

DR. GRUBER: I could, yes.

MS. DREW: All right. Since you spoke up, we're going to ask you to do your report.

This is Dr. Marion Gruber, who is going to give us an update on the Center for Biologics, Evaluation and Research, Food and Drug Administration, vaccine activities.

Agenda Item: Update on the Center for Biologics, Evaluation and Research, Food and Drug Administration Vaccine Activities

DR. GRUBER: Thank you very much.

My update is rather short today. I wanted to mention that since the last ACCV update that we had in June 2011, the Office of Vaccines did not approve any new vaccine, except that on July 18, as also noted in the

meeting booklet for ACCV, we approved the 2011-2012 influenza vaccine formulation for the six vaccine manufacturers that are licensed in the United States to produce and distribute influenza vaccine for the United States.

We have, in addition, a number of vaccines currently under review. These include, for example, a vaccine to prevent infants 2 to 16 months of age from getting meningococcal disease. These are vaccines that are already licensed for use in older children and in adolescents and adults. They are now under review to be given to infants.

We also have a vaccine that is already licensed for use in infants, the pneumococcal conjugate vaccine. This vaccine is under review to prevent pneumococcal disease in adults 50 years of age and older. And there is an influenza vaccine containing four influenza strains, the so-called quadrivalent influenza vaccine, currently under review.

So the office is keeping busy with reviewing new vaccines.

Lastly, what I wanted to mention is that we, unfortunately, have a change of leadership in the Office of Vaccines, just because Dr. Norman Baylor, who is the current director of the Office of Vaccines Research and

Review, has decided to leave the FDA to pursue other endeavors. He has been our office director for the last 6 years. He has served the Center for Biologics for, I think, the past two decades. I want to mention that he really has shaped the Office of Vaccines in many ways. He has made tremendous contributions to the office and CBER and the FDA. He has led this office through many very significant challenges in the world of vaccines. We really will miss him in the many vaccine-related issues that confront us on a daily basis.

Until a permanent director has been appointed, as the deputy director of the Office of Vaccines, I have agreed to serve as acting office director of the Office of Vaccines after Norman's departure at the end of this month.

That's all I wanted to inform the committee about today. I'm happy to take some questions if there are any. Thank you.

MS. DREW: Any questions from the Commission?

(No response)

Thank you, Dr. Gruber. There are no questions.

DR. GRUBER: Okay, thank you.

MS. DREW: Is Jennifer Hamborsky on the line?

MS. HAMBORSKY: (via telephone) We're here.

MS. DREW: Okay, great. We are now going to move to the review of the vaccine information statements.

Who is there speaking?

MS. HAMBORSKY: It's Jennifer Hamborsky and Skip Wolfe.

MS. DREW: Thanks.

Agenda Item: Review of Vaccine Information Statements

MS. HAMBORSKY: We're thinking we could start with rotavirus, because you guys reviewed that in June. The revisions are very, very minor. The only thing that occurred was that a history of intussusception is now a contraindication. There is a new bullet in section 4 noting that.

If anybody has any other comments, that should go pretty quick, since we just did this in June.

MS. HOIBERG: I just have a comment on the rotavirus vaccine, the number 2 where it talks about better hygiene and sanitation have not reduced rotavirus very much in the United States. Could we just take that "very much" out and just say that it has not reduced rotavirus diarrhea in the United States, or maybe has not reduced it significantly or something? It just doesn't sound like good English. Maybe "Better hygiene and sanitation has not been very successful in reducing rotavirus diarrhea."

MR. WOLFE: Unless it's true that it hasn't reduced it at all, I don't think we can say that, but we

can find another way to say that it has only reduced it slightly.

MS. HOIBERG: Okay.

MS. HAMBORSKY: Any other comments?

MS. HOIBERG: Yes, I'm sorry. In number 3, where it talks about the dosing, why is it so specific to say 14 weeks and 6 days?

MS. HAMBORSKY: Because it can't be given after 15 weeks. It's very specific. It can only go up to 14 weeks and 6 days.

MR. WOLFE: This is something that ACIP has been doing, because the times that you say 15 weeks, it's not clear to people whether they mean the beginning of 15 weeks or the end of 15 weeks. They wanted to make it so specific that nobody could possibly misunderstand it -- although they will anyway.

MS. HOIBERG: Yes, they will.

Then this is my comment. You can kind of like put it through the entire thing. I know that we have talked about this at length, but it still really bothers me where it says, "What should I do?" under the moderate to severe problems. It just says, call a doctor or get the person to a doctor right away. I still really want to stress that it should say, call emergency services or get them to an emergency department immediately. When I think

of getting somebody to the doctor, I think of getting them to my practitioner. I don't think about a hospital. I think that in these really bad cases, they need to be directed very specifically to call your emergency services, because not everybody has 911 -- but for it to say, call emergency services or get them to the emergency department, the closest emergency department or urgent care center.

MR. WOLFE: Is there anyone still on the Commission who was -- we discussed this several years ago and decided not to say that, and I can't remember why.

MS. PRON: We discuss it in June, I believe. I don't remember what the outcome was. I thought that it was going to change. Did it have to go through CDC or was there some other reason why it didn't change?

MR. WOLFE: Well, the discussion we had at the ACCV meeting -- we decided not to change it there. I can't remember the rationale.

MS. WILLIAMS: I think that section is different than if somebody has a moderate or severe problem. If you compare 4 and 6, 6 is where -- call a doctor or get the person to a doctor right away. Sarah, is that where you are talking about 911?

MS. HOIBERG: Yes. If they experience -- what if there's a moderate to severe problem? I just don't think that to call a doctor or get the person to a doctor right

away is strong enough language, and I think it's misleading. Honestly, when I say, call a doctor, I don't think about calling a hospital. I think about calling my doctor. I don't know. I just think that --

MS. PRON: I'm looking at our minutes from June. It did say that Mr. Wolfe agreed to consider wording that would reflect the gist of the discussion, which included calling emergency services.

MS. WILLIAMS: A lot of times -- and I know we said this before -- if you call the doctor, the doctor's recording clicks in and says, call 911.

MR. WOLFE: That's true, if it's an emergency.

MS. HOIBERG: Right, but that's one extra call.

MS. WILLIAMS: Exactly.

MS. HOIBERG: Those are seconds that are crucial. You know what I mean? It's like, yes, if you call a doctor, it says, if it's an emergency -- but I really think that it should be, get a person to a hospital or emergency place right away. If I had waited to call my doctor, if I had waited on my doctor, I would have been in big trouble with my child. I'm smart enough to call 911, and hopefully a lot of people are. But we talk about it needing to be -- I just don't see what the big deal is. Why can't you say to call emergency services?

MS. HAMBORSKY: I wasn't involved in it prior to

recently, but the other feeling that I had was that there are other people who review these. There are other groups. There are consultation meetings. There is public comment. At some point there was somebody who was very adamant about not instructing people to call 911 because they were concerned that they would call 911 for not serious reactions --

MS. HOIBERG: People do that all the time. I think that just falls along the line of you all wanting to simplify something that doesn't need to be simplified, such as the dosage of a certain vaccine. I think the idea of simplifying and thinking that people are going to call 911 -- people call 911 for stupid reasons all the time. But these are children's lives that are at stake, and some people read these and really do what it says. I don't understand why it can't say to call emergency services.

I'm done beating the dead horse, apparently.

MS. HAMBORSKY: We'll go back and we'll have to go through and see. As committed to changing it as you are, there were some people who were committed to not changing it. We're just going to have to figure out -- maybe we can balance that with going back -- when we go to the consultation meeting, which would include the other outside agencies, just like the Commission here has kind of changed their thinking, maybe we can present this and the

consultation meeting will change their thinking, too.

MS. HOIBERG: Okay.

MS. WILLIAMS: You all may not know the answer to this question, but what does the package insert say?

MR. WOLFE: We don't know offhand. They would all be different. I don't know if there is standard wording on package inserts. The package inserts aren't really designed so much for the patients.

MS. WILLIAMS: I understand.

MS. HAMBORSKY: Is the FDA person -- Marion, I think -- is she there? Would she know?

DR. GRUBER: I do not know right offhand. I have the package insert in front of me. But I don't think that we would put that type of language in there. I'm looking at it. I don't see -- I don't think we would put language like that. I would have to look at patient packages. It only has a reporting-of-adverse-events section. For instance, the RotaTeq, the Merck rotavirus vaccine, tells you that parents or guardians should be instructed to report any adverse reaction to their health-care provider. The health-care provider should report all adverse events to the U.S. Department of Health and Human Services, the VAERS system, the vaccine adverse event reporting system. Then it gives you a toll-free number to call VAERS. But that's the extent of it in the package insert.

MS. PRON: I think the issue that came up in June was that right before this section it talks about a serious allergic reaction, including difficulty breathing. If you are putting in here that they need to call their doctor right away, you're wasting time. That was really the concern.

DR. FEEMSTER: I think we also were looking at the phrase where it says call a doctor or get the person to a doctor right away, which implies kind of skipping the call-a-doctor part and getting them to a hospital as soon as possible.

MS. PRON: It doesn't say hospital, though. It says to a doctor.

DR. FEEMSTER: You have doctors in clinics and hospitals. I think that was the --

MS. HOIBERG: But a parent is going to think, my kid's pediatrician. That's who they are going to go to.

DR. FEEMSTER: So do we have to be explicit about emergency services or saying to get someone to any kind of provider right away? Is that strong enough to imply, call 911 if you need to.

MR. WOLFE: If we are specific in saying emergency services, would that --

MS. PRON: That would help.

MR. WOLFE: But maybe emergency services aren't

readily available. Then maybe we're being too specific the other way.

There may be some reasonable, less specific language we can use that will -- I don't know what it would be, but we can be thinking about that. Get the child to a place where they are going to receive medical attention.

MS. WILLIAMS: I'm sorry, I know that we are covering plowed ground, but when we went down that road, we then got into a parent putting a child that can't breathe in the back of their car. Let's face it: If you have this situation, you need an EMT. You don't need to be in a car with a child who can't breathe.

MS. HAMBORSKY: What if we said something like, "This is a medical emergency. Seek treatment"? Then leave up to them who they call. Something like that: "This is a medical emergency. Seek treatment." In some places it may be calling the fire department. It may be calling 911. It depends on where you are.

MS. WILLIAMS: In order to short-circuit this, would it be appropriate for you to go back to your consultation committees and simply request that some written document for thinking or analysis be provided back to us so that we can take that into consideration when we make our recommendations? This is clearly something that has been recurring as a topic periodically.

MR. WOLFE: Yes, and we can discuss it with people here who have actually been in clinical practice and people who -- we can get a variety of opinions just within our office, if we need to, and we might come up with some good ideas.

MS. WILLIAMS: That sounds really good.

MR. KING: Before we move on, I heard you say that you might use the phrase “seek treatment.” Maybe we should put the word “immediate” in front of the word “treatment.” It would be “seek immediate treatment.” That might create the sense of urgency that’s required.

MR. WOLFE: Anything to make it sound as critical as we can.

MS. DREW: In section 7, where you reference the program, we have actually updated that wording on all of the other VISs. We need to say that people should learn how to file a claim as opposed to “may file a claim” by calling the phone number. That was probably a cut-and-paste error. If you look at all the other ones, we have changed them before.

MR. WOLFE: You’re right, that was just a cut-and-paste. It will reflect the latest wording.

MS. DREW: Okay, if you could just do that.

MS. HAMBORSKY: Is that everything for rotavirus?

MS. DREW: It looks like it.

MS. HAMBORSKY: The next one we'll do is hepatitis A. That's similar to rotavirus, in that the only thing that has changed since the last time it was reviewed at ACCV is a bullet for the use of vaccine for post-exposure prophylaxis, and another bullet was added about indications for people adopting a child from an endemic country.

MS. HOIBERG: My only recommendation is in section 3, the last bullet, tell your doctor if you are pregnant. The safety of hepatitis A for pregnant has not been determined, but there is no evidence that it is harmful to either pregnant women or their unborn babies. The risk, if any, is thought to be very low.

If it has not yet been determined, how can we say that there is no evidence that it's harmful? It's too big of a question mark for me. You are saying that it hasn't been determined if it's safe, but there's no evidence saying that it's harmful. But you can't prove that it isn't, so maybe pregnant women shouldn't get it.

MR. WOLFE: I'm not sure, but I think this wording is right out of ACIP.

MS. HAMBORSKY: And it also may come from -- and the FDA person may be able to help with this -- I think because of the way the categories are, they don't test it on pregnant women, but there may have been a pregnancy

registry. That's where they would be saying there is no evidence that it's harmful, if they collected data from the pregnancy registry. But the safety of it hasn't been determined because they didn't test it in pregnant women.

MS. HOIBERG: I'd guess I would like to hear Marion's --

DR. GRUBER: We're still talking about the rotavirus vaccine, right?

MS. HOIBERG: No. We're talking about hepatitis A.

DR. GRUBER: The hepatitis A vaccine -- that is absolutely true -- has not been tested in pre-licensure trials in pregnant women. The package insert then states that the safety of the vaccine has not been tested and we cannot really make any statement. But you are absolutely right. The pregnancy category C that is being assigned is not a contraindication. The pregnancy category C says even though there are no adequate and well-controlled studies in pregnant women or even animal models, if the decision is made that the vaccine is clearly needed -- because, let's say, the pregnant woman is exposed to the virus or there happens to be an outbreak of hepatitis A -- then vaccination of the pregnant woman is called for and the vaccine can be administered. In other words, pregnancy category C says, give if clearly needed. That's a

risk/benefit call, a judgment call, there.

But it is true that we have not studied hepatitis A vaccine in adequate and well-controlled studies in pregnant women. You know what? If you ask me if we have a pregnancy registry for hepatitis A, I do not believe there is one. But I could be mistaken. I would have to look this up real quickly.

MR. WOLFE: I don't think there is one now, and I'm not sure if there ever has been.

DR. GRUBER: I don't think there has been. I'm pretty sure, actually, that there hasn't been. Usually I would be aware of this.

MR. WOLFE: In any case, the decision on whether or not to vaccinate is going to be with the provider and not the patient. That's why we say, tell your doctor.

MS. HOIBERG: Is there any way -- because I realize that it does say that some people should not get the hepatitis A vaccine or should wait -- is there any way to add something in there, that if you are pregnant -- like just with what Marion said -- it should be given only in extreme circumstances, that it's not just a routine --

MR. WOLFE: We could say that, but that seems like unnecessary wording. We say, tell your doctor. The doctor is going to be the one making the decision. It's not going to be the patient who determines whether the

situation warrants it or not, I don't think.

MS. PRON: How about if you just eliminate the last two sentences, "but there's no evidence that it's harmful to pregnant women or their unborn babies," and "the risk, if any, is thought to be very low"? If you don't have the information, you could just end it after the first two sentences.

MR. WOLFE: We'll check and see what the ACIP statement says. If it is, in fact, true, it's nice to reassure the patient that if the doctor does decide to give it to them, it's not going to be harmful.

DR. GRUBER: The point is, it could very well be that there is no evidence because, simply, there are no data. There are some data on other vaccines in pregnant women, but for hepatitis A vaccine, I am not sure what data we have available on the safety of this particular vaccine in pregnant women. One should really look into this. If there are really data from published literature that sort of supports the safety, that's one thing. But if "no evidence" really means "no data," then perhaps one should consider revising the wording a little bit. That would be my suggestion.

MR. WOLFE: We can check and see what evidence ACIP looked at before making their recommendations, whether they are extrapolating from other inactivated vaccines or

whether they actually have some data.

DR. GRUBER: That is a good idea. My guess is that perhaps it is an extrapolation from other inactivated vaccines, but I don't know that for sure.

MR. SMITH: Dr. Gruber, maybe just one final point before we leave this particular topic. I don't want to jump ahead to the meningococcal VIS. In that instruction as it relates to pregnant women, what the VIS states is that MCV4 has not been studied in pregnant women, but the recommendation -- and I believe it's consistent with the package insert -- is that it should be used only if clearly needed.

I guess my question would be if the hep A package insert would include, potentially, a similar recommendation, even though, as you suggest, there may be no data in that particular population. It may be worthwhile to check the package insert and ensure consistency on this point.

DR. GRUBER: The package inserts do have these statements under the pregnancy category. That is a category C. That's straight out of the regulations, the law. That says the vaccine should be given only if clearly needed. That is language that is actually prescribed by law that has to go under the pregnancy category C. Since the hepatitis A vaccine is a category C, that language is

in the package inserts.

MS. HOIBERG: Then that last part should be -- I really think that that “but there is no evidence that it’s harmful” should be completely taken out, because that’s an assumption, and I think it’s a dangerous one. I think that they should then replace it with what the package insert says, that it should only under extenuating circumstances be given to pregnant women. That’s what I think it should say.

MR. WOLFE: We’ll look into that.

MS. HAMBORSKY: We’ll go back and see, like the discussion earlier, if there truly is no data or where it came from in the ACIP statement.

DR. GRUBER: The hepatitis A Havrix, they say in the package insert -- under “Use in Specific Populations,” it says safety and effectiveness of Havrix have not been established in pregnant women and nursing mothers. If you go down to section 8.1, which is the pregnancy section, that’s a pregnancy category C. That says Havrix, in this case, should be given to pregnant women only if clearly needed. That is what I was referring to. That is the category C language which is prescribed by law. That’s always used if you don’t have well-controlled studies in pregnant women.

MR. WOLFE: Okay.

MS. HAMBORSKY: Say the wording one more time, the exact wording that is prescribed by law.

MR. WOLFE: We have that.

MR. SMITH: If you look at the next VIS that we look at, under number 4 -- some people should not get meningococcal vaccine -- one of the bullets uses the language. Consistency, given the pregnancy category, between the VIS sheets seems to make sense.

MS. WILLIAMS: Are we talking pregnant and nursing, pregnant or nursing?

MR. WOLFE: There is a general ACIP recommendation that any vaccine except smallpox can be safely given to a nursing mother.

DR. GRUBER: Again, if you look at the package insert, for instance, for the GSK hepatitis A vaccine, we always have a pregnancy section and a nursing mother section. The nursing mother section says for the GSK hepatitis A vaccine that it is not known whether Havrix is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised in Havrix administered to a nursing woman. It says that caution should be exercised. That's what we say. But again, that's because we don't have any data, really. There have not been done studies in nursing mothers.

MR. WOLFE: I'm looking at the ACIP statement.

The wording is slightly different than what we have here, but it says essentially the same thing, that the theoretical risk is low. There is no link to a reference there, so I'm not sure -- we'll just have to talk to the hepatitis A people who wrote this and see if there is any basis other than the category C for their recommendation.

MR. KING: I have a question. The Ig, which is the immune globulin -- I think I'm pronouncing that correctly -- that gives immediate temporary protection. How long does that protection last for?

MR. WOLFE: I don't know.

DR. FEEMSTER: They are antibodies, so they will circulate for a couple of months or longer. Every immune globulin is a little bit different, but it would be a matter of probably months.

MS. HAMBORSKY: Where is --

MR. KING: That would be under "When?" So is that an alternative for a pregnant person?

DR. HERR: There are risks to that, too.

MR. KING: Is it the same risk?

MS. HAMBORSKY: I would probably have more concern about giving Ig to a pregnant person for hepatitis A than the vaccine.

Do you know what category it is for Ig?

DR. GRUBER: I would not know that, no. I'm

speaking strictly from the vaccine perspective here. If I would take a guess, I would say C, but I would have to look this up. Immune globulin -- that's the Office of Blood. I would have to look this up. Sorry, I cannot speak to that.

MR. WOLFE: And the ACIP statement does not mention Ig as an alternative for a pregnant woman.

MS. WILLIAMS: It's a blood product.

MR. KING: So is it even of a greater risk than the actual vaccine?

MS. HAMBORSKY: Greater risk of -- we don't have statistics on the adverse reactions related to Ig.

DR. HERR: Where is this statement coming from? If ACIP does not recommend the immunoglobulin for this condition, where is this statement coming from?

MR. WOLFE: We recommend it for travelers who don't have time to get the series before they travel.

DR. FEEMSTER: It's in the Redbook, under hepatitis A and prevention.

MS. HAMBORSKY: A long time ago, before there was hepatitis A vaccine, it was standard to give Ig for travel. What they are saying is -- and we have to look at the travel recs -- if you are going to a place where hepatitis A vaccine is indicated and you don't have time to get the vaccine, you can get Ig to get immediate protection. If you are going in 3 days to someplace where there is a known

risk of hepatitis A, you will have some protection from the Ig that you wouldn’t have time to get from the vaccine.

MS. WILLIAMS: As long as we are on the travel section -- maybe I just am not reading it correctly -- we have the second paragraph that says, if you are traveling, you have to start the vaccine series, which means two shots, at least 1 month before traveling. But then the last paragraph says that two doses of the vaccine are needed for lasting protection and to give them 6 months apart. The traveler is not going to get the series if they don’t start until 1 month before. So it’s a little confused.

DR. FEEMSTER: I think the idea is that if you get one dose, that will provide enough of an immune response to get you through your travel period, but if you are talking about longer-lasting immunity, then two doses, 6 months apart, is --

MR. WOLFE: Exactly.

DR. FEEMSTER: That completes the series.

MS. WILLIAMS: But temporally it doesn’t work.

MR. WOLFE: Those are the actual recommendations. There may be a clearer way of stating it.

MS. WILLIAMS: Is there some way to put travelers’ information separate from best protection? That whole section is just a little confusing.

MR. WOLFE: We'll think about ways to reword that. The concept that we just talked about is accurate, though. For the vaccine to be effective, you should get one dose a month before you travel. For those who can't get it a month before they travel, then Ig might be recommended. If you don't have time to get the 6-month dose and you need longer-term protection, it's still necessary to get that, but you can get that when you return.

DR. FEEMSTER: Would it be helpful to move the two phrases, the "for best protection" phrase and the phrase in the section in the box, to the end and maybe just have something that says "For Travelers" in italics or something? These are the recommendations specifically for travelers. First you have all of the standard -- this is what children need, you need two doses 6 months apart for full protection, everything that applies to everybody for whom the vaccine is recommended. Then you have the section that speaks specifically to travelers.

MR. WOLFE: Yes, that's a good idea.

MS. WILLIAMS: Exactly.

MS. HAMBORSKY: We just have to think about that, because this is in the "When?"

DR. FEEMSTER: It wouldn't change the wording, just the order of the phrases.

MS. HAMBORSKY: But that's more talking about indication than when. We have to think about, if we change it that way, would it then go more into a different --

MS. HOIBERG: I don't think so, because when you are traveling, you need to have it.

DR. HERR: Why not just leave out "for best protection"? Just leave that out. Just start with "Travelers."

MS. WILLIAMS: I agree with Kristin. It's just mixing categories of people within the paragraph. This is simply paragraph structure.

MR. WOLFE: Yes. We'll see what we can work out with that.

MS. PRON: I want to go back to number 3 again. I wasn't sure whether we settled that last paragraph about pregnancy, because we got into the traveler. But is it true, then, that you will be changing that to say, like it does in meningitis, that it should be used only if clearly needed?

MR. WOLFE: We'll see what our reviewers here think, but that's a possibility. I can't say for sure what we will change it to.

MS. PRON: I thought that was in the product insert.

MR. WOLFE: It might not match the product insert

exactly.

DR. GRUBER: It not always matches what's in the product insert, but, as I mentioned before, the product insert is written strictly by what data are available and have been submitted by the manufacturer to support a statement. We really cannot put any other claims in the product insert. We need to really look at what data have been submitted. Again, if we have not seen data on the safety and effectiveness of a product in pregnant woman, we will put in a statement that the safety and effectiveness have not been demonstrated, and then we put in the pregnancy category C that says, give only if clearly needed.

In the ACIP, they have other considerations for why they would put certain recommendations for a certain vaccine. It's not necessarily the same, as was just stated.

MS. HOIBERG: I strongly, strongly urge you to take the whole two sentences out that talk about that there's no evidence that it's harmful to pregnant women. It's just simply not true. They haven't done the research, so we don't know whether it is or not. Therefore, I think it should be taken out.

MR. WOLFE: It is true, but it may not be complete.

MS. HOIBERG: You could say that there's no evidence that it's harmful, but I just -- because the only reason that there is no reason is because you haven't done the research. So there's no evidence that it's harmful and there's no evidence that it is. Just take it out. Really, blatantly, it's a safety issue. You're talking about pregnant women and their babies. To just throw it out there like it doesn't matter is disgusting to me.

MS. WILLIAMS: But I think the issue is, if you have a pregnant woman who is a nurse who gets a needle stick, you have a cost-benefit analysis about potentially giving hepatitis to their child versus getting --

MS. HOIBERG: Right, so then they need to put in there that in certain circumstances to go ahead and have it. But I don't think that they should just --

MS. WILLIAMS: I should retract that. A needle stick would probably be a candidate for immunoglobulin. That was the lawyer talking medicine, and she shouldn't have done that.

MR. WOLFE: We'll see what evidence ACIP has looked at. There may not be any evidence from studies, but there may be a lot of practical evidence from the vaccine being inadvertently or intentionally given to pregnant women over the years that suggests that there is no risk.

MS. HAMBORSKY: Right. We just need to check,

because it is written that way in the ACIP statement. We need to find out -- someone may have done an analysis of VAERS data. We just need to check and see. That's the way it's written in the ACIP statement. There may be some evidence and it just is not cited as a resource.

MR. WOLFE: But we'll check all of that before making a decision.

MS. WILLIAMS: I have a comment on section 4 if we are ready to move on. The sentence says, "If these problems occur, they usually last 1 or 2 days." Is this a place where we want to say, if they last longer, see your doctor?

MR. WOLFE: Well, if that's really a recommendation we want to make.

MS. WILLIAMS: I don't know. What I'm wondering is, I'm reading this and my child has a headache for 5 days now, is that something -- we are telling them, moderate or severe, to seek medical help. It may be a mild problem, but you seem to be limiting it so that it's only mild if it's 1 or 2 days. The question is, if it lasts longer than 1 or 2 days, does that mean that it's moderate?

MR. WOLFE: We can check on that. It may just mean exactly what it says. It usually lasts 1 or 2 days, but it could last longer, and if it does, it may still not be a big deal. But we'll check and see if that's actually

the case or if there is something that people should do if it lasts longer than that.

DR. FEEMSTER: It also could mean -- for example, in advising families if there is a fever after a vaccine, if it lasts longer than 1 or 2 days, sometimes the recommendation is to come back in because you want to make sure it's not from something else. So it's not just the vaccine, but an evaluation to see if these symptoms are related to something else. If you were to put that statement in, it might be just to make sure your child is evaluated for any etiology with those symptoms.

MR. WOLFE: That's a good suggestion. And that would apply to other VISs, too.

DR. FEEMSTER: Under section 2, when we list all of the bullets for who should be routinely vaccinated, it is all children between their first and second birthdays. The third bullet says children and adolescents through 18 years of age who live in a state or community where routine vaccination has been implemented. Does it make more sense to say children older than age 2 and adolescents through 18 years of age? If all 1-year-olds need to be vaccinated, then all 1-year-olds need to be vaccinated. So can we say children older than age 2 and adolescents? To me, then it suggests that only 1-year-olds who live in places where routine vaccination has been implemented need to be

vaccinated.

It was just a little confusing to me, because you already say that all 1- to 2-year-olds have to be vaccinated.

DR. HERR: Why don't we add "who have previously been unimmunized"?

DR. FEEMSTER: That's a good idea.

MS. PRON: Rather than "living in communities"?

DR. HERR: It says children and adolescents through 18 years of age who have previously been unimmunized who live in states or communities where routine vaccine has been implemented because of high disease incidence or the other part. It just implies that they haven't already been immunized. So it's okay to immunize all of the other people.

MS. PRON: I thought it was on the recommended list of ACIP immunizations.

DR. HERR: It is.

MS. PRON: So whether your community has high disease incidence or not, it's recommended.

DR. HERR: But what we are asking here is -- we say we give it to 1-year-olds and then we skip to the next one that says we want to give it to 18-year-olds or adults who are living in these communities. What about somebody who is 3 who has not been immunized? They are not 1

anymore. There are some vaccines, like the rotavirus, that you are only going to give during a particular period of time.

DR. FEEMSTER: It needs to be clarified.

MS. HAMBORSKY: If it understand it, it's getting at the catch-up issue. There isn't a firm everybody-needs-to-be-caught-up. The people who need to be caught up are the kids who are living in communities with high risk.

DR. FEEMSTER: So children over the age of 2 and adolescents.

MS. HAMBORSKY: Right.

DR. FEEMSTER: Okay. So maybe just saying that -- the idea is that you want to vaccinate all young kids because they are at increased risk of infection in general. Once they are older than age 2, it just matters whether or not you live in a place where you need to have more vaccinations.

DR. HERR: Another alternative would be with the first bullet. Some children should be routinely vaccinated with hepatitis vaccine: All children, beginning between their first and second birthday.

MS. HOIBERG: Because this is like -- it just goes up -- this is 12 to 23 months of age. Why not 24 months of age?

DR. FEEMSTER: Because once you hit the age of 2,

then you are not in that high-risk category. I guess you could say 23 months --

MS. HOIBERG: But it's not the same as, like, with rotavirus, where you are not supposed to get it after a certain --

DR. HERR: You guys hash it out. You got our input. You hash it out.

MS. HAMBORSKY: We'll look and see if there is a way we can add the older-than-2. We have to talk to the hepatitis people here, because this is getting at the catch-up issue.

DR. FEEMSTER: I didn't look at the official ACIP recommendation. It just sounded confusing reading through it on the VIS.

MS. HAMBORSKY: We're looking at the schedule right now.

MR. WOLFE: The catch-up schedule for hepatitis A -- one of the footnotes says it's recommended for children older than 23 months who live in areas where programs target older children or who are at increased risk.

DR. FEEMSTER: Maybe we could just mirror that and add that "greater than age 23 months" to the statement here.

DR. HERR: It's under "When?" The first thing

under “When?”: In children, the first dose should be given at 12 to 23 months. Children who are not vaccinated by 2 can be vaccinated at later visits. We have a catch-up phrase right there under “When?”

DR. FEEMSTER: I guess the goal is just to make sure the who is consistent with the ACIP recommendation.

MS. HAMBORSKY: And it says children 23 months of age and older. So we could say children older than 2 and adolescents through 18.

MR. WOLFE: Routine at 12 through 23 months, and anything after that is catch-up or a special situation.

MS. DREW: My question would be, if we are talking about the people in the second and third bullets there, are we talking about people who should be getting a second vaccine because they need long-term protection? That’s what is not clear to me. Let’s assume that all babies get it before they are 23 months. Do kids living in places such as mentioned in here need a second shot? Is that what you’re trying to say?

MS. HAMBORSKY: No. What it’s getting at is, the universal recommendation for all children 12 through 23 months is relatively new. It used to be not routinely recommended. It was based on risk. There used to be a very complicated -- it was very complicated about who vaccine was indicated for at certain ages, and it was risk-

based. Then we went to the universal recommendation of all kids 12 through 23 months. This other bullet is getting at all of those kids who are not 18 yet and didn't get vaccinated because they weren't living in a high-risk area, but now there is this universal recommendation that they should have gotten it when they were 1 to 2. So it's the catch-up part of it.

MS. DREW: Okay.

MS. HAMBORSKY: Any other comments for hep A?

DR. GRUBER: People from FDA looked at these VISs and we had some minor comments that I would just like to run by. The first one is actually not that minor. This is under section A, "What Is Hepatitis A?" the bullet that says sometimes people die as a result of hepatitis, about 3 to 5 deaths per 1,000 cases. We wanted to get clarification of what the real denominator is here. Is it really death rate amongst hospitalized patients or amongst reported cases or is it more than that? We feel that this figure of 3 to 5 deaths per 1,000 seems to be high, unless the denominator is the hospitalized people or those that are reported. Or is it total cases? We feel that needs to be clarified.

MR. WOLFE: We'll check. I have the ACIP statement here. I'm not sure if I can find that figure immediately, but we'll check.

DR. GRUBER: Okay. The other comment is, under section 2, on the second page, where it says other people might get hepatitis A vaccine in certain situations, and ask your doctor for more details, the second bullet says unvaccinated people who have been exposed to hepatitis A virus to prevent infection.

Our experts are suggesting that that should be modified to say unvaccinated who have been exposed to hepatitis A virus no more than 2 weeks prior. Basically, it depends on if you have been exposed and then you are going to be the shot or it's not sort of unlimited. There is a certain time window there. The suggested revision that was submitted is unvaccinated people who have been exposed to hepatitis A virus no more than 2 weeks prior, to prevent infection.

MS. HAMBORSKY: Okay.

DR. GRUBER: The last one I think is very minor. That's under section 4, under mild problems, where it says soreness where the shot was given, it says about one out of two adults and, I think, up to one out of six children. Our comment to that is, because we have two hepatitis A vaccines, Vaqta and Havrix, and the adverse events vary slightly, we were suggesting, when one speaks of the one out of six children, to sort of precede this with the word "about." Then the slight revision would be, about one out

of two adults and about one out of six children.

MR. WOLFE: Let me just explain. When we say “up to,” we say that because if there have been several different studies or if there is a range of data -- and I’m not sure what they were in this case; one of them might have been one out of three and one was one out of six -- we usually just say “up to” the higher number instead of saying “about,” if there is a fairly broad range with different studies.

That’s the reason. That doesn’t mean that we have to keep that. But that’s why we say “up to” instead of “about.” If there were two studies and the results were very similar, we would say “about.” If there were several studies and the range might be a little broader, then we usually say “up to” and use the higher number.

DR. GRUBER: Okay. Again, I thought that was a minor comment. The biggest comment was the one in the section 1.

So that’s from this side. Thank you.

MS. WILLIAMS: I have two comments for section 1. I realize that we’re jumping around. In section 1, we talk about transmission, then we talk about symptoms, and then in the last sentence we talk about transmission again. Again, this is paragraph structure. Would the last sentence that starts “A person who has hepatitis A” be more

appropriate to be put up with the first sentences that talk about transmission?

MS. HAMBORSKY: Yes, we can move that up.

MS. WILLIAMS: My second question is, under "Hepatitis can cause," the second bullet, jaundice, you have, parentheses, yellow skin, then you have eyes. I'm assuming that what you mean is yellow to modify the word "eyes." But just to be clear, I think what you mean is yellow skin, yellow eyes, dark urine.

MR. WOLFE: Yes.

MS. WILLIAMS: It might confuse some people. What about the eyes?

My last comment is in section 2 -- we may have discussed this, and this is a question -- under the bullet, "Persons who use street drugs," is that the all-encompassing phrase that we are trying to use there?

MR. WOLFE: I think that's a colloquial phrase that someone suggested we use.

MS. WILLIAMS: Okay. Would the words "or illegal" -- were you trying to get at needles?

MR. WOLFE: Injection and non-injection drugs. It says users of injection and non-injection illicit drugs. That's the wording in the ACIP statement. I think "street drugs" is just our euphemism that we believe more people will understand.

MS. WILLIAMS: What's that language?

MR. WOLFE: Injection and non-injection illicit drugs.

DR. EVANS: Skip, can you remind us, what is the education level that you are trying to be consistent with in wording?

MR. WOLFE: Anyone, really. We try to make it accessible to anyone who can read. There is not a specific education level that we are shooting for.

DR. EVANS: "Illicit," though is certainly a harder word.

MR. WOLFE: Definitely, yes.

MS. HOIBERG: "Illegal" you could use.

DR. EVANS: But it doesn't have to be illegal.

MR. WOLFE: We could probably say drug users, and that would mean just as much to most people.

MS. WILLIAMS: I'm not objecting to the word "street." I was just wondering if it was as all-encompassing as you wanted. My view would be to add those other words.

MR. WOLFE: I'm trying to remember back. I'm pretty sure it was our hepatitis people who gave us that term. I believe that's probably the term they used in their educational materials.

DR. DOUGLAS: From health literacy, the average

reading level for the American public -- not any special minority group, but the American public -- is 8th grade. Too many of us know friends who are like us. To decrease the reading level, you decrease the number of syllables in a word. It is actually much more powerful than you would imagine. Just going to “street” from “illicit” is a decrease, and you are taking out a three-syllable word. The number of your syllables is important.

MS. WILLIAMS: Again, it’s not an objection. I was just trying to --

MR. WOLFE: I think that’s where it came from. I’m pretty sure that came from our hepatitis B people, because that’s the term they found was effective.

MS. HAMBORSKY: And, frankly, given the average age of all of us, the people who are parents in their 20s now may call it something completely different that we don’t even know. There might be a term from the 1970s or something. I don’t know.

MS. WILLIAMS: If I could just make one more comment -- and this is a general comment for all of these documents -- the health literacy comment is critical. I know that in hospitals we recommend that the consent forms be written at a 5th-grade level, and there is a process called “smogging,” where you can rate the literacy of each document. I was just wondering if these documents go

through that process.

MR. WOLFE: Frankly, I don't think that is a very effective way to measure readability.

MS. HAMBORSKY: For these documents, because there are some words -- if you take meningococcal, the next one -- it seems like SMOG and different readability formulas have been applied to these, but then when we actually looked at them, we couldn't really -- they weren't valid, because there is no other way to say "meningococcal." It skews them. It just throws them off. There are just certain things where there is no other way to say them with these medical words.

MR. WOLFE: Which is why we tried to periodically do some focus group testing with them, to get actual parents to look at them and let us know how readable they think they are.

MS. HAMBORSKY: Which we just did recently, this winter, our communications group. I actually went to the focus group with them. We did parents in five locations, stratified by all kinds of socioeconomic levels, education levels, children levels. They are still testing very well.

MS. WILLIAMS: That's very good information and reassures me about the products that you are turning out. I thank you for that information.

MR. WOLFE: I will also say that if it were up to

Jennifer and me, they would be a lot simpler than they are. Sometimes we are overruled by epidemiologists who insist on saying things a certain way. Just a gripe that we have.

MS. HAMBORSKY: Actually, going to the focus group thing and watching the moms read these, it really was eye-opening how much -- for lack of a better word -- brand recognition these sheets had. As soon as we turned them out, everybody was, like, oh, yeah, that's the vaccine sheet. It was very, very helpful to go and watch them.

MS. WILLIAMS: If you have an opportunity to have someone on your task force or committee, may I recommend Sarah?

MS. HOIBERG: I'm a parent.

MR. WOLFE: So are we.

MS. HAMBORSKY: So are we, yes. I have a 3-year-old who actually is in VAERS.

Are we done with hepatitis A?

MS. DREW: I think so.

MS. HAMBORSKY: Let's go to meningococcal. Would you like me to go through the sections that have changed? Maybe with this one, what we will do is just go through it, section 1, section 2, and have everybody give their comments, instead of jumping around.

Are there any comments for section 1?

MS. WILLIAMS: Yes. For the words "college

freshmen," is that the group or college students?

MR. WOLFE: The studies were very specific about that, that it was only freshmen living in dorms who were at increased risk, weird as that is.

MS. WILLIAMS: So it's not college students living in dorms.

MR. WOLFE: No. It's freshmen.

MS. WILLIAMS: Okay. That's my only question there.

MR. WOLFE: I don't know, if you are a 30-year-old freshman, whether that would apply to you or not.

MS. WILLIAMS: Or dating a freshman and staying over in the dorm -- not that that ever happens.

MS. HAMBORSKY: Any other comments for section 1?

(No response)

Moving on to section 2, there were a couple of changes here. The first one, we removed the sentence saying that the vaccines protect 90 percent of people who get the vaccine. That was from an FDA comment about the seroresponse rates differing by lab. We also removed the wording about MCV4 being better than MPSV4 at preventing person-to-person spread or providing longer-lasting protection. That was based on one of our CDC SMEs.

The biggest one here -- and when I say FDA, we are talking about an additional review that goes through

Maureen Hess, and I'm not sure who she then sends it to -- our contact person at FDA for additional review is Maureen Hess. FDA suggested mentioning that there are two different MCV vaccines, that only one is approved for children down to 9 months, and that neither vaccine is licensed for children younger than 9 months.

In the group here, the opinion was that that would be a little confusing, since we are already saying that there are two types of vaccines, and adding that there are two brands within one type might be harder to understand. There was an additional recommendation for Menactra. Menactra and Menveo are virtually the same, except that Menactra is licensed down to the younger age. Because a provider will be giving only one of them, it will be the provider that will be available to answer the questions if necessary. So they didn't think that mentioning the difference was important in this section.

MR. WOLFE: In other words, from the parent's point of view, the fact that there are two different types of vaccine, the polysaccharide and the conjugate -- for the two conjugate vaccines, the recommendations are similar enough that it's not really worth the effort to point out differences between them, when the provider is there to explain, if necessary.

DR. GRUBER: I remember Maureen discussing that

at a meeting. What we really have to be careful of -- even though the meningococcal conjugate vaccines, the Menactra and the Menveo, are similar enough, one has to really keep in mind that these vaccines are actually different. Even though they may use conjugation technology in their manufacture, they are manufactured by different manufacturing processes. The term “similar enough” -- one should really be careful using that. You’re absolutely right, if the provider is there to explain that. On the other side, I don’t know where there is harm to say there are two kinds of vaccine -- one is the polysaccharide and the other is the conjugate vaccine -- and make a little sub-bullet and say, preferred for people 55 years of age or younger, there is only one that is currently approved in kids as young as 9 months of age. I don’t know why this would be so confusing. But I have not been in these focus groups and couldn’t really speak to that. But I think it was just our concern. Even though they are two conjugate vaccines, they are still different products.

MR. WOLFE: This is the type of question that we have to deal with with many of the VISs: How much information do we include that is really useful to the parent in this context, and how much is going to make the VIS so complicated to read that they are going to skip over stuff? I don’t think there is any cut-and-dried answer to

that. We just have to look at that with everybody VIS and then make a decision.

MS. HAMBORSKY: In the focus groups, just the words themselves -- getting through the VIS was very difficult for most of the participants. Then, when it came to the different products, most of them said, well, that's the doctor's decision. The doctor is going to pick which vaccine. I may not even have a choice.

DR. HERR: I think we need to sometimes remember that these statements for the physician to replace ACIP recommendations nor Redbook recommendations. They are more to educate the family about what the vaccines are. We can get too technical on these things.

MR. WOLFE: Exactly. And I think that's a very common trap people fall into, thinking that the VIS has to say everything there is to say, which isn't really the case.

MR. KING: I don't think, though, that it is a problem for both of them to be mentioned. If it is to educate the parents and the public, there's no reason why we wouldn't just leave the two of them there, as we have it here.

MS. HOIBERG: We did that with the HPV vaccine.

MR. WOLFE: There is a range of -- we have on one end of the scale DTaP, for example, where there are several

DTaP formulations, and we don't even mention that on the VIS. At the other end of the scale, there is HPV where we have two separate VISs because the vaccines are different enough that trying to explain the differences in one paper would be too confusing. This falls somewhere in between, I think.

MS. HAMBORSKY: Trying to explain to the average parent the difference between the two conjugate vaccines is very different. It's very difficult. The conjugate and the polysaccharide -- they kind of get that. But then drilling it down even more into trying to separate the very minor differences between the two conjugate vaccines, other than the licensing, the age indication, is very difficult.

MR. WOLFE: I guess the question you have to ask is, from the parent's perspective, do they need to know that, and if they do, why? Are they going to do something different if they know?

MS. HOIBERG: Is one better than the other? Does one carry a little less risk? What's really the difference?

MR. WOLFE: No. They are identical from that perspective.

DR. GRUBER: I do not think that the FDA meant to explain the differences between the two vaccines in terms of how they are made and what they do. To say that only

one of them is really licensed and has been studied for safety and effectiveness in babies 9 months of age and up is something that we thought is useful to state.

But I'm hearing the conversation. On the other side, these VISs are also living documents. They are fluid. I mentioned in my overview that one of these vaccines right now is under review to be given to infants as young as 2 months of age. When that takes place, maybe then you would consider differentiating between them, because then you have a real difference. Right now we are talking about 2 years and up and we have 9 months and up.

Very different considerations have been going into even the approval process for 9 months versus 2 years and up. I still believe that mentioning that one of these conjugate vaccines is indicated for kids much younger and that there is a difference is not too much. But if you feel it's too confusing for the parents, we have not been sitting in these focus groups. We will leave this up to the experts. But I think when Maureen talked about the difference, she wanted for it to be made clear that only one of these two conjugate vaccines is licensed in subjects younger than 24 months.

MR. WOLFE: I see your point and Maureen's point. On the other side, I would argue that a parent with a child down to 9 months old -- the doctor is only going to be

giving them Menactra. So in a sense, it's not necessary that they know that there is another vaccine that is not licensed for that age.

Again, it gets down to how much information a parent needs about the vaccines in this situation before it starts to become too confusing.

MS. HAMBORSKY: Also it's only children with certain medical conditions in that 9- to 23-month-old. We don't know how big the group is of 9- to 23-month-olds, because it's only ones with certain medical conditions.

MR. WOLFE: That's something we can continue to look at. There is a continuum between how much information is helpful and how much is confusing, and we have to walk a fine line sometimes.

DR. GRUBER: I see your point. I don't want to belabor that.

DR. FEEMSTER: If we are okay moving off of that topic, before we leave section 2, I just have one question about the very last sentence: They do protect many people who might become sick if they didn't get the vaccine. Because we are talking about the vaccine only containing some of the types, would it be more accurate or better to say that they do protect many people who might become sick if they are infected by the types in the vaccine? That's what we are really saying, that it's protecting you against

the types in the vaccine, right?

MR. WOLFE: Right.

DR. FEEMSTER: That sentence just sounded a little --

MR. WOLFE: We have dealt with this same issue in other VISs. We can look at those and see how we worded it and see if it makes sense to change that.

DR. FEEMSTER: Similar to HPV and saying that it will protect you against --

MR. WOLFE: Pneumococcal and others, yes.

MS. HOIBERG: She just brought that up, and I'm reading it now. Does that mean that the people who get vaccinated are protecting people who didn't get vaccinated, because they don't get sick and so then they don't pass it on? Or is that saying that people can get the vaccine even after they get sick?

DR. FEEMSTER: There is herd immunity, probably.

MS. HOIBERG: Is this talking about herd immunity or is this talking about --

MR. WOLFE: That wasn't really the issue. It's just people who would be infected.

DR. FEEMSTER: Your own protection.

MR. WOLFE: Yes.

MS. PRON: Maybe the English doesn't read right, but the intent is that some of you could get the disease if

you don’t get the vaccine, not all of you, because there are other strains that it’s not going to protect you against. So it seems accurate in its intent. Maybe it’s the wording.

DR. FEEMSTER: Exactly. Maybe just a specific --

MR. WOLFE: The previous sentence is important to understand that one: Cannot prevent all types of disease.

DR. FEEMSTER: But it may protect you if you’re infected with the types contained in the vaccine.

MR. WOLFE: Yes.

MS. HOIBERG: Okay, I get it. I’m sorry.

MS. HAMBORSKY: Anything else in section 2?

(No response)

Let’s move on to section 3.

MS. WILLIAMS: I have a comment about section 3. In the “Other people at increased risk,” it says microbiologists who are routinely exposed to meningococcal bacteria. Isn’t it laboratorians or laboratory workers? You don’t have to be a microbiologist to be working with meningococcal bacteria or be exposed to it around the lab.

MR. WOLFE: That terminology probably came from the ACIP statement. We can broaden that.

MS. WILLIAMS: If you look at -- it might have been on HAV -- page 2 of the hepatitis, bullet number 3, it says persons who work with HAV-infected primates or who

work with HAV in research laboratories. I think maybe it's "persons who work in meningococcal laboratories," or something like that.

MR. WOLFE: We just pulled the language out of the ACIP statement. We can broaden that.

MS. HAMBORSKY: We could say persons who work in a laboratory who are routinely exposed to meningococcal.

MS. WILLIAMS: You have already answered my freshmen comments. You should know that some colleges don't have freshmen anymore. They have first-years. But I'm not suggesting you change it.

DR. FEEMSTER: I have a couple of questions, comments. Under "Other people at increased risk," would it be better to say -- it's my understanding that the recommendations between 9 and 23 months of age are for three things: They have a complement deficiency, travel, and exposure to some kind of outbreak. At least for right now, it's not recommended if they are asplenic for any reason. Would it be better to say anyone over the age of 2 years who has a damaged spleen or whose spleen has been removed? I thought that there was at the last ACIP meeting some question about whether or not you definitely wanted to give the vaccine to asplenic children under the age of 23 months.

MR. WOLFE: I'll have to go back and look at the

minutes for the last meeting.

MS. HAMBORSKY: You're right. There was actually prolonged discuss about the asplenics.

MR. WOLFE: I'm not sure if there was a vote on that or not. Was that the one where the vote excluded asplenic children? I think it was.

DR. FEEMSTER: It says it in the slides from the ACIP transcript, but I don't think it was published in *MMWR*. But I think there was a vote on it.

MR. WOLFE: I think they voted for everything except the asplenic children and excluded that from the vote. I would have to go back and check the notes.

DR. FEEMSTER: If that's the case, then can we say anyone over the age of 2 years or 23 months?

MR. WOLFE: If that's actually the recommendation, yes.

DR. FEEMSTER: That would be important for parents to know.

MR. WOLFE: The other thing that we noticed when we looked over this is that when we are talking about other people at risk, we don't say how many doses. I think we had better do that. It's a single dose for them.

DR. FEEMSTER: For whom?

MR. WOLFE: For the other people at risk.

DR. FEEMSTER: Yes, unless you have a certain

medical -- but I guess you talk about that. That was also confusing. Yes, it is one dose, but if you have some of these medical conditions, you need two doses.

MR. WOLFE: Yes, so we need to make that explicit. That's just something we neglected to put in.

DR. FEEMSTER: Along those lines, in that italicized paragraph -- children between 9 and 23 months -- when it jumps to "and older persons," it makes me think that you are jumping up to adults. Could we say infants aged 9 to 23 months and children and adults up to age 55 years? As I read this, all 9- to 23-month-old kid need two doses, if they need the vaccine, and all children do as well.

MR. WOLFE: Just say anyone else with certain medical conditions?

DR. FEEMSTER: Anyone else or all children and adults, just so everyone knows and it's clear that it's the continuum.

MR. WOLFE: We're not talking about the elderly.

DR. HERR: Can you say that again? I was thinking of something else, and I missed it.

DR. FEEMSTER: Nine- to 23-month-olds need two doses 3 months apart. I think all children, adolescents, and adults with certain medical conditions, if they need the vaccine, would need two doses.

MR. WOLFE: We could just strike the word "older."

DR. FEEMSTER: Yes.

DR. HERR: I'm confused on the whole idea of two doses, and when, in general. Then, when they become teenagers, do they get another one?

DR. FEEMSTER: If you don't have a medical condition and you are a teenager, you get one dose and then a booster, whereas this is about just two doses at the beginning.

DR. HERR: But does the child who gets it at 2 get another one later on?

DR. FEEMSTER: There is a booster dose schedule, in my understanding. But here you just say, talk to your doctor about the need for booster doses.

DR. HERR: This is probably new. I haven't heard any of this.

MR. WOLFE: The algorithm is so complicated.

DR. FEEMSTER: Yes, it is. It's like every 3 years if you are a young child, every 5 years if you're older. It is very confusing.

MS. HOIBERG: But it just says here that if the first dose in the series is given after the 16th birthday, a booster is not needed.

DR. FEEMSTER: That's true, but that's just for

adolescents who are otherwise healthy. This is under the "Other people at increased risk."

DR. HERR: And you don't go to college. You don't become a first-year or a second-year or whatever they call them.

DR. FEEMSTER: It is true that it is a complicated algorithm. But maybe just saying any child or adult who has a medical condition needs two doses, and then to talk to your doctor about the need for booster doses -- that is kind of all over the place.

MS. HAMBORSKY: Anything else in 3?

(No response)

In section 4, we had a note here. We added the information about the pregnancy registry.

MR. WOLFE: That was an FDA suggestion.

MS. HOIBERG: I have a question on the second bullet. It says anyone who has had a severe or life-threatening allergy to any vaccine component should not be the vaccine. Tell your doctor if you have any severe allergies. Where would one find the vaccine components? How would one know that you had a reaction to a particular component?

MR. WOLFE: That's why we say to tell your doctor if you have any severe allergies, because we can't expect people to know what is in the vaccines. But we do assume

that people will know if they have an allergy. If they tell the doctor, then the doctor can cross-check that against the package insert or against a list of what the components are.

Just a couple of years ago, we made that change on all VISs, because it was an always an issue -- how are people going to know? It seemed like the only pragmatic way around that was to assume that people know if they have allergies, and if they do, tell the doctor.

DR. HERR: We'll get into packaging later or some other time?

MR. WOLFE: Get into?

DR. HERR: The vaccine packaging.

MR. WOLFE: As it pertains to the VIS?

DR. HERR: Or about the reactions, about the latex.

MR. WOLFE: Oh, latex.

DR. HERR: We can talk later if you want to talk about it.

MR. WOLFE: We can talk about it now if you would like to. From the parent's point of view, I think it's the same issue.

I think what Tom is referring to -- we had kind of a private email exchange that latex is not technically a vaccine component. It has to do with the packaging.

My position is that, from a practical point of view, that doesn't matter to the parent. If they are allergic to latex, they should tell their doctor, and then the doctor will be able to find out whether the packaging for that particular vaccine does contain latex.

DR. HERR: But the packaging isn't really labeled. The boxes aren't labeled.

MS. HAMBORSKY: That's an FDA thing, as far as the labeling of the packaging.

DR. HERR: I understand that. Marion is here.

MR. WOLFE: But the package inserts do say whether the packaging contains latex, and we have published in our website and in our textbook, the Pink Book, a table that shows, as up-to-date as we know, which vaccines are packaged with latex. So there is something that the provider can refer to.

DR. HERR: But it should be obvious.

DR. GRUBER: Definitely if there is a latex component in the packaging -- that is, in the tip of the syringe or whatever, or in the stopper of the vial -- it will say so in the package insert.

MS. PRON: But that's too late. Even for the provider, from a safety perspective, it would be best to be on the outside of the vial or box.

MR. WOLFE: That's not something we can settle

here, but, yes, I agree.

DR. HERR: I agree, it's not anything we can settle here. It's just the issue that needs to be looked into a little bit more.

MR. WOLFE: But, Tom, from the point of view of the VIS, are you satisfied that what we say is adequate or would you rather change it?

DR. HERR: It's hard to say, because all this stuff varies from vaccine to vaccine. Not all vaccines have latex stoppers.

MR. WOLFE: One thing we could do is, if we think that's an important -- I don't know how many people actually have an anaphylactic hypersensitivity to latex --

MS. HOIBERG: It's a big enough issue that hospitals and doctor's offices stock non-latex gloves. Everywhere I have been, there are non-latex gloves. So it's a big enough issue to where doctors and hospitals have made that a standard of care. For the most part, most gloves are latex-free now and powder-free and all that kind of stuff just because of the severe allergies. And sometimes you don't know that you're allergic until you come in contact with it.

MR. WOLFE: Right. Well, there's contact allergy and then there's anaphylaxis, which -- but I guess the point I was going to make is, if we think that people may

not pick up on that otherwise, we could change every VIS to say tell your doctor if you have any severe allergies, including latex. That wouldn't be a --

DR. HERR: That only really matters if it deals with that particular vaccine. Our acellular DTaP does not contain latex.

MR. WOLFE: It really wouldn't hurt for them to tell the doctor anyway, and the doctor can say, don't worry because there's no latex in this one. It's about erring on the side of caution, I guess, to put it on every one. Sometimes they change, too.

MS. PRON: I'm looking at the two VISs that we have already approved, and they are different. For rotavirus, under that section of who should not get it, it does say tell your doctor if your baby has any severe allergies that you know of, including a severe allergy to latex. Then under the hepatitis A, it says anyone who has a severe or life-threatening allergy to any vaccine component should not get the vaccine. Tell your doctor if you have any severe allergies. All hepatitis A vaccines contain alum and some hepatitis A vaccines contain 2-phenoxyethanol. Anyway, that one lists specific components. They are not consistent.

MR. WOLFE: We're not consistent because ACIP is not consistent. If ACIP lists specific components, we

usually do, too. That's the reason for that. Some ACIP statements do and some don't.

DR. HERR: Can we just then ask this to be sent back to the other powers that be, ACIP, and discuss with FDA how this can be remedied, and then come back with some suggestions?

DR. GIDUDU: There is some wording in the general recommendations on latex. I'm wondering whether there are two tiers here. There is latex in gloves and latex in parts of syringes. Then there are types of latex. The one with natural rubber has more impurities and has more susceptibility for severe reactions. So I agree, maybe a discussion needs to occur.

MR. WOLFE: We couldn't really hear you very well. Are you talking about the difference between natural rubber and latex?

DR. GIDUDU: Let me try again. I was saying that there are two levels here. We are looking at latex in gloves and latex in the needle or the vials. The recommendation may be geared to those two approaches. There is already some wording in the general recs around latex that you can borrow from.

It may be confusing. When a provider is asking, there are allergies to latex in gloves and then there is also the parts of the syringes.

I was also saying that there's the natural rubber and there is also the synthetic one. The one that has natural components has more tendency to cause more severe allergic reactions.

MR. WOLFE: I think ACIP lumps them together, though, when they make their recommendation.

DR. GIDUDU: It helps to make that clarification.

MR. WOLFE: For our purposes, once the parent or the patient tells the doctor that they have a latex allergy, then it's up to the doctor to take it from there and decide whether vaccine can be given or not and then can ask more questions, of course, if necessary.

DR. HERR: We do need to look into things that we can do to make it more obvious to the provider.

MR. WOLFE: Yes. We can do that in ways other than on the VIS, though.

DR. HERR: I understand that. This really just provided a vehicle for me, because it came up in the office and I went, oh. I had never thought about this before.

MR. WOLFE: It would be nice to see that on the package.

MS. HAMBORSKY: Any other comments in that section?

MS. HOIBERG: I have a comment in 5. Can we move on to 5?

MS. HAMBORSKY: Sure.

MS. HOIBERG: Just at the bottom, where it talks about mild problems and they mention that you could have a -- that a small percentage of people who receive the vaccine develop a fever, fever is also listed under severe problems. Should we go ahead and specify low-grade fever under mild problems?

MR. WOLFE: Yes.

MS. HOIBERG: Just a mild fever, but if it reaches temperature above -- I don't know -- a certain -- what's a low-grade fever? If it's over 103, 104, depending on the child -- because babies run really high fevers.

MR. WOLFE: I don't see that we mention fever under the severe problems.

MS. HOIBERG: We do.

MR. WOLFE: In a sense, that's hypothetical, if you see a high fever. I think they are saying that for meningococcal, high fevers have not been reported.

MS. HOIBERG: In 5, it says a small percentage of people who receive the vaccine develop. So I'm reading and I'm, like, okay, so they develop a fever. But then in number 6, what if there's a severe reaction. But it does say a high fever. I wouldn't have put it down if I hadn't seen it. What constitutes a high fever? If somebody spikes a fever, depending on the age of the person

receiving the vaccine --

DR. HERR: From a practical standpoint, a high fever can be anything to some people. Many times I get phone calls and the child has a high temperature and it's 100.8. It all depends upon the comfort level of the parent.

MR. WOLFE: I guess it depends on other factors, too, because we have --

DR. HERR: No, no, no. I'm saying what the person thinks is a high fever --

MR. WOLFE: -- more prescriptive and let that be a clinical decision.

DR. HERR: Right. So the fact that they are going to call their physician about it -- fine, that's exactly what they should do. One way or the other, they should call their physician and let the physician interpret that kind of a reaction and then deal with it. I would just pass on trying to quantify it, one or the other. It's a worry factor, and it will vary -- unless you are going to write the numbers down and people really believe it. That doesn't always fit, because it's really the condition of the child, not the severity of the fever, that's important.

MS. DREW: I know this may be another formatting thing, but the box with the brief fainting spells is under severe problems. Is that really appropriate? Could we

move that up to either mild problems or moderate problems? It makes it look worse than it is.

MR. WOLFE: It probably isn't meant to be under severe problems. It's probably meant to be a general statement.

MS. DREW: That's what I thought, because it was in a box.

MR. WOLFE: That may not be as obvious in the Word version as it will be in the final version.

MS. DREW: Okay.

MS. WILLIAMS: I have a follow-on to that comment. It seems to me that this is a comment relative to all vaccines, so why is this box not on every sheet?

MS. HAMBORSKY: This has more to do with the syncope and adolescents, since this is a vaccine that's primarily given to adolescents.

MR. WOLFE: We had suggested putting it on all VISs, just as a precaution, because of ACIP's move toward strictly evidence-based recommendations.

MS. HAMBORSKY: They had the evidence for the syncope with adolescents.

MS. HOIBERG: The part where it says sitting or lying down for about 15 minutes after getting a shot, especially if you feel faint, can help prevent these injuries -- is there any way to allow -- because a lot of

the adverse events can happen within 15 minutes of vaccination, shouldn't all people, especially parents with babies and stuff like that, wait 15 minutes after each --

MR. WOLFE: I believe AAP does recommend that more strongly than ACIP does.

MS. HOIBERG: I think that it's only just a few shots that they do that with. It's with the older kids that they are waiting. They are not doing it for the little ones.

MR. WOLFE: You may want to observe for anaphylaxis and you may want to observe for syncope. For syncope, it's more related to adolescents.

Again, I wouldn't have any problem with putting that on all VISs either. We can look into it.

MS. HOIBERG: That would be greatly appreciated. Thank you, Skip.

MR. WOLFE: I don't know if it will fly, but we can try.

MS. HAMBORSKY: There is something in the general recs, too, that talks about 15 minutes. There is something in the general recommendations that talks about observing for 15 minutes for anaphylaxis.

MR. WOLFE: I can't remember how strongly it's stated, but it is in there.

MS. HAMBORSKY: Just as an aside, when we tested

this box, some of the parent said they had never gotten out in 15 minutes anyway. Practically, that's what the parents were saying. They come in and they give the shot. It takes at least 15 minutes to check out. I'm just saying what the parents said. They said they were around for 15 minutes easily.

MS. PRON: That's not true in all locations.

MS. HAMBORSKY: I know. I'm just saying that --

MS. WILLIAMS: The other thing is, you can be in checkout, but then you're at the desk and the child is standing next to you or fidgeting trying to go outside to the hallway. They are trying to get out. So, yes, it may take 15 minutes to check out, but a lot of times you're standing at the desk behind other people in a line.

MR. WOLFE: ACIP's general recommendation says providers, particularly when vaccinating adolescents, should consider observing patients, with patients seated or lying down, for 15 minutes. It's to decrease the risk of injury should they faint. That is an ACIP general recommendation. It's a recommendation to providers, not to parents, but it can't hurt to mention it to parents, too. I think we could make a strong case for putting it on all VISs.

MS. PRON: I agree with that. I also agree that any injectable, because of the IOM's report -- it says,

clearly, regardless of antigen in the injectable, there's a causal relationship with syncope. I think that should be on every injectable, about sitting or lying down for 15 minutes.

MS. WILLIAMS: I concur. The other thing is, this talks about after the shot. Is there any reason why -- and I know we have talked about this before -- shouldn't people be sitting down for the shot?

MS. HOIBERG: Both the provider of the shot and the recipient should be seated at the time to ensure a correct -- the injection be correctly -- if you're above, then they're going in and they're getting that shoulder pain. We were told in one of the reports that we were given a couple of meetings ago that both should be seated so that you are going straight in, so that you're not coming above and risking the frozen shoulder syndrome.

MR. WOLFE: I don't think on a VIS we should be getting too deeply into --

MS. HOIBERG: Well, no, you don't need to do that. The whole lying-down issue, I think, is very important to be put on -- the 15-minute waiting period should be put on all of the VISs, if that's possible.

MS. DREW: This is a really valuable discussion that I think we should continue maybe at the next meeting. But we're starting to run a half an hour behind, and some

people have transportation issues at the end of our meeting. So if we could finish up on this section.

MR. WOLFE: Everything from here to the end is standard on all VISs -- unless somebody has comments on the sections we have already discussed.

MS. PRON: I'm assuming that for number 6 on this one, as with the other two VISs that we looked at today, some clarification about immediate action or emergency, whatever the wording you are going to come up with about severe reactions, is going to be on all of them.

MR. WOLFE: Yes. If that changes on one, it will be changed on all of them.

MR. KING: Just one final comment. I know that we don't have time and we do need to move this to another topic. The pre-shot component probably should be addressed somehow, whether not it's a vaccine information statement or not. It might make sense to have it there, only from the perspective that we talk about the what, we talk about the who, we talk about the when, so why not talk about the how on the vaccine information statement because of the fact that we know from the IOM report that, in fact, you can get the frozen shoulder or the deltoid bursitis from the how part of it. So it may be something that we should -- at least this way, a parent would say, wait, we need to do this differently.

MR. WOLFE: In reality, I wonder how many parents would do that.

MS. HAMBORSKY: I don't know if a parent is going to know if it was actually given IM versus subcutaneous. Obviously, with an oral versus an injected or FluMist versus injected -- differentiating between making sure that the nurse or the medical assistant did IM or subQ, my guess is that would be a little bit too much information for the parent.

MR. WOLFE: And if we're concerned that people are not using correct administration techniques, there are other ways to fix that than through the VISs, I think.

MS. HAMBORSKY: It's not that there aren't tons of administration errors. We know there are tons of administration errors. I don't know if clinicians would want parents saying, I don't think you gave that right.

MS. HOIBERG: I think that parents need to be more informed. We could really lessen the amounts of injuries that we are seeing if the shot is given correctly. A lot of the syncope cases wouldn't even come into play because there wouldn't be syncope, because the child was lying down. A lot of the frozen shoulders wouldn't be in the system because it was given correctly, with the person sitting down and the provider sitting down. You know what? It doesn't have to go on the VIS, because -- let's be

honest -- most people don't read the VIS. But if we can talk about educating providers, which is what we have been talking about a lot, that's what needs to happen. There needs to be a bulletin out on how to give the vaccine correctly. But that's a topic for another day.

MS. HAMBORSKY: And here in our branch, we do have a lot of training and education materials for nurses, physicians, medical assistants, pharmacists that address appropriate administration. There's a whole appendix in our Pink Book that's dedicated to nothing but proper administration.

MR. WOLFE: We're trying.

MS. HOIBERG: Thank you.

MR. WOLFE: Thank you. This has, as always, been a stimulating discussion.

MS. DREW: Thank you. Maybe if you folks are available for our next meeting, we can actually put this down as an agenda item and continue the discussion.

MR. WOLFE: Definitely, because, for one thing, all the VISs that are now interim we want to make final. That means that a lot of the ones that we have, bit by bit, we want to get through ACCV.

MS. DREW: Thank you.

I think we need a brief break, even though we are running a little late. If everybody would just take 5

minutes, then we'll come back and try to move through it so that the people who have transportation to catch can do it.

(Brief recess)

MS. DREW: We're resuming now. Our next speaker is going to be Rosemary Johann-Liang, from the DVIC, who is going to give us her clinical update. Also Candice Smith, the medical reviewer from the DVIC, is going to give a report on rotavirus vaccines and intussusception. I don't know if these are going to be together or as separate reports.

Agenda Item: DVIC Clinical Update/Rotavirus Vaccines and Intussusception

DR. JOHANN-LIANG: Good morning, everyone. That was a short break. Hopefully everybody is regrouping here.

Changing gears just a bit, I'll give you an update. Remember yesterday with Vince from the Department of Justice? He was giving you all their latest numbers. It looked like he was providing you with numbers from May to August. The way I always update you all is by quarters of the fiscal year. So this will be updating you on the last complete quarter, which is the third quarter of fiscal year 2011, which would be March to June.

We'll talk about some of the numbers and demographics, what vaccines, what adverse events. Then I would like to turn to following up on the IOM report

presentation that Dr. Clinton gave yesterday and what our next steps will be, very briefly. We want to spend a little bit more time today on the rotavirus vaccine.

Rotavirus vaccine -- the background information has been talked about at ACCV a number of times. However, many of you are new commissioners to the group, and we thought it would be a good time to give a little bit more comprehensive review of rotavirus. We are going to probably come back to you in December for some action items, if things go down the line that way. We have a lot of things to cover, so we thought this would be the best thing to focus on today and give you just a little briefing of what we are seeing at VICP as far as rotavirus claims, so that you can at least get a flavor of what we have.

This is the same slide that I was showing last quarter. We really had a very big year last year as far as claims were concerned. It looks like, as Vince talked about yesterday, for the current projections, the claims coming in, probably, at the current rate, will not be as high as last year. They will probably be a little less than 400. It’s still much more than it was in previous years. But we are thinking it will either stay the same as last year overall or end up being a little bit less. These are all non-autism claims. Interestingly, during the third quarter of fiscal year 2011, we did not have any new autism

claims at all.

So these are the numbers. You can see that the numbers are a little bit down since the second-quarter report. It's April to July. That's the third quarter. The last quarter is August-September. This is an error, sorry. It should be March to June, because the last quarter is July, August, and September.

This is just adding on the green bar to the same graphic you saw last quarter. It shows you that our display of the age bands remains pretty similar across our quarters this year. Thirty-five percent or so are pediatric claims, which means less than 18 years, and 18 and above, which we consider adults, are really -- two-thirds are adults right now, adult claims.

These are the vaccines that petitioners are alleging caused their injury. Again, influenza remains the number-one vaccine being alleged for injuries, followed by HPV and tetanus, meningococcal. The infant series is for the babies less than 1. There are multiple infant vaccines that are given. It's hard to kind of tease those out. So this is the display of vaccines alleged.

Adverse events: This is just to explain some of the acronyms that are used just so we could fit these acronyms into a slide for the next one. So you can refer to these. Many of these you are so familiar with, like

Guillain-Barre and SIDS, sudden infant death, et cetera.

These are actually the diagnoses, where, after the medical review, the reviewer determines that this is what that case actually ended up being. The vaccines, remember, were the alleged vaccines. These are actually after medical analysis review of the cases that we actually had enough records to be able to review during third quarter of fiscal year 2011. GBS remains the most common adverse event that the medical analysis shows, followed by a variety of other demyelinating diseases, as explained in the slide before, transverse myelitis and ADEM and chronic inflammatory demyelinating polyneuropathy, which is the CIDP. So the demyelinating diseases -- remember, GBS is also peripheral polyneuropathy; it's a demyelinating neurologic condition -- those really make up a large proportion of the diagnoses after review, followed by other neurologic adverse events.

IOM was charged with looking at, not vaccine-specific adverse events per se, but these injection-related conditions. That's what we see in our claims as well. That still does make up quite a proportion, about one-tenth of our claims in the third-quarter review, followed by rheumatologic.

We had a number of death cases that we reviewed.

The PNES -- this is psychogenic non-epileptic

seizure -- these are people claiming that they have seizures, and yet when you do the EEG, which is looking at the brainwaves, it's really normal. It really seems to be -- we are seeing, interestingly, several cases of these during the review that we haven't seen before. They are usually coming in now with HPV vaccine claims.

Again, as we discussed at the last clinical update, we do have a proportion of these patients who, upon review, really do have genetic and underlying disorders. Even though they are alleging that there was something going on with the vaccines, the majority of times, when you actually do the review, it's really a manifestation of their conditions, what the reviewers have analyzed, and not necessarily anything -- it's just that temporally they received vaccination, but, actually, it's a manifestation of their underlying disorders.

Then we had a whole bunch of miscellaneous conditions, including the intussusception. IS is intussusception. I think during the third quarter we had one case of rotavirus intussusception. Actually -- I was looking in my BlackBerry -- we have another claim that just came in of rotavirus and intussusception. So they are few and far between. It's an infrequent claim. That's why that's lumped in together there as miscellaneous -- one here, one there, et cetera.

Any questions thus far? I'm going to turn now to following up on what we're going to do now that we have the IOM report.

The charge went to the IOM in April of 2009. Usually you say, looking back, it just seems like yesterday. But in this case, I have to say, I don't feel that way. It has been a long, grueling couple of years. Geoff is such a taskmaster.

So in April of 2009, we gave the charge to the IOM, and then they began to look for the committee members that would comprise the committee to work on the charge that was given to them. The charge given to them -- you have seen this before. Remember, unlike previous IOM reports, we really asked them to not only look at the epi literature, but also look at what they now classify as mechanistic evidence, which addresses biological mechanisms underlying different theories, et cetera. The whole chapter 3 is on a lot of the issues that we had asked them to address.

You heard a lot about these eight vaccines that we asked them to review. Remember -- the dates are important -- in April of 2009, there really wasn't anything going on with rotavirus vaccines at that time. Rotavirus is one of the vaccines that we did not ask them to address. That was right before the pandemic for H1N1 hit. We did

not ask them to address H1N1 because we didn't know about it. We did ask them to address influenza seasonal vaccines, which they did. So that's important to keep in mind.

They released a public report on August 25. They are right now doing briefings to everybody. Dr. Clinton did a wonderful job yesterday briefing you all.

Now that we have the report, what are we going to do? The whole reason for the IOM report, for the purposes of the Vaccine Injury Compensation Program, was that we really felt the vaccine injury table -- the program actually started off as a table-based program. It is really no longer that. We really are off-table in discussions, reviews all the time. So we really felt it was time to update the table. The IOM study was really to give us an independent, external -- you know, the experts in the field -- scientific review of the current science so that we really can be scientifically based. So we have done that. We have the report now.

What else will be in our thoughts as we go in to update the table? The IOM study looked at the current science of all of these adverse events and vaccine pairs. Remember, 158 adverse events and vaccine pairs were addressed by the IOM. Many of those are really based upon what we asked them, based upon the claims, the alleged

claims, that are coming in. People may say there's no science with this adverse event and this vaccine at the current time. However, if a big proportion of our alleged claims are that vaccine-adverse event pair, we really felt compelled, from our perspective, to request IOM to look at everything -- everything -- in a very independent way and give us the current science. So that's kind of how our process went.

So we really have a good bulk of the information that we need for our day-to-day work as we look through the cases and medically analyze the information.

We also wanted to add to the IOM study information that is coming from us in a group format. That's something that we have been trying to give you updates on as we have some time to look and pull information together. Some of them have been published. We published the SIRVA, the shoulder injury-related vaccine administration, paper, which I think was really sentinel in helping the IOM. We got that in in time. Remember, IOM would only look at published literature, peer-reviewed published literature, and we were working like crazy to get that paper in so it could be part of the IOM review. That's the deltoid bursitis that they came back with. So that was good.

The CRPS was presented to you. You heard Dr.

Clinton yesterday. CRPS is, besides syncope, the other one that they could not really say favors acceptance, just because there is not enough information out there. But they were kind of thinking there is something going on. That's something that we presented to you last time. We are working that up further to hopefully put it in -- we have to put it into peer-reviewed literature. So that's what we are working on.

Then we talked about some of the adverse events. That's looking from the injection-related to the administration part. We are also analyzing different adverse events. We published the anaphylaxis case series. That is going to be very important, because, remember, there are -- I can't remember exactly -- there are five, I think, favors-acceptance, causal link that IOM came down with. They were anaphylaxis to different vaccines. Many of those vaccines currently are listed on the table, but they do not have any adverse events in the table. So we will be updating those after the review.

Then, obviously, we are continuing to look at different vaccines. We talked about the fact that H1N1 is really not part of the IOM. However, we as a group -- and you guys are included in this process, obviously -- we are going to have to make a determination about what we do with H1N1 now. That's part of the antigen now. That monovalent

H1N1, which was a standalone vaccine during the pandemic, is now folded into our seasonal vaccine. Our program is actually seeing claims. We are starting to get them now. Remember, there's a little time delay after people get injected and then they want to make a claim to the program, et cetera. We are starting to see seasonal vaccines with H1N1 included. So that will be a point of discussion. That's a little bit different than how IOM came to us with their review of the influenza.

But what's really important -- and this is another driving-home point that I get from the IOM report -- the influenza vaccines, although they are all lumped together as influenza vaccines, are different vaccines year to year. What goes into the trivalent, the three-prong, vaccine -- those things are not always the same. Of course, we are thinking of them sort of like globally together. But we also need to think about, seasonally, are there differences? I think that's an important point to think about, therefore realizing that the H1N1 now being part of the seasonal vaccines -- again, different than previous seasonal vaccines. We are waiting for the active surveillance information from the pandemic time regarding the H1N1 influenza vaccine. It's generally thought to be -- there have been reports out from the post-surveillance from China in the *New England Journal*. There

have also been a couple of other reports out, which all show really no increased signal, particularly in regards to GBS that we are all concerned about. But we are still waiting for the final analyses to be presented from the active surveillance. Remember, there was a slight signal that was published in *MMWR* very early on in the initial screening for H1N1 active surveillance following the initial pandemic.

So it's still coming your way, and we'll discuss it further in the future.

We also say, as part of that continuous monitoring, aside from the external review, aside from the group information that we are trying to pull together from our claims information, we are also continuously monitoring the literature and seeing what is going on in the world of vaccine safety. Obviously, that is what we do as the medical folks here. Recently, something that we have been following very closely -- there was preliminary information presented in the October 2010 ACIP -- is now published. Based upon *The New England Journal of Medicine* publication and the editorial which accompanied it, we thought it was timely for us to give you a background today. We are not asking for any action items today. This is something to update you on the most current science and understanding of rotavirus vaccines. Then you guys can go home and ponder

about it at your leisure, and then we can come back to it next time.

So I'm going to turn it over to Dr. Candice Smith. Candice has been working with us for quite some time, I would say a couple of years now. She is a pediatric infectious disease physician out of Stanford. She actually has done research in rotavirus. We're very fortunate to have her as part of our working group.

We have formed a very small working group with our Office of General Counsel member and the pediatricians of our program to really jump on this newest published information and to look at everything. We want to look at everything, put it all in perspective, to bring that information to you and to think about what our next steps would be.

DR. SMITH: (via telephone) Like Rosemary said, we do want to give a little bit of an overall perspective on rotavirus disease first, even though some of you have heard it before.

Rotavirus disease, we know, is the most common cause of acute, severe gastroenteritis, and may result in severe dehydrating diarrhea and fever and vomiting. Virtually all children will get rotavirus disease by the time they are age 5. This is a disease that has equal rates in developing countries versus developed countries.

In developing countries it is much more serious. It accounts for about 500,000 deaths per year. In the United States it causes far fewer deaths, but causes a significant burden of disease. It caused, before vaccine started for it, about 300,000 ER and doctor visits each year and 50,000 hospitalizations.

The complications of rotavirus are obviously severe dehydration and death resulting from that severe dehydration. Important to note that the younger the child, the more severe or persistent the disease is. Before vaccination started, we had about 1 in every 40 children in the US who had rotavirus disease requiring hospitalization for IV fluids.

This slide is important. It shows how the rotavirus disease and the burden has changed since United States vaccination began in February of 2006. The graph shows the percent of the rotavirus tests positive by week throughout the year. As you can see, we have this black dotted line that shows pooled rates from 2000 to 2006, all before vaccination. You see that we have this big peak in the winter -- every winter, a big, big peak of rotavirus. It fills up all the children's hospitals with these little dehydrated children. Year by year, as vaccination has started, we see a significant change in the burden of disease. We have far less burden of disease. We have a

change in the peaks of disease and how long the season goes -- much shorter season, much smaller peaks, and so on. So the vaccines have had a remarkable effect on the rotavirus burden in the United States.

I thought it was important to go through the rotavirus intussusception story, go through the history just a little bit. In 1998, the United States licensed Rotashield. It was a rhesus-strain rotavirus vaccine. It was a live oral vaccine. Starting in August 1998, it was given. By the spring and summer, there were noted intussusception rates that were increased among the vaccinees. They published *MMWR* in July of 1999 that showed that there were 15 intussusception cases reported to VAERS. They really saw this clustering of the cases after the first dose, in that tight window just a few days after the first vaccine was given. Because of these reports, the CDC suspended Rotashield vaccination. Then they had three different large studies look particularly at what the rates of intussusception were in vaccinees. The studies generally showed that there was a 30-fold risk of intussusception in the 3 to 7 days after the first dose of the vaccine. Because of the findings of the studies, the ACIP withdrew the recommendation in 1999.

Important to note that as these studies went in depth to the rates of intussusceptions, they basically saw

that there was 1 case of intussusceptions per about every 10,000 vaccinated infants. Important to note is that they kind of moved forward into the next generation of vaccines.

I thought it was important to talk about what naturally occurring intussusception is, in case people are not completely familiar with it. Intussusception is a telescoping of the bowel. A part of the bowel moves forward and goes into the further portion of the bowel. As that bowel wall telescopes in, it pulls along with it the blood supply. As the blood supply kind of gets pinched off, then the damage to the bowel occurs.

We don't know why it happens. The causes aren't well defined. It's uncommon. Only about 1,400 children each year in the United States get it. Infants up to 2 years old are the most common children who get it. It usually happens between 4 months old and 10 months old, with the peak time being a 26-week-old to a 29-week-old. It's really low in those first 2 months of life.

When you guys were discussing the rotavirus VIS statement, there was a question about why 14 weeks and 6 days was the upper limit. It was because of this data, that the intussusception risk is really quite low early on in life and then it starts really having a rapid rise after the first 2 months of life.

As far as the demographics, we know it's more

common in males. It's more common in Hispanics. It's more common in African Americans.

It varies by region. The United States has rates, and our rates differ from all the other countries. Our rates differ by region within the United States. So the West and the Northeast are higher than the South and the Midwest. Obviously, there are cultural and environmental factors that determine this. We are not clear which ones act significantly.

We do know it's associated with anatomic defects. We do know that there are multiple different infections -- respiratory infections, adenovirus infections -- that are associated with intussusception.

It is treated with either a contrast enema to reduce that telescoping or, if the contrast enema is not successful, then they will go to surgery. In the United States it's about 50 percent successful with the enema to reduce intussusception and 50 percent end up going to surgery.

Overall, the morbidity and the mortality in the United States is low. We are talking about, usually, they get admitted, the intussusception is reduced, and they are going home the next day or within 2 days and recovering really well. Recurrences do happen just naturally. Ten percent of the time we have a recurrence.

Going back to the Rotashield vaccine from 1999, why was it associated with intussusception? A specific biologic mechanism was never discovered. The leading theory has been that because this was a live oral vaccine, during the peak period of viral replication and then shedding, there was this local inflammatory response in the intestine and this ended up triggering an intussusception. We know that, looking specifically at that strain, the rhesus strain, of the rotavirus vaccine from 1999, it had high replication and it had high shedding. More than 80 percent of all the people who had the vaccine would have high replication. The timing of the high shedding was 3 to 7 days, which completely coincided with the high-risk intussusception period.

We had a side effect profile with this vaccine -- fever in 30 percent and an increased risk of vomiting and diarrhea. So overall, it felt like this was when the vaccine was replicating and this was when we were having a lot of side effects and reactogenicity from it.

As they went forward, we have now two different rotavirus vaccines, Rotarix and RotaTeq. I'm going to talk about Rotarix first.

Rotarix was licensed in the United States in 2008. It is the one that is used less frequently in the United States, mostly because RotaTeq preceded it by almost

2 years, and a lot more people feel like it's just what they have been using for longer.

To review what this is, the Rotarix is one strain and it is an attenuated human rotavirus. So they just have weakened a natural human rotavirus strain. The theory is that an attenuated human strain should not provoke an intussusception, as the natural rotavirus does not. They also looked at shedding rates and the reactogenicity of this particular strain. The side effect rate was very similar to placebo. The shedding rates were 40 percent to 80 percent after the first dose, peaking in that first week.

They did very large pre-licensure trials with both of the rotavirus vaccines. This slide goes over the pre-licensure study that was done for Rotarix. It was done in 12 different countries, given the charge to kind of be powered, have enough patients to rule out a risk of intussusception, much less than that of Rotashield vaccine. Rotashield vaccine again was about a 30-fold risk. This was looking at a tenfold risk and getting enough patients to do that. This was a much larger vaccine trial than normally is done.

This slide goes over the intussusception results from the pre-licensure data. Out of these 60,000-some patients, they had 26 positively adjudicated definite cases

of intussusception. When you look at the cases that are just within a 31-day period of any of the doses, they had almost completely equal rates of vaccine and placebo group who had intussusception, six from the vaccine group, seven from the placebo group. They did parse that out and look specifically at the first dose and the second dose. Within the first dose, the relative risk was .5 -- very low -- and the second dose was .9.

They felt very reassured by this large pre-licensure trial that they were not seeing an increased rate of intussusception. The really interesting point from this pre-licensure trial is that they followed about 20,000 of their vaccinees out to the year mark, and what they found was that they had a much lower rate of intussusception in the vaccine group versus the placebo group. About a fourth of the patients in the vaccine group compared to the placebo group had intussusception. So there is this question about whether or not having the vaccine is protective in the long term against intussusception.

Rotarix has had some extensive studies in the postmarketing period. All of these studies are from outside the United States, but it’s important to kind of go through them, as Rotarix use in the United States is increasing. This slide was presented at the ACIP meeting in October 2010. I really want to look at the first study

that's discussed, in Mexico. GSK did a self-controlled case series. It's the largest postmarketing study for intussusception to date. They basically had 1 million infants in their cohort of patients that they were following. Within the 1 million infants, they had 459 intussusception episodes.

Then they did a self-controlled case series and they showed that the 0-to-30-day period after the first dose had an incident rate ratio of 1.8. That was something that was borderline significant. They did see within that 0-to-30-day period a clustering of cases within the 1-to-7-day period. After that, they did change their package insert to note that there was a borderline significant increased rate of intussusception based on this data.

I think we'll go to the next slide to discuss the Mexico and Brazil studies and the Australia studies, because in the interim between last year's ACIP and now, they have been published, so we'll go over the published data in this next slide.

Looking at the Australian data, they calculated their baseline historical rate of intussusception form the period before they started vaccination and then they looked at how many cases of intussusception they were expecting from history and then compared that with what they were actually seeing in the 2007-2008 period. As they looked at

Rotarix and whether or not it was associated with intussusception, after the first dose in the 1 to 7 days, they saw an increased relative risk. It was 3.45. They did not see an increase after the second dose. So it seemed to be just that first dose.

Note that this was a very small number of cases. They basically were expecting .9 cases from the historical rates, and they got three cases. They caution that we need further larger studies to look at this data.

So that's the Australian data. Now let's go over to the Mexico and Brazil data.

This was a case series and a self-controlled series as well. When you look at the Mexico data, they also found something similar. Again looking at the 1 to 7 days after the dose, we had an increased incidence rate. They found an incidence rate of 5.3. With the second dose, they also looked, and they found no increased rate for the second dose.

They had the same exact study setup in Brazil, and they actually found the opposite there. With the first dose, they found no response, and with the second dose, they did find an association, with a lower but still increased rate of 2.6.

The paper discusses at length that they feel like this discrepancy between the Brazil and the Mexico data is

basically because Brazil gives the rotavirus vaccine with the oral polio vaccine, and we know that that really decreases the immune response of the rotavirus vaccine. So they basically say that first dose doesn't really act like the first dose as far as the immune response because it's combined with oral polio vaccine. The second dose is acting more like the first dose.

MS. HOIBERG: Can I stop you right there? Why are they using the oral polio when we know for a fact that that actually causes polio? Did the pharmaceutical companies just ship down all the old oral polio and give it to them?

DR. SMITH: You are wondering about Brazil?

MS. HOIBERG: Yes. Why do they use the oral polio?

DR. SMITH: Oral polio is used in developing countries basically for the better herd immunity, because their immunization rates aren't incredibly high. That's a really good question. I actually don't know what the vaccine supply is in Brazil and what their options are. But it is something that needs to be investigated, because the oral polio is given throughout South America and many countries in Africa. It is something that needs to be further researched.

MS. HOIBERG: Yes, it does. Thank you very much.

DR. JOHANN-LIANG: One thing, though -- I don't know about the polio per se. I don't think that what you're asking actually is what's happening. But as far as rotavirus vaccines go, we actually met the Ministry of Health head person when we were down at ACIP last year. We just happened to run into them waiting for a taxi or something. We were talking about why in Mexico -- the lady was from Mexico -- they were using Rotarix, not RotaTeq. It really has to do with how the companies come in and do a contract. They do a competitive bid and they get the vaccine that would be the most cost-effective for their country. So --

MS. HOIBERG: Right, but I want to know why something that we took off our shelves because it was causing polio in our country -- why are we sending it to another country? That's what I want to know.

DR. JOHANN-LIANG: I don't think we are sending our polio vaccine to Brazil. Each country makes a determination for their country what the best vaccination would be program and series for them. We don't make a vaccination determination for their country. Brazil -- I don't know what their analysis came up with, but probably what Candice was saying was a big part of it. It really has to do with the uptake of vaccination and what would be best. The oral polio is really for herd immunity effects.

That's probably the main reason.

Any additions, Jane?

DR. GIDUDU: Most of the countries have different procurement systems. For Africa, I know that UNICEF procures vaccines, and there's a cost involved. Lots of the differences are around that kind of issue. But I really doubt the US sends their oral polio to any country.

DR. SMITH: Just one more point. The WHO guidelines for worldwide polio eradication are to generally finish up -- the countries that are using oral polio for herd immunity, when they get significant vaccination rates that are good, would change to inactivated polio. That is the plan. But I think they are waiting to get uptake of their immunization rates before they move on to that stage.

Moving on, that is the end of the research update regarding the Rotarix vaccine. Again, all that data is from outside the United States.

Oh, I did want to make the point before we move on from Rotarix that both the study from Australia and the Mexico and Brazil study did look long-term. They basically looked a full year out. I think Australia looked 9 months and Brazil and Mexico looked a year out. They showed no overall increase in intussusception rates. They were basically saying, we're seeing these little increases right after the first dose, but if you look at our total rates of

intussusception, they are not increased. In fact, sometimes they are decreased overall from what we were expecting.

RotaTeq is the vaccine that's used much more frequently in the United States. It is a vaccine that takes a bovine rotavirus backbone and takes components of human rotavirus and combines them into a human-bovine reassortant. It does five different strains. That's why it's often referred to as rotavirus 5. The theory in making this vaccine is that the bovine strain doesn't replicate much and doesn't do much shedding in humans, and so it shouldn't provoke that immune response that, in theory, was causing intussusception. The shedding rates are really low. The side effect profile is the same as placebo. They felt like this was a good vaccine to move forward into the clinical trials.

The next slide talks about the pre-licensure trial for RotaTeq. Again, we had 72,000 patients from 11 different countries in the study. Eighty percent of the infants came from Finland and the United States.

The next slide looks at the intussusception results from this pre-licensure trial. We had 32 cases of intussusception. When you look at how many of those were from the vaccine group versus the placebo group, they parsed it into within 42 days of a dose, 42 days to a year

of a dose, and longer than a year after the dose. They basically found within a year 13 from the vaccine group, 15 from the placebo group, so not an increase in risk of intussusception from this data. They also found something similar. Looking at the year point, they had a decreased rate in the vaccine group versus the placebo group of intussusception.

Now, they did specifically look at that first dose. There were no cases of intussusception within 42 days of the first dose. They even parsed it down to 14 days, and there were no cases of intussusception within 14 days of the dose.

So they felt good moving forward out of the pre-licensure period and licensing this one. Since 2006, this has been licensed in the United States.

We have multiple studies in the postmarketing period. This slide comes from last year's ACIP update. Important to note the CDC/VSD study that was done. Basically, the VSD is a large federally funded collaboration of eight managed-care organizations and the CDC, and they have done three different studies of RotaTeq and intussusception. The first study was early on enough that they compared those babies who had had RotaTeq versus those babies who had other vaccines, but not RotaTeq. They found a relative risk of .5 -- so on risk seen at all. The

subsequent VSD studies have looked at concurrent -- their controls have been other vaccine recipients. As time has gone on, that pool of patients in this VSD study is getting larger and larger. This most recent VSD study has almost 900,000 doses, and they are seeing no increase in the rates of intussusception. Particularly, they are looking at that 1-to-7-day period and they are seeing no increase in the relative risk. In 30 days after the first dose, they are not seeing a risk either.

So from the largest amount of United States data, they feel like they have excluded a risk as far up as 1 to 65,000 or 70,000. That's our biggest amount of United States data.

Going on to the next study, Merck also has done a study in the United States where they compared those patients receiving RotaTeq versus those receiving DTaP. They actually didn't parse out just dose 1. They were looking at all doses combined. The study was powered to look at 0 to 30 days. They found a relative risk of 0.8 for intussusception during the 0-to-30-days. Because of the data, especially with Rotarix, pointing at the first week after vaccine, they weren't powered to kind of do a post ad hoc and look at the 1-to-7-days, but they did, and they found that the relative risk was 2.8. You can see that their confidence intervals go from 0.3 to 139, simply

because they weren't actually powered to look at that analysis. But they felt like the 2.8 was borderline significant, but hard to tell because they weren't powered to look at it. Again, that was for all doses combined.

The Australia data has been published since ACIP, so I want to go to the next slide and talk about the Australian data.

DR. JOHANN-LIANG: Candice, can you hold on one second?

Do you want to make a comment?

DR. GIDUDU: Yes, I was going to mention one correction. VSD has 10 sites now, instead of eight. Secondly, the RotaTeq study will soon be published. It's in CDC clearance. It should be out later this year.

DR. JOHANN-LIANG: The VSD that Dr. Smith is talking about Dr. Gidudu is correcting. It's 10 sites, managed health-care organizations, in the US, and also this whole VSD analysis of RotaTeq will be published soon as a publication. These are all preliminary presentations from meetings.

Let's go on.

DR. SMITH: So the Australian data was interesting. Again, like the Australian data from RV1, they compared it to the historical background rate. They saw an increased rate after the first dose. They basically

again said that just within that 1- to 7-day period after the first dose, they were seeing a relative risk of about 5. Important to note that this is the only definite data saying that there is an association with intussusception, again to know that it's from a very small number of cases, just three cases, when they expected .6. Specifically looking at the second dose and the third dose, with the second dose they had three cases and they expected five; for the third dose, they had zero cases and they expected six. So they highlight that they are only finding risk in the short period after the dose 1 and that the subsequent doses do seem to be protective. They again say that they are limited by their small number of cases and that we need further larger studies. But again, this Australian data is the only data that really points towards an increased risk. The United States data is not replicating that same amount of risk in our studies.

The next slide just goes over the continued recommendations from the CDC. They state that some but not all of the studies suggest a possible, very low risk of intussusception caused by the rotavirus vaccines. They specifically note that the benefits outweigh any risk and that the vaccines prevent more than 50,000 hospitalizations and hundreds of thousands of office visits from dehydration due to rotavirus disease in the United States.

They state that hypothetically vaccines could cause a small increase of intussusception each year, but again the benefits outweigh the risk, and they continue to recommend them.

That's it.

DR. JOHANN-LIANG: Thank you so much.

I'm going to just move on rather quickly because we're running out of time, just to give you what our program's experience has been for the second-generation rotavirus vaccines.

Remember that currently rotavirus vaccine is a row in the vaccine injury table, but we do not have any injuries listed. The intussusception that was associated with Rotashield, where the claims were paid out -- that was years ago. When that vaccine went off the shelf and was no longer being manufactured or marketed or anything, we didn't have any claims. That whole thing went away.

With the second-generation vaccines being manufactured and being given out, rotavirus vaccines are now listed again as a row on the table, but there are no injuries listed yet. So that's the background.

For our experience, this is after analysis. These are rotavirus vaccine claims with intussusception as the correct diagnosis. There are 12 of them by the end of fiscal year 2010. There have been three more since then in

fiscal year 2011, and we just got another one. It's a very infrequent claim compared to influenza and demyelinating diseases. The breakdown: nine boys, three girls, age range from 8 to 31 weeks. It looks like it breaks down to a third, a third, a third after each of the doses. You can see that the onset range is very broad for each of those doses.

Dr. Smith has shown you that, in general, in the background it's about 50/50, with surgeries. There were more surgeries for the kids that made the claims to the program than the background.

Interestingly enough, many of these kids -- 67 percent, actually -- had alternative factors, meaning they really had a reason for the IS, aside from the vaccination, such as actually being born with a malrotation of the gut, which is one of the main reasons why babies may develop a telescoping of the gut as in intussusception.

The reason why these are all RotaTeq, as Dr. Smith explained, is because RotaTeq is what's being used in the US now.

I will try to get with the person at CDC to see if we can get some updated distribution data in the US for rotavirus vaccines for you. But it's my understanding that it's RotaTeq that is mainly the uptake in the US. But as we move towards the future, Rotarix will be distributed in

the United States. So it's not like Rotarix is not going to be used in the US. It will be used, both vaccines. But clearly up to now, it has really been all RotaTeq use. That's why we are seeing those claims here.

Some things for us to think about -- you have been given a very nice background overview of what the disease is about, what the vaccination has been developed and manufactured to prevent, what the worldwide considerations are. But, really, we are thinking about the national vaccine claims coming to our program.

Some of the very simplistic numbers -- remember, for Rotashield, there was a very high attributable risk. Whatever is happening with these new second-generation vaccines, if there is an attributable risk, it's much, much lower. That may be why in the United States there is just not enough data out there to even see a signal. We are not seeing anything in the US right now. These signals are coming from Mexico, from Australia. But there it is. It's there.

What we wanted to show you today were the recent publications of postmarketing studies. Remember, premarketing, pre-licensure, they did large safety studies and they didn't see anything. We have given you a very thorough presentation of the most recent data information.

Currently in the US postmarketing, as I said

RotaTeq is still mainly used. There is limited available intussusception data, but it is going to be the VSD. That's the largest information that we have, 10 managed organizations. That information will be published, we understand, very soon from CDC. It will probably be years before we have any information on Rotarix, because that's just starting to get an uptake in the United States.

So those are the considerations for you to think about.

What are we doing about it, from our perspective? We have this rotavirus working group that we have started. We have already done a lot of work. We are presenting to you the information that we have. We looked at everything, and this is what we have. What we are considering is working with our Office of General Counsel colleagues to think about putting together a notice for public rulemaking. I will be presenting a shortened version of this information to the Immunization Safety Task Force later this month and see what our colleagues from different agencies -- what their thoughts are about the most recent publications on rotavirus vaccines.

We will bring this back to you in December, and possibly for a formal vote as to what we should do about addressing rotavirus vaccines and intussusception as far as updating the table.

Again, rotavirus vaccine was not one of the vaccines that we asked IOM to do a thorough review on. You have basically gotten all the data that we have on this. We will be taking rotavirus separately from the IOM information and bringing that to you in December. It will be a good trial run to see how we can do this. We are hoping that, as far as IOM vaccines, those eight vaccines, and the injection-related -- we will be forming small working groups with our CDC Immunization Safety Office colleagues and our Office of General Counsel folks to work on IOM information and to develop what we think should be the next steps about updating the vaccine injury table from the IOM information and also the information that we have from the VICP.

That will take some time. I will give you an update on where we are by December. Then most likely our timeline is -- we do want to meticulously and methodically go through everything, but we are hoping that we can really push it forward sooner than later, and hopefully bring all of that information to you maybe for the March ACCV. So a lot will be happening in the next year or so, we're hoping.

That's our tentative plan.

Any questions?

(No response)

MS. DREW: Thank you, Rosemary and Dr. Smith.

Dr. Jane Gidudu is going to give us an update on the Immunization Safety Office, Centers for Disease Control and Prevention vaccine activities.

Agenda Item: Update on the Immunization Safety Office, Centers for Disease Control and Prevention Vaccine Activities

DR. GIDUDU: Good afternoon, everybody. I'm happy to be here to represent my Immunization Safety Office. My director couldn’t be here. He sends his greetings.

I’m going to be talking about recent discussions in the June ACIP. I’ll be mentioning issues around the influenza discussion and provide a brief update on febrile seizures, as well as maternal Tdap vaccination, the use of meningococcal conjugate vaccine, use in high-risk individuals. Then I have selected recent ISO publications that you have in your handouts. There are a lot of materials we publish, but these were the ones we selected for you.

If there is a bit of time, we may be touching a little discussion on Gardasil interval. I don’t know whether you still want that discussed a little bit. But it will be very brief.

I just want to mention that this is the same vaccine that has already been mentioned by Rosemary. The

vaccination formulation is the same as last year. The emphasis here is that it has the same three antigens that include the monovalent H1N1 pandemic influenza vaccine. I want to also just remind you, on the recommendations for vaccination, that routine annual vaccination is recommended for all persons 6 months old and older. Vaccination should optimally occur before the onset of influenza activity. Vaccination should also continue to be offered throughout the influenza season.

There are multiple vaccines that are expected during this season. They are all outlined in additional slides. What I want to highlight here is that there is a new intradermally administered TIV vaccine, Fluzone Intradermal. That was licensed this year in May. It's indicated for persons aged 18 years up to 64 years. Again, annual vaccination is recommended for optimal protection against influenza infection.

There was a lot of discussion on egg allergy. Allergy to eggs must be distinguished from allergy to influenza vaccine. Severe allergic anaphylactic reactions can occur in response to a number of influenza vaccine components, but such reactions are very rare. A review of VAERS reports in CDC in adults noted that four reports of deaths occurred that were caused by anaphylaxis following influenza vaccine over a 15-year period. The vaccine

companies were not really reported, but these have been reported in VAERS.

A prior severe allergic reaction to influenza vaccine, regardless of the component suspected to be responsible for the reaction, is a contraindication, as you all know, for influenza vaccine. As mentioned yesterday, all currently available influenza vaccines are prepared by inoculation of virus into chicken eggs. Hypersensitivity to eggs has been listed as a contraindication in most of the package inserts. However, as more evidence comes out in recent years, studies have indicated that vaccines can be safely administered in persons with egg allergy.

So ACIP recommends that persons who have experienced only hives following exposure to eggs should receive influenza vaccine. However, because studies published to date have looked at only TIV and not the live vaccine, it's recommended that these people get the trivalent inactivated vaccine. The vaccine should be administered by a health-care provider who is familiar with the potential manifestations of egg allergy. These vaccine recipients should be observed for at least 30 minutes after they get any vaccine dose.

Also persons who have symptoms that are listed here in the fat box on the left -- cardiovascular, respiratory, GI symptoms -- who usually require epinephrine

should be referred to allergists or experts who are dealing with allergic reactions.

All vaccines should be administered in settings in which personnel and equipment for rapid recognition and treatment of anaphylaxis is available. Basically, you need to have epinephrine and be able to use it.

Some people who report allergy to eggs might not be egg-allergic. Egg allergy can be confirmed by a persistent medical history of adverse reactions to eggs and egg-containing foods, plus skin and/or blood testing. Lastly, a previous severe allergic reaction to influenza vaccine, regardless of any component suspected to be responsible for the reaction, is a contraindication to receiving influenza vaccine.

I'm going to change gears and talk a little bit about febrile seizures. I gave an update during the last two meetings on febrile seizures regarding the signal that was identified in our VSD. VSD has followed up more than 200,000 children 6 months through 4 years of age during the previous influenza season. The analysis so far indicates an increased risk of febrile seizures for concurrent TIV and PCV13 vaccination. The increased risk was greatest in children ages 12 through 23 months when the two vaccines were given during the same health-care visit. In this group about one additional febrile seizure occurred among

every over 2,000 children who were vaccinated. Most children who received the other vaccines -- it was the PCV13 that was most common.

Further investigation is under way to determine the contribution of other childhood vaccines that may be contributing to the increased risk of febrile seizures. CDC has determined that no changes in the immunization schedule are necessary at this point.

There was discussion on maternal Tdap vaccination. Women's health-care providers should implement a maternal Tdap vaccination program for women who have not previously received Tdap. Health-care providers should administer Tdap preferably in the third or late trimester. This is at least after 20 weeks of gestation. Alternatively, administer Tdap immediately after delivery.

I'll mention a little bit about the meningococcal vaccine. Children aged 9 through 23 months who are at increased risk for meningococcal disease should receive a two-dose series of the vaccine, 3 months apart. This group includes all the conditions that are listed here:

· Those with complement component deficiencies.

· Infants who are in defined risk groups for a community or institutional outbreak.

· Infants who are traveling to an area where meningococcal disease is highly endemic or highly epidemic.

· People who are traveling, like Muslims, for the Hajj or people who travel to areas in the meningitis belt. This is largely in Africa, from West Africa to Central Africa.

It does not include children with functional or anatomic asplenia because of the concern with interference with immunogenicity of the pneumococcal vaccine.

I will now mention a few highlights in the papers you have. You can read them for yourselves. Again, most of these are around H1N1.

Petro Moro, who is one of our colleagues, and others looked at adverse events following administration to pregnant women of H1N1 vaccine that were reported to VAERS. The objective here was to evaluate and summarize reports in VAERS, which, we all know, is a spontaneous surveillance system with limitations. The study population was pregnant who received the H1N1 vaccine to assess the potential vaccine safety problem.

The method here was review of reports that were reported to VAERS from October 2009 through February 2010.

This graph indicates the number of reports that were sent to VAERS. Most reports, as you can see, were between October and November, and then they reduced. So as expected, due to the massive vaccination campaigns, there was an increase during the active phase of the pandemic.

The summary here indicates that at least 3 percent of the reports received following H1N1 vaccine involved pregnant women who reported to VAERS. Twenty percent of the reports were classified as serious, and 294 reports. Of these reports, 288 were inactivated vaccine, as expected, and we had a few of them that involved live vaccine, six of them.

The most common pregnancy-specific adverse events were spontaneous abortions. We had stillbirths. The most common non-pregnancy-specific adverse event was allergic reaction.

A review of VAERS reports in pregnant women who received the H1N1 vaccines, in summary, revealed no unexpected patterns or unusual adverse events that were reported in VAERS.

Another study by Lee and others in VSD prospectively conducted monitoring of H1N1 vaccines, as well as seasonal influenza vaccines during the 2009-2010 season. The Vaccine Safety Datalink, which monitors safety on just under 10 million members in the US, in 10 managed-care organizations -- this is electronic data on vaccines and pre-specified adverse events that are updated weekly for signal detection. They looked at the period of November 2009 to 2010.

Again, the results here indicate that over 1

million doses were administered for the monovalent vaccine, above a quarter of a million doses for the live vaccine. For the seasonal, it is about 2.7 million and under 200,000 doses for the live attenuated vaccine in VSD. As of May last year, there were no significant associations noted in the analysis for GBS and most neurologic outcomes and allergic and cardiac events. However, for the monovalent vaccine, a statistically significant signal was seen initially and observed Bell's palsy in adults aged 25 years and above. But this was dismissed on subsequent analysis, after they adjusted for a lot of factors.

In conclusion, there was no major safety problem following the H1N1 or seasonal influenza vaccines. This is more reassuring data.

The next paper, which is Glanz and others, again in VSD -- the objective here was to look at the safety of trivalent inactivated influenza vaccine in children 24 months to 59 months and to evaluate the risk of medically attended events in the sub-cohort of children who had multiple annual doses of TIV over their lifetimes. Again, the setting here -- they used seven managed-care organizations. The period is from October 2002 to March 2006 data. The participants again are aged 24 to 59 months who received at least one dose of TIV. The exposure here was vaccination with TIV. The main outcomes were medically

attended events in inpatient and emergency settings, with those various risk windows.

The results: Nine met the diagnosis for their screening criteria using ICD-9 codes. After medical review, statistically significant associations were mainly for GI conditions and fever. But none of the events seemed to be severe or had any major complications. In a second reanalysis, there was an apparent dose response for vaccine and allergic reactions in the 1-to 3-day risk window. The conclusion here was that there was no evidence for severe medically attended events following vaccination with TIV among children 24 to 59 months.

That's it.

I wanted to say something regarding Gardasil and dose interval, which was a question that was raised. But we can have this discussion first, if anybody has questions.

(No response)

Thank you.

MS. DREW: Thank you.

Dr. Mulach?

MS. BERNSTEIN: (via telephone) Hi. It's Jessica Bernstein. I'm standing in for Barbara Mulach.

MS. DREW: Thank you. You will be giving an update on the National Institute of Allergy and Infectious

Disease, National Institutes of Health vaccine activities.

Agenda Item: Update on the National Institute of Allergy and Infectious Disease, National Institutes of Health Vaccine Activities

MS. BERNSTEIN: I want to start off by talking a little bit about the goals of the NIH vaccine research and development program. I'm just going to briefly outline what those goals are:

· One is to identify new vaccine candidates to prevent or ameliorate diseases for which no vaccines currently exist.

· To improve the safety and efficacy of existing vaccines.

· To design novel vaccine approaches and strategies.

· To develop innovative technologies, like new delivery methods and new techniques for vaccine stabilization.

· To conduct and support research on issues related to vaccine safety.

I actually just have a brief update today.

I have spoken before, as has Barbara, about our vaccine safety program announcement that is signed on by five NIH institutes and CDC. This was released originally in 2008. I have mentioned it before at ACCV, but I wanted

to just briefly outline it since there are some new commissioners.

Because there are five institutes signed on, and CDC, we allow for flexibility in the funding sources. The PA is written to include a variety of research topics. It's designed to be broad and flexible as far as considering applications. I want to also give some examples that are put forward in the PA as topics of interest:

· Immunology research, including optimizing immune response to vaccinations.

· Comparison of vaccine schedules using genomics to identify differences that may be predictors of adverse events.

· Identifying biomarkers that may help in predicting predisposition to adverse events.

The PA was set to expire this month. I'm pleased to report that we are extending it through January 2012. We have also applied to extend it for 3 more years, so we're waiting to hear back about that.

MS. HOIBERG: Did you have slides on this?

MS. BERNSTEIN: I don't have slides, but I can provide bullet points if you would like, to be forwarded later, and a link to the program announcement.

MS. HOIBERG: That would be great, thank you.

MS. BERNSTEIN: Is there any other information you want about it?

MS. HOIBERG: No. I think that's okay.

MS. BERNSTEIN: I can keep you updated as to the approval process for extending it for another 3 years. That's still in the works. I'll let you know.

MS. HOIBERG: Thank you.

MS. DREW: Thank you.

Next we will call upon Michelle Williams, our ACCV member, to give a report from the Workgroup on Future Science.

Agenda Item: Future Science Workgroup Report

MS. WILLIAMS: The workgroup has met several times. We have essentially agreed on our charge, if you will. Remember, this is a question from the Commission stimulated by a feeling, which we are trying to validate, that the medical information contained in the claim files, regardless of the outcome of the claim, may have some clinical interest to investigators which could advance the public health goal of vaccine safety for future vaccine recipients. Again, that's an assumption. It's not tested. So our charge is to determine if that is the case, and if it is the case, essentially what the barriers are to accessing that information and if they can be overcome, and if indeed there is information that is useful out there and

there are investigators interested in using that information. Part of this comes from the fact that as the claims increase in number, we have more aggregated information.

We have already identified a few barriers to the usability of that information that we are going to follow up on, including some legal analysis and actual physical analysis. I know when we talk about the claims information, a lot of times people talk about the database, and in actuality it's not really a database, but a disparate collection of files.

So we will be working further on that. We do not have an action item for you today. But we'll keep you posted.

The second issue is that the Commission referred to the workgroup a comment made in the public comment period of one of our meetings as to making a recommendation that autism cases be put in moratorium until future science could be developed. As it turned out, the chief special master -- we requested some information on that question, some help with that question, because we felt it was essentially a request about claims that were in process that is really, said in legal terms, a request for pending a claim by someone who is not a litigant or a petitioner or a petitioner's attorney. We weren't quite sure what to do

with that. I know the chief special master is listening, and I think she may be able to share the answer that she gave to our workgroup with the public, if she is still on the line.

MS. CAMPBELL-SMITH: I am. Good afternoon. This is Trish Campbell-Smith, the chief special master at the Office of Special Masters.

Effectively, the Omnibus Autism Proceeding was the most generous scientific stay at the request of petitioners that has occurred in the history of the program. That turned largely on the number of claims that were involved. There was a period of better than 5 years that was afforded for petitioners to allow, quote/unquote, the science to develop.

The two particular theories that were put before the three autism special masters, the theory concerning MMR and a particular theory concerning the thimerosal component of, at the time, thimerosal-containing vaccines -- those two theories that were put before us were considered and rejected.

Now the Omnibus Proceeding has effectively disbanded and is no longer being treated as a coordinated proceeding, but is proceeding independently. Those petitioners who desire to move forward must do so and have received innumerable communications, orders and the benefit

of extended status conferences, if so desired, with petitioners, to understand what is necessary to move forward. Those who have identified themselves as desiring to move forward are moving forward, many on theories that do not pertain to autism as the injury -- table injuries and other types of injuries. But for those that are moving forward and attempting to get experts, there has not been a request for a scientific stay from any petitioner or counsel who is in the program. That's what we would be responsive to here in the program.

I will say that, as a general matter, in much smaller omnibus proceedings -- meaning those with a dozen cases or so -- effectively, what it amounts to is a scientific stay, so to speak, that would benefit a number of related cases. If there were similarly situated cases with similar injuries and petitioners or counsel could identify specific studies that were under way and were relevant to the claim or the injury that had been addressed in this particular case, there might be afforded a brief or modest stay, somewhere short of 6 months, to allow petitioner or counsel, if so represented, to advise the sitting special master or the assigned special master of the development of that theory. But general studies that are taking place that would provide background information or something like that are much less likely to receive that

kind of favorable consideration.

In short, it has not been an issue in the autism cases or current petitioners and counsel that are electing to move forward on other theories. But the opportunity to obtain a brief scientific stay is available in instances where a number of cases might be affected and ongoing studies that are identifiable, relevant, and specific to the issues before us can be demonstrated to be under way.

MS. WILLIAMS: Thank you, Chief Special Master.

Unless there is a follow-up request from the Commission, I think the workgroup's feeling is that that answer is sufficient, and we will take it off our workload.

That concludes my report.

MS. DREW: Thank you, Michelle.

We're coming to the end of our meeting here, but we now have some business for the Commission. We have the nomination and election of a new chair and vice chair on the schedule. I wonder if anyone has some comments on this.

Agenda Item: Nomination/Election of New Chair and Vice Chair

DR. SMITH: One of the things that we were speaking about, at least as an option and maybe a dialogue in advance of the nominations and elections, is ascertaining your interest to serve as chair for maybe the

next meeting or next two meetings of the ACCV and then move to have one of the new commissioners serve as vice chair, to get a better appreciation of the responsibilities and the activities of what the two positions do, so that on a moving-forward basis there will be this rotation of an experienced commissioner serving in one of the two capacities and then one of the other two positions, someone that's a little bit newer.

As maybe a way to introduce that topic and discuss it amongst the commissioners, I would be very curious to hear your perspective as well, Sherry.

MS. DREW: I personally think that makes a lot of sense. I know there has been some discussion among various commissioners. I think if anyone has any objections to that line of thought, maybe they could speak up now. Otherwise, maybe we can think of a way to achieve that.

I personally would be happy to stay on for a meeting or two as acting chair. I'm not sure if you would need to have an election for that. What you might want to do at this point, today, is elect a person as acting vice chair for the next meeting or two.

MS. WILLIAMS: I can't see people, so I don't know if people are nodding heads.

DR. EVANS: Michelle, hold that thought for a second. There's a bit of information here that we all know

about that others don't know about, and that is that the three replacements for the new members have been approved and have accepted, but they did not do so in time for this meeting. We expect that they will be available to serve in December.

This year has been unique, for a number of reasons -- earthquakes, everything, but also the fact that we brought on six new folks at once. Now to bring three more on, as some of you have pointed out, certainly begs the question about whether that's the most optimal way of doing it, and will there be enough transition of knowledge, experience, and so on?

What I would like to do -- and I think this can be worked out -- is go ahead and have the new members come to get oriented and observe the meeting in December and then the three members, if they are willing to stay on, and then we'll take it from there. We might even continue something those lines. There was one suggestion that Sherry continue to serve as chair for an additional meeting beyond that.

The point is, I think that, now until December, we can certainly count on there being this overlapping. You can decide what you would like to do in terms of election of officers with that understanding.

MS. PRON: I have a question. We cannot elect a

vice chair because we don't have a chair?

MS. DREW: No. We can elect a vice chair. I was just suggesting, if we elect a vice chair, that it be not for a year term, but just until such time as there is an election of both officers -- an interim vice chair.

MS. PRON: I don't understand why there has to be an interim.

MS. DREW: Because that person may want to become the chair after another two meetings.

MS. LEVINE: You are also able to elect Sherry as chair and then, in a few meetings, have another election to have a new chair. There's nothing in the -- it just says that the members shall select a chair and vice chair from among the members.

MS. DREW: We have traditionally been doing it every year, but it apparently doesn't have to be ever year.

DR. EVANS: This is the only vaccine advisory committee where the members actually make the selection.

DR. SMITH: Sherry, just a quick question maybe as follow-up to the email that you circulated to the Commission earlier this week. What interest has been expressed by members of the Commission in response to that email?

MS. DREW: We had Dave mention that he is interested. Michelle is not interested at this time. And

nobody else has actually mentioned any interest in serving now. I think everybody is a little reluctant, given that this is really only the second meeting that they have attended and been able to observe at.

MR. KING: Can I speak to that for a moment? Part of the germination of the idea of having someone either as an acting vice chair or a vice chair with Sherry as the chair was so that we would be involved to some degree in understanding what the process is in terms of setting the agenda, doing the back-scene type of work that occurs prior to the start of the meetings, so that, when Sherry's replacement comes on board, we at least have some level of knowledge of how this works and we're not all green forever. That was one of the reasons why we suggested it.

To be honest with you, several of us thought that Michelle should be the chair, but Michelle, in her Sherman-esque way, has made it clear that that was not good at this time.

MS. WILLIAMS: I can't hear you.

MR. KING: So I have offered to work as a vice chair, to really understand how it works and what it is. But in order to do that, we as a Commission need to say, let's do it this.

So it's an idea. It's out there. It can be

accepted or rejected.

MS. PRON: I would like to propose a slate. Do we operate by Robert's rules? How do we operate here? Sherry for chair and Dave King for vice chair, until such time as another election --

DR. SMITH: Second.

DR. DOUGLAS: And another election will be held in a meeting or two.

MR. KING: Whenever you want.

MS. DREW: Okay, all in favor.

(Chorus of "Ayes")

MS. DREW: Any opposition?

(No response)

MS. DREW: The motion is passed.

Next we have the public comment portion of our meeting.

Operator, this is our public comment portion. Would you see if we have any folks who would like to make a comment at this time?

OPERATOR: If you would like to make a public comment, you may press *1.

One moment, please.

Our first comment is from Jim Moody.

Agenda Item: Public Comment

MR. MOODY: Good morning. I want to specifically

thank Michelle Williams and the chief special master for their comments regarding the ongoing issue of staying the autism cases, however they are to be labeled going forward. On behalf of NAA, where we have a lot of pro se petitioners, we take this information back to the petitioners bar. It's our hope that these cases can go forward. There are a number of scientific studies that are under way that are of relevance to this question.

I think more broadly, one of the issues coming up -- more and more federal committees are accepting this as a gap in the science now, which is the lack of baseline data on unvaccinated children -- I believe there is going to be an IOM committee convened to work on that issue. That would obviously take 1 or 2 or 3 years to complete. I think that would give us much more comprehensive data on a lot of the adverse events going forward. I know that's longer than the 6 months that the chief special master mentioned. But as I said yesterday, I think it's an absolute moral and legal duty that all cases of injury be compensated. If it takes time to do that, then so be it. That is the plan set forth by Congress. The urgency in the program was designed to protect petitioners, not to punish petitioners.

Certainly my interest in going forward is to make sure that all of the cases of injury be compensated. I

certainly would appreciate and thank the Commission so far for its help in ensuring that that goal is taken care of as the science continues to develop.

Thank you.

MS. DREW: Thank you, Mr. Moody.

OPERATOR: At this time there are no more comments.

MS. DREW: Thank you.

This ends our public comment portion. Now we have future agenda items.

Agenda Item: Future Agenda Items

MS. DREW: I know we have mentioned a couple of future agenda items today, the VISs in particular and also getting certain information on injection practices out to practitioners. We may want to schedule those for some discussion.

Does anybody have any other suggestions?

MS. HOIBERG: We have had a couple of emails go back and forth about the questions about dosage of the Gardasil. Dr. Gidudu, is that what you were going to talk about?

DR. GIDUDU: Yes.

MS. HOIBERG: So we could put that on the agenda for next time.

MS. DREW: All right.

MS. PRON: I think the issue of whether or not we get to make a recommendation for a labeling of latex-containing vials of vaccines.

MS. DREW: I was including that in getting information to practitioners.

MS. PRON: Actually, that was a recommendation to the FDA, I think, because they control what labeling is on packages.

MS. DREW: Okay.

MR. KING: Do we have an agenda group that's going to be --

MS. DREW: No. That was another thing I was going to mention. I'm sorry, I let a couple of people escape before I asked for volunteers for the agenda committee. Sarah, Dave -- you're on it as the co-chair. Is there anybody else?

DR. EVANS: What I was going to say is that some of the areas that you are talking about really get into this interaction between CDC and FDA and recommending bodies and so on. I want to be sure that whatever we put on the agenda is appropriate. What I would like to do is do some background investigative discussions and then go to the agenda committee and figure out with you all what is appropriate to be put on and discussed.

I just wanted to make that clear. You can tell,

just the way that Marion was reacting to some of the discussion back and forth, that these are things that they toss around and have trouble with themselves. It just is the nature of the beast. That's why, for example, in your meeting books there is that workgroup paper by Neil Palsy(?) back in 1995 where they went over many of these issues about labeling and recommendations and the disconnect between the bodies.

This is something we can talk further about with the agenda committee.

MS. DREW: All right. Are there any other issues?

(No response)

I would like to hear a motion.

MS. HOIBERG: I motion.

MR. KING: Second.

MS. DREW: Everyone in favor?

(Chorus of "Ayes")

Anyone opposed?

(No response)

MS. DREW: Here we go.

(Whereupon, at 12:40 p.m., the meeting was adjourned.)