UNITED STATES
COURT OF FEDERAL CLAIMS

COLTEN SNYDER BY AND THROUGH KATHERINE SNYDER AND JOSEPH SNYDER, HIS NATURAL GUARDIANS AND NEXT FRIENDS,	)	
Petitioners,	)	
	)	Docket No.: 01-162V
v.	)	
SECRETARY OF HEALTH AND HUMAN SERVICES,	)	
Respondent.	)	

REVISED AND CORRECTED TRANSCRIPT

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1220 L Street, N.W., Suite 600
Washington, D.C. 20005-4018
(202) 628-4888
hrc@concentric.net

IN THE UNITED STATES COURT OF FEDERAL CLAIMS
OFFICE OF SPECIAL MASTERS

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Respondent.	)	

Courtroom 56
U.S. District Court
401 West Central Boulevard
Orlando, Florida

Thursday,
November 8, 2007

The parties in the above-entitled matter convened, pursuant to notice of the Court, at 9:00 a.m.

BEFORE: HONORABLE DENISE K. VOWELL
Special Master

APPEARANCES:

On Behalf of the Petitioner:

CHRISTOPHER W. WICKERSHAM, SR., Esquire
Wickersham & Bowers
501 North Grandview Avenue, Suite 115
Daytona Beach, Florida 32115
(386) 252-3000

APPEARANCES: (Cont'd)

Also On Behalf of the Petitioner:

THOMAS B. POWERS, Esquire
Williams Love O'Leary & Powers, P.C.
9755 Southwest Barnes Road, Suite 450
Portland, Oregon 97225-6681
(503) 295-2924 / (800) 842-1595

On Behalf of the Respondent:

ALEXIS B. BABCOCK,Esquire
U.S. Department of Justice
1425 New York Avenue, N.W.
Washington, D.C. 20005
(202) 616-7678

On Behalf of the Respondent:

VINCENT MATANOSKI, Esquire, Assistant Director
VORIS E. "VO" JOHNSON, JR., Esquire
KATHERINE C. ESPOSITO, Esquire
U.S. Department of Justice
Civil Division
Ben Franklin Station
P.O. Box 146
Washington, D.C. 20044
(202) 616-4136

C O N T E N T S

WITNESSES:	DIRECT	CROSS	REDIRECT	RECROSS	VOIR DIRE
Bertus Rima	824	905	933	938	--
Brian Ward	939	977	993	--	--
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Ronald Kennedy	995	1004	--	--	--
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E X H I B I T S

RESPONDENT's EXHIBITS:	IDENTIFIED	RECEIVED	DESCRIPTION
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P R O C E E D I N G S

(9:00 a.m.)

THE COURT: We're on the record in the Snyder case.

MS. BABCOCK: Oh, I'm sorry.

THE COURT: That's all right. It's nice if we're on the record before we start calling witnesses.

Dr. Rima, if you'd step up to the witness chair and raise your right hand.

Whereupon,

BERTUS KAREL RIMA, PhD

having been duly sworn, was called as a witness and was examined and testified as follows:

THE COURT: Thank you. Please be seated.

DIRECT EXAMINATION

BY MS. BABCOCK:

Q Good morning, Dr. Rima.

A Good morning.

Q Would you please state and spell your name for the record?

A Okay. My name is Bertus, B-E-R-T-U-S, Karel, K-A-R-E-L, Rima, R-I-M-A.

Q And what is your profession?

A I'm a virologist.

Q Now could you briefly describe your

collegiate and graduate education?

A I was educated as a chemical engineer in Delft, the Netherlands, and graduated there in 1970 with what was the Anglo-Saxon equivalent of an MSC, specializing in bacterial genetics. I then went to do a PhD in Canada for five years in bacterial genetics and then went to Dublin and to Belfast and wanted to do postdoctoral work on measles virus. And I have stayed there ever since and progressed through the ranks.

Q And where are you at currently? The Queens University of Belfast?

A Queens University, Belfast, yes.

Q And what is your position there?

A I am head of the School of Biomedical Sciences. And at the moment, I am involved in the reorganization of the medical faculty with a person who was in my school and now is the head of the School of Medicine and Dentistry. So I'm involved, essentially involved, in reorganizing the whole of the medical faculty there.

Q Now do you also teach?

A I do both at undergraduate level as well as postgraduate level, although with the amount of administration that I do at the moment, the amount of

undergraduate teaching I do is relatively limited. But I do still have about seven postgraduate students in my lab.

Q And you alluded to it earlier, but what has been the primary focus of your research, the literary research?

A The primary focus of my research has been paramyxoviruses and particularly neurovirology of measles. Canine distemper and mumps virus is more or less what I do at the moment as well as the pathogenesis of these viruses. So that is the main focus of my work at the moment.

I have been in measles virus work for about 33 years and started that off with the original SDS-PAGE gel to look at proteins. We went through RNA, the cloning and sequencing phase, PCR phase. And essentially we are now focusing more on the pathogenesis of the virus.

Q And about how many articles have you published on measles virus?

A I haven't counted them accurately, but it must be well over 100, plus a substantial number of articles on canine distemper as well as on mumps.

Q And you've also written book chapters and other publications?

A I have, yes, about 20 odd book chapters. I am responsible primarily for the Encyclopedia of Virology in mumps as well as the author of textbooks in medicine on mumps as well.

Q And have you been an invited to lecturer or given talks on measles?

A Oh, yes, quite a few times. Twenty, 30 times at least. And I've been involved in a number of evaluations and WHO groups to look at measles vaccination as well.

Q You also review scientific papers for journals?

A I do. It's a matter of trying to limit that, but I certainly will do one a week.

Q Okay. So that's about 52 a year?

A About 50 a year, yes.

Q Okay. Are you currently or have you ever been on the editorial board of journals that might be relevant to the litigation here?

A Yes. I'm on the editorial board of the Archives of Virology, which is a relatively low-ranking journal. I have been 15 years on the editorial board of the Journal of General Virology, which is about the third-ranked in the world, the most prominent European journal. I've been editor of that

for five years, and I'm still on the board. And I've been invited just to join the editorial board of the Journal of Virology, the ASM Journal.

Q And do you sit on any research panels?

A Not at the moment. I have sat on quite a lot of panels in the past, but I just simply don't have the time to sit on grant panels at the moment.

Q Do you have any learning society memberships? And just the most important ones that would be relevant to us here.

A Yes. I'm a member of the Society for General Microbiology where I am also on the council of the organization. That's a large-membership organization, about 5,000 members in the U.K. and Europe. And I am a member of the American Society for Microbiology.

Q And you were an expert in the U.K. MMR litigation, correct?

A I was, yes.

Q So it's fair to say you've spent a substantial amount of time working on that litigation?

A I did. I was asked to come on board and work with the lawyers who represented the respondents in those cases, which were the vaccine manufacturers. I was asked in late 1999 or early 2000, I can't

remember, and I worked for over five years on that, with different levels of intensity obviously because the case took off slowly. And then in 2003, we had to produce expert reports. But I was very much involved in the earlier stages of that work, trying to bring the legal teams up to speed in measles virology.

Q And as you just stated, you produced an expert report for that.

A I did. It is a two-pronged report which since has been redacted and has been made available to the Court here. The first part is essentially very much a general description, which I think is noncontroversial as it's simply to educate people. The second prong is really much more focused on my assessment of the claims for presence of measles virus in tissues of various claimants.

Q About how much were you paid for your time?

A I was paid about $160,000.

Q And of that, how much of that went to your academic institution for scientific research?

A After tax, I donated half of the proceeds of this to my academic institution.

Q And before today, how many times have you testified in a legal proceeding?

A I've never testified. As you know, the

McCabe case never came to court.

THE COURT: As we said to Dr. McCabe, welcome.

THE WITNESS: Thank you.

BY MS. BABCOCK:

Q Did you review the Snyder case materials in preparing your report?

A I did.

Q And by your report, I'm referring actually to what we may have called the supplemental report from you, because obviously the UK report was prepared for the ligitation there.

Did you also review any materials from Cedillo?

A I did. And obviously I submitted an affidavit in that particular case. That affidavit was terminated by a statement which essentially said that I wished to revise my opinion if indeed I will be allowed to talk more about what I had seen and what I had experienced in the case. And luckily, because of the redacted report now being available, I can now make a complete disclosure of the content of my report, which obviously was more extensive than the affidavit you have in the Cedillo case.

Q And have you been present to hear the

testimony of Dr. Kennedy and Dr. Kinsbourne in this proceeding?

A I have.

Q Now, during Cedillo and in this case, there was a fair bit of discussion about immune changes that are observed after a measles virus infection vaccination. Actually it was after a measles virus infection, and then there was an effort to extrapolate those immune changes to the MMR vaccine. Based on your research and knowledge, are there any clinically relevant immune changes following MMR?

A Well, I'm obviously not a physician. I'm not as involved in this, but actually I've studied this field quite a lot and I have never seen any clinically relevant immunosuppression after vaccination.

Q And can you briefly describe with MMR the attenuation process that results in the MMR vaccine for measles?

A Well, obviously there's three components, and I don't know whether you wish me to go through all three of them. Certainly in the case of rubella, I would be a bit shaky on the actual process that has taken place.

But as far as the measles virus is

concerned, it was passed through a number. You had first of all monkey kidney cells. And then essentially this process culminated in a number of passages in chicken embryo fibroblasts. And the virus occasionally is grown by some manufacturers in eggs.

Q And is it fair to say that the intent of the attenuation process is to make the virus less virulent?

A Yes, although that is measured in a very pragmatic sense in terms of the ability of the virus upon infection in human beings to cause clinical symptoms. So the actual molecular knowledge that we have doesn't really allow us to identify at this particular time which mutations are relevant. We certainly know a large number of mutations that have occurred during a particular attenuation process, but we are not able at this stage to say this is the important mutation that makes a particular virus attenuate. But that's part of a very large research program that I've been involved in.

Q Is it fair to say that the current formulation of MMR is an attenuated version of the Edmonston strain?

A It is. All measles vaccines used in the world come from that particular strain.

Q Which of the clinical findings -- and again, realizing that you're not a medical doctor -- but of wild measles virus infections do we typically see, if any, following MMR?

A The only one that is indicated and occurs is the thrombocytopenia at a very low rate. But that is rare and it is transient, but that's about it. There is a certain amount of fever in some of the children, but that is the main aspect.

When the original virus was put on the market, the Edmonston virus was not that well attenuated, and a more attenuated vaccine has been developed since. And that particular vaccine, the original vaccine actually still shows the occasional Koplik spots, but that is no longer the case now. And essentially what we see is a situation that fever is practically the only sort of clinical symptom that we see.

Q For about how long has this new vaccine you said is the more attenuated version, how long has that one been commonly administered in the United States?

A I think that must have come out late '60s, early '70s. I don't know exactly when it came to the U.S.

Q But quite some time?

A This is a long time.

Q Is pharyngitis a recognized reaction to the MMR vaccine?

A (Nonverbal response.)

Q Is otitis media a recognized reaction to the MMR vaccine?

A Of the vaccine, no. That is with the wild type.

Q Has the MMR vaccine ever been associated with SSPE?

A It has not.

Q What about MIBE?

A There are two cases in the literature that I'm aware of, the Bidmun case which was referred to earlier in the week by Dr. Kennedy. And that turned out to be -- sorry?

Q Could I just clarify, I think it was Dr. Kinsbourne.

A Sorry, sorry, yes. And that's the case in which the child turned out to be immunosuppressed and had an immune deficiency, although that wasn't recognized at the time. That child throughout the decades has been well described in the literature.

The second case is one that we have

identified about 30 years ago in Belfast with a child who had received the Schwarz vaccine, which is the same as the variety and strength in a more attenuated vaccine. And in that case, the child died of giant cell pneumonia but had infection in the brain and in all the tissues that we looked at. So those are two cases I know of.

Q Sure. Can I back up to Bitmun for a minute? You said there was immune suppression? Are we talking about mild immunosuppression, or was this a significant --

A No, in the case of the Bidman case, I don't know. I can't remember when the actual immune deficiency was identified.

Q But it was significant?

A It was. And in the case of the second case that I described, this child had -- anemia, so I couldn't make out accurately.

Q And that child died.

A So these were essentially unrecognized immunodeficient children which should not have been vaccinated but were obviously.

Q Okay. And I just need to make this clear now. By unrecognized immune deficient, the postulate here is that to some extent, there might have been

some unrecognized immune deficiency. We're talking about far more significant.

A Oh, yes. Definitely in the Belfast case. In the virus in the Bitmun, it was less well described.

Q Now you described acute disseminated encephalomyelitis in your report.

A Uh-huh.

Q What viruses have, you call it ADE, we usually refer to it as ADEM, been associated with?

A The viruses that can cause that are measles/mumps/rubella, vaccinia, varicella and influenza. There are some classical mumps with which that has been associated on occasion.

Q So a number of different viruses.

A Yes.

Q Has measles virus ever been shown to be in the brain of children affected by this condition?

A No, it hasn't. But obviously studies are quite limited because it is not often fatal. And in that sense, it is a situation where there's not a large number of material available. But in those cases that have been looked at, we haven't been able to find it.

Q So, no?

A The answer is it always difficult in science to prove the absence of something. There is no evidence for it, but that doesn't mean that it isn't there. In essence, because the general opinion in the field is that there is some form of an immune reaction that is set off and essentially leads to a reaction that is manifesting itself as encephalitis.

Q Now is measles an RNA virus or a DNA virus?

A It's an RNA virus.

Q Which is more stable?

A The DNA is much more stable. I mean, that's well-demonstrated. In fact, we can look at the -- DNA, or we certainly could look at the -- RNA, it's so unstable that essentially the viruses need to be able to replicate constantly in order to maintain themselves. And that's where there is a substantial difference in terms of persistence between DNA viruses and RNA viruses.

Q So it's possible for a DNA virus to remain in a latent state for a lengthy period of time.

A Yes. Oh, yes. That's very well actually demonstrated in the case of shingles in the elderly who have had chicken pox in the very early, much earlier stage of the virus stage, which you rely on viruses like -- but cold sores and Epstein-Barr --

Q But with an RNA virus such as measles, it needs to be replicating?

A It needs to be replicating, and so in that sense, it's not considered a latent virus. There is an active replication process that needs to be there to sustain the virus throughout the period of symptoms. I think this is particularly in the case of SSPE where that's about eight years. We do need to recognize that there is a time that that virus has to replicate in order to be able to maintain itself.

Q Now Dr. Kennedy discusses an R protein in his report, contending that it's produced by ribosomal frameshifting?

A Uh-huh.

Q Does this protein exist in measles virus?

A No, I've never heard of it. I've been 33 years in the field, attended all the conferences on measles, and I've never heard of this. Ribosomal frameshifting is a process that does occur in other RNA viruses but not in measles.

Q And Dr. Kennedy also stated in his slides on Tuesday that CD46 was the primary receptor for the vaccine wild type measles virus. Do you agree?

A I don't. Its main receptor is CD150 or SLAM. And even I refer to the paper that we have that

was produced in Belfast in this vaccine case, which essentially is a little bit alike in that even in that case, we are at this moment looking at the distribution of the virus in this child's tissues which are still available to us. And even in that case, the virus is still entirely limited to the lymphopickering (ph) system.

Q Now Dr. Kennedy also discussed a high-titer measles virus in his report, suggesting that the increased mortality in girls could be due to the viral persistence and with immune factors at play. I think we've already established that that's not a vaccine that's ever been administered in the United States, but are you personally familiar with these vaccination trials?

A Yes. I mean, I was part of the review group that WHO put together in order to look at that particular issue in 1992. And we had to come to the conclusion that there was indeed an unexplained higher risk for girls to die after the administration of this vaccine.

That particular evaluation was an interesting one in the sense that if you put the two genders together, the effect was just simply on the statistical borderline. We were really quite unclear

and unsure as to whether or not there was a real effect or not, because this was looking closely at cases that had occurred in various countries, and the studies had been replicated in a number of cases in countries.

And essentially you couldn't define exclusion criteria after the fact. So there were falls, there were traffic accidents, there was anything. We couldn't really exclude anything. But nevertheless, it was clear and it was replicated that in girls, there was this excess mortality. And so the WHO decided that these trials with high titer vaccines should be discontinued.

The main reason for them having to try and go into the children at an earlier stage with the vaccine is so that there is this window of opportunity for the virus to maintain itself. That is caused by the fact that at some stage, children lose the maternal antibody that they get.

If you then do a vaccination program at too early a stage, you end up in a situation where a large number of children simply have too much maternal antibody left for them to get the good thing from that vaccine. And so you have to wait with your program until a time that the maternal antibody level has

waned in almost all the children.

And so what we found was essentially that that needed to be 12 to 15 months. But what was tried was to go in with a higher titre vaccine from the remnants of that maternal antibody. So that was the idea behind it. And I think it was quite a sensible idea, but at the same time, when this effect was noted and replicated in other countries, there was really no option but to stop the trial.

Q So do you think it's appropriate to extrapolate and suggest that the reason that this might have existed were because of immune dysfunction?

A No. I mean, there's been several attempts to try to look at what the reason behind this is. And essentially studies have been attempted, but none have been able to be conclusive as to what happens in those cases. And these cases have been followed up for several years afterwards.

Q What are the measles antibody levels you see in the CSF of patients with SSPE?

A The antibody levels in SSPE are extremely high, and that is primarily based on the fact that there are resident B cells in the brain which start to make antibody that is measles-specific. And this leads to the situation where in SSPE, you have

oligoclonal bands that are the products of a set. A small set of B cells make these antibodies and have been put there in very, very high levels in the CSF of SSPE patients.

Q And with SSPE, does measles virus affect some areas of the brain and not others?

A No, it doesn't. It is diffuse, although we can show anatomical spreads, that it's spreading both through the sinus and also --

Q So it affects -- I'm sorry, you may continue.

A Sorry?

Q So it affects everything?

A Yes. It's diffuse throughout the brain.

Q Any evidence it causes altered cytokine levels?

A No really very good evidence, no.

Q Can you briefly discuss the clinical symptoms of someone with SSPE and MIBE.

A Well, it starts off usually with deficits in attention, difficulty to concentrate and usually is followed very quickly by degeneration, and there are four different stages recognized. And in the final stage, the children lapse off into coma. Death follows almost invariably. But there are stages with

seizures and seizures in various levels in between that that form a relatively well-defined staging of the process.

Q And have you ever had occasion to work with Andrew Wakefield?

A I did. As you can imagine, I worked on measles for about 15 years before Andy started. And I was quite interested. As a person who was interested in the sequelae of measles, I was quite interested to see what he had to say about the work in laboratories on viral disease. And so in 1992, I attended the first meeting with him where we had a number of measles virologists come together with him to look at material that he had produced.

And he was essentially asking the opinion of a number of people who were fairly well-respected and had had long experience in this field to see what they made of the claims. And I attended two of these meetings I think, and I came to the conclusion that whatever material was put in front of me was highly selective. When criticisms were made, they were not followed up.

So I was confronted with so-called measles viruses inside the cell which essentially turned out to be clathrin-coated pits and not measles virus,

which I pointed out. The size wasn't right. That sort of thing developed into a situation where I became somewhat frustrated by the fact that criticism that was leveled at the data that we were shown really wasn't followed up.

And then essentially in 1995, we had a situation where one of his MD students produced an abstract for a meeting that I was attending and asked me whether I wanted to be coauthor on it and I asked so, first of all, I would like to ask what the data were. And when data were presented to me in terms of sequence analysis, one of Andy's students told me that essentially it wasn't the Edmonston strain but that it was because it had the same simple single mutation in a particular position.

And I said, well, that's interesting because that was exactly a mutation which is present in the clone that I sent you, and so essentially that would have indicated contamination at that time. And when that wasn't retracted, then I formally withdrew my collaboration with Andy Wakefield.

And so I have been since 1995 involved in first of all looking from a different perspective of his at his claims for the involvement of measles in infecting inflammatory bowel disease, which was a

difficult period because it changed. We had notices all the time in strains of measles, wild-type measles viruses to vaccine measles viruses to measles and mumps in the same year. It was a very difficult time.

In '92, which is in my CV, it led to a situation where in 1998 I think, '99, I can't remember exactly, the Medical Research Council in the U.K. convened a meeting in which essentially we had hearings with Andy and several experts in the field. The general conclusion of everyone present was that there really was no substance to the claim that measles vaccine or measles virus was involved in the actual infectious bowel disease syndrome that he described. The only person that didn't agree was Andy Wakefield, and at that time, he had started to work on the autism case, but I wasn't aware of that.

Q So, just to summarize it, you had an instance where you worked with him, you identified concerns. Because of that, you didn't work with him any longer.

A Well, yes. I mean, my main concern was a rather difficult situation where I found that the criticisms I made were not acted upon. Then essentially you have to stop the collaboration, as several others have had to do as well. I mean, there

were people from the Westbury Group, a very well-known group working with measles. They were involved with Andy at the same time, and they withdrew from that collaboration as well. So it involved my other colleagues.

Q Switching gears, have you ever heard Paul Dyken?

A No, I hadn't, not until I came here.

Q Okay. And switching gears again, now on to the Uhlmann paper. This topic has been covered in quite some depth, and so we will certainly attempt not to duplicate what was already presented in Cedillo. Is it safe to say that you have identified a number of concerns with the Uhlmann paper?

A With the Uhlmann paper, yes. I mean, part of that is in my original affidavit in the Cedillo case and is read very well and extensively criticized in my redacted report that's available to the Court.

Q How much confidence do you have in the reported results based on those concerns?

A I have no confidence whatsoever.

Q Now Dr. Kennedy takes issue with Dr. Bustin's observation of a C-to-T substitution in the F-gene probe in the Uhlmann paper, asserting that this was done for purposes of allelic discrimination.

A Uh-huh.

Q Can you just explain quickly what allelic discrimination is?

A Okay. I think it's best if we would go to the last slide that I had.

THE COURT: All right. At this point, can we get these marked?

MS. BABCOCK: I'm sorry. Would it be Respondent's Trial Exhibit 4?

THE COURT: It would be.

(The document referred to was marked for identification as Respondent's Trial Exhibit No. 4.)

THE COURT: And are those slides numbered?

MS. BABCOCK: Yes.

THE COURT: Okay.

MS. BABCOCK: So we are on page 9.

THE WITNESS: Okay. So --

BY MS. BABCOCK:

Q Well, let me set the groundwork here. I'm just wanting in general what is allelic discrimination. We'll discuss it in more detail later.

A Okay. Well, allelic discrimination is a

test that's been devised to see whether people are having in their DNA largely just a copy of the same allele, the same sequence, or whether there is a mutation involving the parental chromosomes or whether most of them are of the second allele, and I have described that in my report.

It is a technology which works quite well when you have two 50/50 of DNA, with 50 on one allele and 50 percent on the other allele. Unfortunately, the Unigenetics Lab started to apply this to RNA work under conditions which are essentially experimental and which I can easily demonstrate to you that they actually failed to develop a proper test.

Q And we will get to that?

A We will get to that.

Q This is just for purposes of I wanted to see when I'm asking questions about whether the suggestion of the C-to-T substitution was done for purposes of allelic discrimination.

A Oh, it wasn't an allele. In fact, it was clearly a mistake. There is nothing in the Uhlmann paper that deals with allelic exclusion.

Q Okay. Were there other techniques used in Uhlmann like solution-based RT PCR?

A Yes. There were essentially four techniques

used in that paper. Solution-based RT PCR, which is an standard technology. There was in situ RT PCR, which was an experimental technology which in my opinion they failed to develop properly. And then there was obviously the background data. Those were the main technologies used.

Q What is immunocytochemistry?

A Immunocytochemistry is a technique that is used in order to demonstrate the protein of a particular virus in a particular tissue. Essentially, what it does is that binds an antibody to that particular protein to the tissue with a large number of controls. Then we add a secondary antibody to the infected antibody to see whether a particular protein of a virus is present in that tissue or not. And that technique was not used in the Uhlmann paper.

Q You answered my question, which is great. We'll move on to Unigenetics. Obviously, in your report, as part of your work in the U.K. MMR litigation, you had the opportunity to examine the tests and records used by the O'Leary Lab?

A What I had looked at, I must say I find myself in a somewhat difficult position, and if I may explain that to the Court. Obviously, my redacted report is available, but there is obviously a large

amount of background material that I have looked at but which I am not at liberty to discuss with you.

Nevertheless, my experience is described in the report, and it's based on having looked at that very substantial amount of material, which involves probably around 300 samples that we looked at in the U.K. litigation of controls as well as claims.

So, in essence, I have to be careful about how far I go into disclosing particular material. That is unfortunately the situation. But what is a very big difference between the situation that I find here and the U.K. litigation, the data that were available to me in the U.K. case would have been the top sheet or the headline figure that is the number of copies of measles F gene. It would be in some cases simply a number of copies. In some cases, the number of copies per nanogram of RNA, so a computation had taken place.

And I would have also then seen the actual data for the cell cycle number at which the -- would have had the circled CT number that -- I looked at and described in detail. And for each of the samples in that particular run as well, I would have seen the laboratory pages that would have indicated how the RNA was extracted and how successful that would be.

Q So you're saying that the clinic's efforts in the U.K. proved their case. They provided you with a lot more information on the testing that was done.

A Data, yes.

Q Obviously, Colten Snyder wasn't a part of the U.K. litigation, but nevertheless, we don't have that information here.

A No, we don't.

Q Nor should I say we would have any information in the Michelle Cedillo case.

A No, the same applies. The only thing that we have here is the number of copies.

Q And you've read materials presented by Stephen Bustin in Cedillo and in his testimony.

A I did, yes.

Q And again, I assure you that as a result of that, we will not be going through how PCR is done and some of the more technical details, because that was very technical, but we also need to cover some issues with you, Dr. Rima.

You've also read the rebuttal opinions filed by Dr. Kennedy and Dr. Hepner in Cedillo.

A I have.

Q During your career, have you developed

//

expertise on PCR techniques.

A Yes. I mean, as soon as it came out, it became quite clear this was a very, very powerful technique. What wasn't immediately recognized, and this was not until a substantial number of situations in literature which involved data that had to be rectified, was how powerful the technique actually was. And certainly the experience of all of us in the particular effect of using the technique is that it can pick up one copy or one molecule of DNA for a specific titer quite easily.

The RNA is a little bit less sensitive because you have to do this reversion scripting. That's the conversion of the RNA into DNA. That in itself is additional multiplications in the whole process. That's a situation where RNA is actually a little bit harder to detect. This is an area where I would have taken some issue with while Dr. Kennedy described immunization through the discussion you had -- in relation to the contamination issues in relation to the -- interactions.

(Electronic interference.)

A RNA actually, it is more difficult to pick up RNA in a lab, and even if you've got a virus and if you are in a laboratory which has a large number of

plasmids around, which are used in order to make standard RNA for the PCR tests.

So I would observe that it is a difficult situation to prove to anyone, but if you ask me what is the most difficult situation, it's that if you have in your laboratory a large number of plasmids that are of a particular virus, then you have a much greater chance of contamination than if you have the actual virus itself.

Q Were there plasmids at Unigenetics?

A Yes. They made them. They grew them in order to make standard RNA's for their standards curves in assays.

Q Did you visit the Unigenetics Laboratory?

A Yes, on two occasions. The first time primarily to look at the IS RT PCR data.

Q Which IS stands for?

A The in situ RT PCR. And I was allowed into a small room. Maybe I was a naive scientist at the time, not having been involved in any legal cases at all, and essentially ended up in a situation where I thought, well, I'm going there and I'll talk this over with John O'Leary and see what we can come up with.

But the only contact I had with John O'Leary was he came in the room and read me a legal statement and said he couldn't talk to me. I said okay. Then I just simply looked at the slides myself. And my only

interaction was with Dr. Shiels, who whenever I said, look, I don't see what it is I'm supposed to see in this particular slide and I see in this red circled area which you say is positive, I see exactly the same outside that red circled area, the only response I got, he said, well, this was Dr. O'Leary's invitation. So we couldn't really discuss this any further.

But being mindful of the fact that we were then getting into a legal situation, I ended up saying to the solicitors that acted for the respondents, well, I'm not a pathologist, so it would be very easy to say in court that what I saw was of course simply based on inexperience in the situation.

So I then went back a second time with Dr. McDonald, who I understand has testified to the Court, essentially to look at IS RT PCR and Tom I think also he took quite a few slides home with him in order to photograph them, and I hope you are aware of that. I haven't read the transcript of his testimony, but I assume that's the area that was covered.

Q Certainly. So it's safe to say you did review the Unigenetics of data?

A I did that directly in the IS RT PCR. I mean, the -- data, I obviously reviewed what I already said, the material that was disclosed to us in the

U.K.

litigation and presented through the allelic discrimination assay.

Q Now Dr. Bustin during his testimony and in his written report discussed concern with the laboratory notebooks.

A Uh-huh.

Q He discussed one example in particular. An attempt has been made to adjust that the problem, this problem he identified, was an isolated problem and was later corrected. Was this your experience in review or your knowledge of that particular lab notebook?

A In terms of the lab notebooks, I have seen that particular alteration that has taken place, the fact that after P28 full stop, material was added later on. Because we didn't get too many cases in which particular samples were disputed or where particular samples were repeated, I haven't been able to myself see any further instances of direct notebook alterations of that kind, okay? So that thought in regard to a first look at the evidence in this case, that's the only evidence that I have seen of that particular instance of the alteration of lab notebooks.

Q Based on your knowledge of that particular

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one, the circumstances, do you think it was later corrected? Do you buy the explanation that was offered in the rebuttal for the lab notebooks?

A It was clearly later corrected. In the U.K. case, we had one submission of that notebook and it came back into the second submission, and then there was an alteration.

Q Now we have the slide up actually about allelic discrimination. A claim has been made they were able to determine whether the measle virus they were identifying is the wild type or vaccine strain?

A Yes.

Q Based on your review, do you think they were reliably differentiating between vaccine strain and wild-type measles virus?

A No, they weren't, and I think this is very extensively dealt with in my report. But I have had direct discussions with Orla Shiels about the way in which he did that, because it wasn't very clear from the material that had been disclosed to us how that particular test worked. But if I may take the opportunity to show a diagram that is in my report?

Q Just one moment. I'm just going to say this is in color at one point, because you'll see according to the legend, different colors are supposed to

represent different things. We may ask leave of the Court to later file a color version so it will be easier to understand.

A Okay. Is this in color?

Q It's tough to tell.

A Okay. I need to see some colors.

Q What I need you to explain is why this does not give you confidence in allelic discrimination assays.

A Okay. Well, the assay works as follows. There are two probes in the RT PCR, one that can interact with DNA that is coming from the vaccines if there was a vaccine present in a particular sample and one that can interact with DNA that would be amplified from wild vaccines. And this gives rise to two different fluorescence values, which are measured in the "Y" axis or the "X" axis.

And so the assay is set up in the following way. A number of tests are being done on material that has been spiked with DNA, actually RNA that is contained in the vaccine sequence. There are also a number of tests that are set up in blue here if you can see it that are spiked with RNA that contains the wild vaccines.

THE COURT: All right. Doctor, I want you

to stop for a minute and describe where on the slides you were using your pointer for the vaccine strain and for the wild-type strain.

THE WITNESS: The vaccine tests material would be these right here.

THE COURT: And that would be the upper right part of the lower right square.

THE WITNESS: It is indeed here, yes. So a cutoff point is defined in that test. Based on the highest point in this set where the vaccine is spiked with the samples, and the value of that is determining where you make the cutoff between the vaccine and wild vaccines.

THE COURT: And by that, you mean the line that divides this slide?

THE WITNESS: That's the line that divides that particular diagram into four.

THE COURT: And that's the horizontal line.

THE WITNESS: The horizontal line, yes.

THE COURT: That's not quite at the halfway mark in the square.

THE WITNESS: That's right. Okay? And the same is then done in terms of the left/right discrimination with a number of samples that are spiked with wild-type RNA.

THE COURT: And you're referring there to the cluster of dots at the upper part?

THE WITNESS: At the top of the diagram.

THE COURT: Of the diagram, along the vertical line.

THE WITNESS: Yes. And so essentially then the most right-handed point of that set of samples spiked with wild-type RNA defines the second cutoff for wild-type or not.

THE COURT: And by "second cutoff," you're referring to that vertical line?

THE WITNESS: That's right. So if you spike them with both, then you get your "Y" data, essentially your indication of the amount of wild-type RNA that is there, and you get that in the upper right quadrant as a set of samples.

THE COURT: And you're circling that more dispersed cluster of dots next to both.

THE WITNESS: That's right. And so here's the wild-type spiked samples. The vaccine-spiked samples appear on both. Then we have a cluster of patient data. This cluster of patient data is actually populated very heavily with one single case of an SSPE that was amongst the litigants in the U.K.

THE COURT: And by that, you are referring

to the more dispersed cluster of dots along the vertical line, below the wild-type cluster you described before.

THE WITNESS: That's right. The controls, the no template controls, or irrelevant templates, are here.

THE COURT: And you're circling?

THE WITNESS: I am now circling the sample in the bottom left quadrant, several of which are open circles are --. And essentially then where we see most of the claimant samples are in this particular position here. They are in this particular cluster, but some of them are on the right-hand side of that vertical line. Others are on the left-hand side of that vertical line.

THE COURT: And you are there circling the cluster of dots in the upper left-hand corner of the box labeled "vaccine".

THE WITNESS: That's right. Thank you for helping.

THE COURT: Lots of experience in describing things.

THE WITNESS: Thank you for making this as correct a transcript as possible.

And essentially what we then have is a

situation where you see that most of the claimants sampled, apart from one case which clearly has a wild-type virus in there, sit in this particular position. And essentially when I started to look at the actual raw data, I came to the conclusion that several of these samples had been miscalled, and that is identified in great detail in my report on pages 32 and 33, and page 32 has been filed, now, has it?

MS. BABCOCK: Yes.

THE COURT: Yes. We have it filed as a separate exhibit.

THE WITNESS: Okay. So essentially there were a large number of instances where when I started to look at the data, they had certainly been miscalled, because particularly now the "X" or "Y" data was mistaken as to where the line should be, and then some of them were actually on the wrong side of the line but were nevertheless called vaccines.

And in many cases, as you can imagine with a distribution like this, a lot of the replicates would have been on that side and the other replicas would have been from that side of the line. And so it ended up in a situation where we then called these vaccines but essentially they were undeterminable.

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BY MS. BABCOCK:

Q So let me be clear with that. If they did a replicate and one showed up on the vaccine side and one showed up on the undetermined side, they could say they have isolated the vaccine strain?

A In the reports, they would have said consistent with vaccine and I'll come back to that later, because they could not by the fact that they had not analyzed the F-gene sequences, the H-gene sequences that they used for this, they had not been able thereby to come forward with a proper allelic discrimination test between all wild-types and all vaccine. And so they had to change their claim to not vaccine but consistent with vaccine.

But indeed there are a number of cases where the replicates were on either side of this line. To my mind, this is a single distribution. There's a bit of spread in it, and maybe we can come back to describe and we will come back if we are going into further detail about the fact as to how that can come about. But this is a single distribution. And essentially in some cases, they simply fell on one side of the line and in some cases on the other, and in some cases, even patient samples would have had to be called wild-type when they would be sitting

basically here or here, for example.

THE COURT: And when you are saying this is a single distribution, you are circling the cluster of dots in both the undetermined and the vaccine boxes that coincide.

THE WITNESS: Contain samples from claimants.

THE COURT: And these are the samples that appear on either side of the vertical line.

THE WITNESS: So I didn't consent that they had succeeded in making a test that really was working properly. Essentially, I think that particular test has never really been published as it had not really been verified, and other laboratories have not begun to follow it, because obviously the question as to where does this signal come from is an interesting one, and we can come back to that if we look at in greater detail the technical RT PCR. So it is not as if there is no signal. We see if they are negative, there is signal. It's just a matter of how much signal is there as to whether they were considered positive or negative.

THE COURT: And by "signal," you're referring to those same dots we just described.

THE COURT: I'm referring to that same

cluster of dots, right.

BY MS. BABCOCK:

Q Stepping away from allelic discrimination for a moment, in the Hepner and Kennedy rebuttal opinions, they both seem to suggest a number of problems can arise in PCR tests where you have low detectable levels of whatever you're targeting. Would you agree?

A Uh-uh.

THE COURT: And that was a yes?

THE WITNESS: Sorry. Sorry. No, I don't agree with that particular interpretation, because it goes back to the point I made earlier about what material is available to us. Both Dr. Kennedy and Dr. Hepner in my mind made an assumption, namely, that the actual headline figure that was reported, in the case of Cedillo 1.67 times 10 to the fifth copies per nanogram, in the case of Colten Snyder 3.4 times 10 to the fourth copies per nanogram, is indeed something that must indicate that the copy numbers in the tests were high. That is not necessarily the case.

BY MS. BABCOCK:

Q And that leads right into my next question. Did you observe discrepancies in the way Unigenetics was reporting their copy numbers?

A Yes, we have had several discrepancies in that particular area. The first one is the following, and that is the most disturbing in my mind. On several tests, I have seen the data for the copy number in one lab, because it might have been 2,400 and a copy done where in the second lab it might have been zero. What then was reported to us was the value of 2,400.

Now a bad scientist would say it's 2,400. Slightly worse scientists would make the average of 2,400 and zero as 1,200. But a good scientist would have said there must be something wrong with my test if one is 2,400 and the other one is zero. But this particular method of reporting was widespread IF tables in which data that have occurring 30 out of 40 samples, and so zero values were ignored.

Q Now accepting for a moment that the high copy number is what it is, it was actually a high copy number, can laboratory problems still exist when you have high copy numbers?

A Well, obviously I think contamination problems have been identified by Steve Bustin and which I have seen and also have been documented quite well in the report by Professor Simmonds. We came to the same conclusion, that there were a series of

problems with the actual contamination that was in the laboratory. That is something that I think is most aptly demonstrated in one of the slides that I brought by and produced for you, and that is, for example, this.

Q Slide 2?

A This is a slide from actually it appears Dr. Simmonds' report, page 72, which indicates the sort of replicance between the two samples that would have been put into a GAPDH of the age determination of a particular sample and of the measles "F" gene. And this is a scatter diagram you get in which the values found for replicate number one are on the "X" axis and replicate number two on the "Y" axis.

THE COURT: And you're referring to the slide on the left side, the "F" gene slide.

THE WITNESS: That's right. And these are samples that would be negative in both cases. Here, for example, we have a sample on the top left-hand side of the diagram in which there might have been approximately 5, 6,000 copies of the measles "F" gene found, but the replicate would have been negative.

THE COURT: So, to make sure I understand the slide, you referred to the dot at the top left-hand corner in saying that that might have been 5 or

6,000 copies.

THE WITNESS: From the level of replicate number two, it might have been 5 or 6,000. I'm just trying to interpret it on the lower-end axis here. And I'm not sure who did that.

THE COURT: And earlier you circled the dot in the bottom left-hand corner.

THE WITNESS: That would be a sample that would be declared negative in replicate one and replicate two, okay? But this sample here, for example, would be a sample that would be 5,000 copies in the one replicate, number two, and negative in the other half.

THE COURT: And that's why it falls in the negative column.

THE WITNESS: That's right.

THE COURT: Because the two runs did not agree.

THE WITNESS: That's right. Okay? And so this would have been a reasonable determination with a reasonable conformance between the two replicates. So if I look at the top right-most dot there, that would have been one in which replicate number one might have been again 5, 6,000 copies, replicate number two, 5, 6,000 copies. Replicate number one might have been in

that same class. So that would have been a reasonable concordance between the two figures.

But all the other dots are providing the difficulty to us, because they should be, as we see here on the GAPDH line where the best theory works, they should be on the straight line. They should form a cluster around that particular straight line here.

THE COURT: And so what you're suggesting as I understand it --

THE WITNESS: What I'm suggesting is that while this test clearly doesn't work, your replicates are very discordant, not concordant, this test worked well.

THE COURT: So if the F-gene test worked, you would expect to see the dots forming a diagonal line from the bottom left to the upper right.

THE WITNESS: That's right. That's right.

THE COURT: Instead, they're --

THE WITNESS: They're all over the place.

THE COURT: Right.

BY MS. BABCOCK:

Q Now it's been suggested that high copies of measles virus, a high copy number necessarily implies that the threshold cycle was low.

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A Yes.

Q The CT was low. First, do you agree?

A No, I don't.

Q What's a housekeeping gene?

A A housekeeping gene is a gene that was used simply because it is present in all cells at relatively constant levels. And so housekeeping genes like GAPDH have a relatively constantly level of messenger RNA in each cell, and that is about 1,000 copies, okay?

So although there is dispute and you'll see some comments in Steven Bustin's report to indicate that GAPDH is not the ideal choice, and we all disagree with each other about what is the ideal choice because you can't always find a situation that you'll have the cell type in which one of these housekeeping genes is upregulated to such a level that you say this is not proper, but a lot of people use GAPDH as a housekeeping gene. So I have no issue with the choice of that particular gene.

But the question that you raise is really an important one, because it affects a lot of the data that we have seen, particularly in the Cedillo and in the Colten Snyder case. The headline figures are very high.

Q Well, the general question is, if there's calculation errors involving GAPDH, that affects the copy numbers, correct?

A It does, because it's normalized to that.

THE COURT: And just let me inject here. The second chart to the right is labeled on your chart "GADPH," but that's just a transposition?

THE WITNESS: That is the housekeeping gene that is used in the test that Unigenetics worked.

THE COURT: I guess what I'm asking, are we talking about the same thing? The title of the slide refers to "GAPDH."

THE WITNESS: Yes.

THE COURT: The slide itself showing the dots refers to "GADPH." Is that a typo?

THE WITNESS: That must be a typo in Professor Simmons' report.

THE COURT: Okay. But we're talking about the same thing.

THE WITNESS: It is the same gene, sorry. I'm sorry about that.

BY MS. BABCOCK:

Q And then I think you were moving on to Slide 3 with the calculations.

A Yes. So essentially the important factor to

recognize, and this is where I think I disagree with the rebuttals of Dr. Kennedy and Dr. Hepner, is that the headline figures as they are reported to us in this case can be derived from a large number of different situations.

And for that, I have to indulge you in a couple of slides to take the type of suit up. Having read some of the transcripts, I can see that there is a potential for confusion about core CTs, high CTs, low CTs, low copy numbers and high copy numbers. Therefore, I will discuss only copy numbers, but remember that it is always based on the CT values.

So, in most of the reports that we see, we see, for example, in the case of Cedillo that there's a reported figure of 1.67 times 10 to the 5 per nanogram of RNA. Now this figure is derived by first of all establishing the number of measles F copies in a given sample volume. That given sample volume is only in the reference data 5 microliters, and they extracted RNA in 50 microliters so they have enough for 10 tests.

And the second thing that needs to be done is to decide and then look at the GAPDH housekeeping gene, messenger RNA. In the same sample volume. So that is how that figure is derived.

Q Moving to Slide 4.

A Moving now to the next slide, so in most samples that I have seen for a report of the copy numbers of measles F in the sample, the actual copy number in that term is from the low end of the standard curve. So we are looking at the right-hand side with Figure 18 in my report. But most of the actual determinations of copy numbers were done in this range on the left-hand range of the standard chart.

Q The right-hand chart. Okay. It's the line which, again, we're going to file this again in color.

A It is the blue line, correct. So this particular diagram is derived from material that the manufacturers of the ABI TaqMan system provide to people who want to use the system, and they compare their absolutely straight standard curve with that of the competitor, which has curves on the outside, which means that if you are working in this low copy number area, you really don't get the proper evaluation of the numbers of copies based on the cycle numbers. And so you see this before at any cycle number over 35, or 40.

In the -- cycle, background PCR is generally distrusted by experts, which allows me to make the

point that most of the values that I've seen are actually outside the standard curve that Unigenetics had in the sample itself. So in most cases, their standard curves were stopping at 500 copies per sample, and so they make the standard curve from 5, I can't remember what it was. I think it was 500,000, and they did indeed take it to the root of ten for each time, and they stopped at 500.

But then they reported copy numbers on the order of well below 500, so then you would be working on this part of the graph where you're working to the left of your last standard in, so you're extrapolating your data from the standard curve, assuming that this is a linear relationship.

THE COURT: I'm not sure I followed that.

THE WITNESS: Okay.

THE COURT: Can you try again?

THE WITNESS: Yes. So the standard curve as determined is set up by making let's say for the sake of argument 50 copies, 500, 5,000, 50,000, 500,000, 5,000,000, okay?

THE COURT: Now I think I understand what you were saying.

THE WITNESS: Yes? But most of the copy numbers that are actually reported in the data are to

the left of that low standard point, so that is an extrapolation. You just assume that the curve continues in this way and thereby you end up in a situation where you assume to make that assumption, and then you assign a copy number to that particular value, yes.

THE COURT: Okay.

THE WITNESS: So that is in itself, and I make reference to that in my report, a deplorable way of doing a test. Most of us like to do a test where the values that we determine somewhere along the line are in the middle of the range of the curve rather than somewhere to the left or to the right of the standard curve. So essentially then we have to look at what is --

MS. BABCOCK: Slide 5.

THE WITNESS: Sorry. Are we going back? No?

BY MS. BABCOCK:

Q No. We're on Slide 5.

A So the number of GAPDH messenger RNA copies that was determined in the sample is often also low. Particularly when that sample of RNA is degraded, we end up in a situation where the GAPDH is low in particular, and a reference has been made by Steven

Bustin to the fact that he can clearly demonstrate where particular RNAs are degraded because the GAPDH copy number becomes low.

Now the manufacturer of the Taqman kits and many independent studies give us a figure of the following kind in that the average cell contains about 10 picograms of RNA, messenger RNA, which in general parlance means every cell has about 200,000 messenger RNA molecules in it. And it's important to remember that figure because we come back to it later.

So of those 200,000 messenger RNA in a cell, about 1,000 of them are GAPDH. That being said, if you have 100,000 copies of GAPDH, you'll say that is equivalent to a nanogram of RNA simply based on the idea that 100 times 1,000 is 100,000, 100 times 10 picograms gives you a nanogram, okay? And so 1 nanogram is the approximate amount of RNA in 100 cells. If we go on then --

Q Slide 6.

A -- we get to the following. The reported headline figure could be based on very different raw data.

Q And this is just to be clear 1.67 going back a couple slides.

A This goes back to the headline figure that

is on the first slide, which in the Cedillo case was 1.67 times 10 to the 5. So you could report that figure of 1.67 times 10 to the 5, which is 167,000, if you had 100,000 copies of GAPDH in your samples. But you would report that also if you had 1.6 million copies of the F in your sample, but a million copies of your GAPDH, yes?

THE COURT: Okay.

THE WITNESS: So just to digress back to the CTs, that would be correct if that was your test because you really would have large numbers of copies. But what is more frequently the case in my experience is the following, that the F copies were low and the GAPDH copies are low, and still the headline figure because of normalization would have been produced at 1.6 times 105 per nanogram. They simply multiplied this figure up by what you need to get from this figure in order to get to 100,000.

And even if it was 167 MDF copies properties and a 100 GAPDH, that same figure would have been reported to us as 1.67 times 105 per nanogram. And this is where I had serious problems with what was being reported in these two cases because all we have seen is the headline figures. We have not seen any of the underlying data that I have seen in the U.K.

litigation as a standard amount of evidence that would have been provided to us.

BY MS. BABCOCK:

Q Let me just clarify that, though. Even when you saw the extra data in the U.K. litigation, were you satisfied that Unigenetics was calculating things properly and identifying?

A Well, on occasion, they made calculation mistakes, and they had a structural mistake in their standard operating procedure because a lot of it was marker-related to base variant of 660 and not 375. It's very technical to go into here. It's not that relevant. All of their figures are off by a factor of two, but we are usually dealing with orders of magnitude in this, although they have immense belief and confidence in their technology so that they said, well, we have 6.63 copies in this particular case.

Now, if we then look at that, so in my experience, the headline figures that were reported were largely coming from data like this. Therefore, it is wrong to say for Professor Kennedy and Professor Hepner that essentially the CTs must have been low because the headline figure is so high. The data are simply not there. There is no evidence in this particular case.

THE COURT: We don't know what the CT figures were?

THE WITNESS: Exactly, we don't know.

MS. BABCOCK: Page Seven.

THE WITNESS: So in my experience from all the data that I have seen from Unigenetics is that the high reported headline figures come from the bottom of the type of unreliable determinations of copy numbers of the MDF and GAPDH. And many of those I even pointed to outside the range of the standard.

I refer you to Table 3, 10 to 17 in Section B of my report, where you'll see many examples of lower values that are reported as high headline figures simply because we had the information in the U.K. litigation available to us, and I started to get information that has been passed to us by the understanding in both the Cedillo and the Colten Snyder case, but it's not available to us.

BY MS. BABCOCK:

Q Now can contamination still be a problem with a high copy number?

A Of course, because it is a sort of somewhat random event, and so if you have contamination and you're contaminating samples, then they will be able to have high copy numbers.

Q And does an entire run need to be positive for contamination to be at play?

A No.

Q Why is that?

A Because it all depends on where you find some of the samples. Again, in the U.K. litigation, we were provided with data for each of the litigants that showed where their samples were on a particular plate, and in many cases, we found that contamination was closest to the row in which the high copy numbers were available for the standard curve. So there was an effect of how the closer your sample was to the extended curve line the more likely it was that you might end up with a measured copy number. That was the threshold sort of effect that can occur during a test.

Q Is it a positive control?

A The positive controls that are returned in the standard curve for that particular application.

Q Just wanted to make sure that was clear. So hypothetically if you had CSF samples next to the positive control, and a whole blood sample elsewhere on the plate, would it be feasible for the CSF to be positive and whole blood negative?

A Certainly so.

Q And that would still be because of contamination?

A Exactly.

Q Now did you also observe variations in runs depending on the day they were done?

A We did, and that is very well documented in my report and even better in Professor Simmons' report where essentially we saw whole runs in which everything was negative and we saw runs in which everything was quite high, and I identified that in my report as areas in which on some days out of 48 samples, there might be some 36 or 37 that are positive and the next day nothing is positive.

Well, you either have biased your samples on the plates somehow, or alternatively you have massive contamination on one day and not on the next. So that contamination problem doesn't disappear as a result of that.

Q Now I wanted to ask you about the testing that was done on Colten Snyder in this case on CSF and whole blood. One was positive, one was negative, correct? The CSF and the whole blood test?

A That's right. The headline figure reported 3.4 times 104 for the CSF, blood was negative.

Q I think it's 3.7 times 104.

A It is 3.7. Sorry.

Q Just nitpicky. The samples were drawn on the same day, correct?

A Uh-huh.

THE COURT: And that was a yes?

THE WITNESS: Yes. Sorry.

BY MS. BABCOCK:

Q Now, accepting for a moment the results, did this make sense for CSF to be strongly positive while whole blood is entirely negative?

A Not to me in the sense that the figure that is described in the CSF of course is one that is again given as a headline figure of a per nanogram basis. We must assume that there must have been some GAPDH copies and that we have a look at extractions out of the RNA. And neither in the measles pathogenesis or the normal infection or in SSPE or in any of the infections do we actually see a large amount of free virus in any of the tissues or in samples like serum or CSF or PBMC's, so it must have come from cells.

And the cell types that we find in the CSF would be the same as those that you would find in the PBMC fraction. So assuming that you had a long-term infection which had gone on for years, I find it very strange that you would have the cells in your CSF as

positive to an enormous extent, and again, we can come back to that later, and the PBMC with a zero copy number.

Q Now again accepting that its valid, how much measles virus would that finding translate to in Colten? Is that a high number?

A In his CSF?

Q Uh-huh.

A It is a very high number.

Q Higher than maximum viremia in wild measles virus infection?

A No, it's very difficult to say that. I mean, the only figure we have is the following, that first of all, there was no measles virus found, okay? All that has been found in his CSF is a copy number of a DNA molecule that is supposedly coming from an RNA molecule, which is supposedly coming from a measles virus infection, so there are a number of suppositions in that.

To say that is a high number is based on a very simple sort of calculation. I've already given the Court the sort of guesstimate that we work with in molecular biology that a cell is not doing 1,000 copies of messenger RNA, but in an acute infection, if I set up one of my best growing viruses, measles

viruses, in one of my easiest to grow cells like the vero cell, I can get about 3,000 copies of measles F gene per messenger RNA per cell. That's the best I can get, okay?

So if you get to figures like 3 times 106 per nanogram, that means that you have three times 104 copies of that particular RNA per cell, and that is three times 104 would be 30,000, okay? So any figure at that level I immediately suspect as completely and utterly wrong in the sense that that is very implausible biologically because it would indicate that that cell would be stuffed with measles F.

And as Dr. Kennedy rightly pointed out, that would have also in order for that to be biologically correct would have also meant that there will probably be 10 times more copies of the measles F, about 80 percent of that figure, measles N, another 80 percent of that with measles M, et cetera, because we have this gradient gene expression that he well described, which I have absolutely no problem with.

So if you get to figures of that order of magnitude, you know that it would have indicated that every cell would be stuffed with measles virus, okay? If that's the case, we don't need to go to any of the

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sort of TaqMan technology or any of the technologies that have been used by Unigenetics in order to demonstrate the presence of the virus in these children because it would have been a double. You would have had positive solution phase. You could have done the immunocytochemistry. You might have even been able to isolate the virus, or it would have been fairly simple. Anyone competent in this particular field would have been able to pick up the virus because it would have been in every cell in very large quantities. So that is where we are in the situation that essentially the headline copy numbers that I described to us are biologically implausible.

Q Did you also review Dr. Bradstreet's 2004 paper?

A I did.

Q Looking at his paper and comparing it to your UK report that was filed, did you determine that several of those children are included?

A That's right, and I have prepared a slide for that.

Q Slide 8.

A So, on the top of that slide, we see that the --

THE COURT: All right. Our copy of Slide 8

looks very different from this.

THE WITNESS: Yes, that's right. Special Master, there is a problem, and that is that I in my somewhat inexperienced method of operation produced an animated slide, so what you see there is a printout of the final animation, and we'll come to that animation.

THE COURT: Okay.

THE WITNESS: The top of this particular slide as we see it there is the Table No. 2 from the Bradstreet paper.

THE COURT: Okay. If you'll give me just a moment then so I can find the Bradstreet paper?

(Pause.)

THE COURT: Mr. Wickersham, can you identify the exhibit number for the Bradstreet paper?

MR. WICKERSHAM: It's Petitioners' Exhibit 188.

THE COURT: 188? Thank you very much.

All right. Thank you. I'm prepared.

THE WITNESS: So in Table 2 of that, this is part of Table 2 only, I haven't shown the controls because the bottom line from the controls is just simply a straight set of negatives. The essential one is autistic spectrum disorder. Do you want me to explain?

MS. BABCOCK: Let me stop for you a moment. I'll just note that Table 2 is on page 42.

THE WITNESS: Okay. First of all, I was able in Table 3 of my report to identify the other two children, and Table 3 in my report deals with the CSF cases in the American cases, and obviously I have only seen these anonymized data. Unfortunately for us, I have not been able to find the data that might have been anonymized but might have referred to Colten Snyder.

BY MS. BABCOCK:

Q So these refer to the other two children?

A The other two children are --

Q In the Bradstreet paper?

A -- No. 265 and No. 498 in my table, which I show an excerpt on this particular slide. And these children there, Child No. 1 is 490 of which a CSF determination was done, and what you see at the bottom table is that the CSF and the GAPDH was 2.9 times 101 and 5.5 times 101, 29 and 55 respectively, and so presumably a figure of 37 or thereabouts would have been used as the figure.

For the measles F, they would have come forward with a determination of 1.1 times 104 and 9.5 times 103. Very high numbers, but as I indicated, my

interpretations are based on contamination. Then multiplying the average of 1.1 times 104 and 9.5 times 103, let's say 10,005, whatever you have to multiply to get from 100,000 to 37, 7,000, you end up in a figure of 2.42 times 107 copies per nanogram.

So Child No. 1 in the CSF had 2.42 times 107 copies per nanogram. That's the sort of figure that you would have seen if you had no other data, that's the headline figure that we're dealing with in this particular case, and that gives rise to that particular headline figure. That headline figure means that every messenger RNA in those cells is measles F, and they're still stuffed with that. It's still a higher number than 200,000 per cell.

So essentially we're in a situation where this is completely and utterly implausible as a phenome. What's interesting is that the other child is 265, had a GAPDH of 9.8 times 101 and 7.4 times 101 if I see that correct. I haven't got a slide on my screen.

Q Yes, that is correct.

A Okay. And given a figure of 6.2 times 103, 5.2 times 103, and the figure is 6.60 times 106, which is the figure that you see in the Bradstreet paper, hence this is the type of data that convinces me that

I'm looking at the right child. We hadn't seen that figure anywhere else. I looked at this fresh frozen biopsy.

Now fresh frozen biopsy, you expect good messenger RNA extractions, and indeed you see the headline figure is going out to 8.2 times 104, 6.4 times 104. The technical figure for the measles F is zero, and maybe you can see that in the copy you have, or 770. And then you see the figure that is then determined, you ignore the zero as per standard treatment of Unigenetics, and you end up with a figure of 1 times 103, and that's the figure that you see in the table here.

Q Okay. So in that middle box, where the black mark is is supposed to be a zero?

A That is a zero, yes. It's red in my original report. I don't know whether a copy, a color copy of my redacted report is available or why that was redacted in such a fast way that it didn't --

Q Do you have color copies?

A Yes, I have color copies.

Q Okay.

A And then the whole blood, a different story again. We see in this particular case whole blood. The reasonable GAPDH had a low number of this certain

set and very high copy number for measles F, four times 103, 2.1 times 103.

Q That's 102.

A Sorry? Is that 102?

Q Two.

A I'm sorry. I can't see them on my screen here.

Q It's okay.

A And essentially that is now in this case done because this is such a high number. This becomes 2.1 copies per nanogram.

THE COURT: And all of this information is from No. 265 on your slide?

THE WITNESS: That's right. That's right.

THE COURT: So whatever claimant number.

THE WITNESS: And what we see in this particular case, 265 is measles F. It gets in the ileal biopsy coming from this information and copy number being this, in the blood PS copy number being 2.1 per nanogram and then in the CSF, 6.6 times 106.

BY MS. BABCOCK:

Q You're referring to Row 2 in the top chart?

A I'm referring to Child No. 2 in that table.

THE COURT: And this is Child No. 2 from the Bradstreet paper.

THE WITNESS: I haven't been able to find in my records where this figure comes from yet, but less than one copy per nanogram. Then one copy per nanogram, let's assume that you have a good infection in one cell that gives you 3,000 copies of measles F per nanogram if you have one in 100 cells infected. So you can see that one copy per nanogram actually means that one in 100 times 3,000 cells, so 100 times 3,000 is 3,000,000 cells is infected.

We've had a lot of debate about that particular type of argument because what it means is to say, well, there are very few systems in the body which will destroy pathogenic effect in which if one out of 300,000 cells wasn't doing what it was supposed to be doing, it is a simple chance of if that was the case, our body wouldn't really work all that well, so in those cases, we have substantial redundancy in all of the functions. And so that is where that figure in itself is not going to give you any explanation for pathology or for clinical effect.

So let's then look at Colten Snyder's case. He was identified as the third child in this particular paper, and the headline figure for him is 3.7 times 104 in CSF. The blood as we've already established was negative, although I have already

indicated why I found that surprising. And then in his ileal biopsy, we have a new type of report in this litigation that says greater than seven.

Now, scientifically, it's very hard to know what greater than seven means. I can understand what less than seven means in a particular instance. It means that it's below viral detection level. But greater than seven was a new form of reporting that Unigenetics came up with, and we asked on several occasions what does this mean. And we never received a proper answer to that particular question. It is still a mystery to me how you could get to greater than seven.

Now there is one potential explanation. That's the following: If you say I have less than one copy or less than 10 copies of GAPDH, so in my denominator, it is less than 10. Then if you divide your numerator by a denominator which is less than, then you get to a figure that is greater than. But if that's the case, you should say there is no RNA in this sample and I shouldn't report it at all.

And one of the most I must say difficult to understand examples I've had is where I have seen the report from Unigenetics where it blithely was reported zero copies of GAPDH, zero copies of measles F, where

the headline figure is zero copies of measles F per nanogram of RNA, which essentially makes no sense. The proper way of reporting that is say I have no RNA to write out all these layers because there was nothing in the samples.

THE COURT: So rather than per RNA, it should have been no RNA.

THE WITNESS: There was nothing.

THE COURT: There was no RNA?

THE WITNESS: There was no RNA, right. And so I think this is where I want to emphasize this particular point, because I think it is important to recognize the paucity of the data that we have here. We have only a headline figure for both Cedillo and for Colten Snyder, and essentially that could have been derived from zero, and five sum copies could be divided from zero and 50 copies divided by 10 copies of GAPDH, that's just a very small copy number of GAPDH.

So, with the absence of that data, it is very difficult for us to know exactly what this particular claim that there is measles virus in his CSF and therefore in his brain is actually based. It's based on a single sheet of paper that comes from a laboratory, which I've already indicated there are a

number of questions first of all about the calculation

methodology, secondly, about the fact that essentially we are in a position where not knowing what the GAPDH was and what normalization factors that have been applied actually allows us to interpret this headline data in any way, shape or form. That is where I think both cases in my opinion are based on evidence which is much less strong than I would have expected to see. That is a disappointment in this particular situation to me.

Now there's a third aspect of this that is relating to the Bradstreet paper, and that is that Dr. Bradstreet refers in the paper to the fact that there has been a demonstration of the nucleocapsid protein, not the RNA but the protein of measles in these cases, and in the paper, he refers to the paper, reference No. 25 by Andy Wakefield, and if you look at that particular reference, there are no data in it. There are only assertions that things have been found.

And what is surprising and astonishing to me that if such data would have been available that the claimants would not have presented them to me in the sense that I would have expected that if you based your claim that there is measles virus in the CSF and you state that these children have been shown to have nucleocapsid protein of measles virus in the tissues

that you then don't actually supply the data that would support that particular aspect of your claim.

So that is surprising to me, but it does highlight to me the rather weak basis on which these cases have been put in front of you, a basis which I think is much weaker than the ones that I have certainly seen in a number of the U.K. claimants' cases where all that data was available. And it is astonishing to me that that data hasn't been provided to us so we can make the proper interpretation of the data.

BY MS. BABCOCK:

Q Now, during his testimony on Tuesday, Dr. Kennedy discussed a gentleman named Professor Cotter?

A Yes.

Q Professor Cotter is also discussed in Stephen Bustin's report and I believe Professor Simmonds' report, and I know Steve Bustin discussed him during his testimony.

A Yes.

Q Who is Professor Cotter?

A Professor Cotter is a professor at one of the London colleges. I think it is The Barts and London Hospital, and he runs a diagnostic laboratory and uses Taqman RT PCRs. He was approached by the

claimants in the U.K. litigation to actually provide a backup and confirmation of the Taqman RT PCR data from the Unigenetics Lab.

Q And based upon your understanding of this specifically through Dr. Bustin's testimony and Professor Simmonds' report, what were Professor Cotter's experiences in attempting to replicate the Unigenetics work?

A Well, there were original problems, which have been identified and which were referred to by Dr. Kennedy, but at the end of the day, Professor Cotter was not able to confirm the data that were provided by Unigenetics. And both a number of Professor Simmonds' data -- let me go back. We had a long discussion in the U.K. case as to whether or not we should try to reproduce the actual data and do the testing again.

And at the end of the day, it came down to this deliberation that essentially none of us could. Having seen the quality of the data that Unigenetics had provided, having seen the sort of questions that we raised about them, we were not in a position to convince ourselves that it would be reasonable to subject the children to the rather invasive technologies of taking ileal biopsies and taking CSFs in order to simply provide ourselves with backup

testing material.

So the respondents never tested the children for the very simple reason that they could not see ethically that this would be the steps you take, although it might well have been a very quick and easy way out of the Court. And so we then had a later series of data, and this is the so-called E-series, which I refer to in my report, I think Steve Bustin refers to and Professor Simmons refers to as well where that actually was split, the samples were split over the respondents and the claimants.

And essentially Professor Simmons not having access to Taqman but having validation of the sensitivity of his techniques which was based on a nested RT PCR approach, and that is essentially why your PCR up was one set of primers, and then you take a set of primers further in and you PCR up again. A very, very tricky technique to perform without getting contamination, but all the data in Professor Simmonds' report indicate that he managed to do that.

And we went as far as I supplied him with a measles strain, a standard material strain which is extinct, which is no longer around so that we couldn't be confusing any sample of any results from his data that is currently circulating and those strains of

measles.

Now Professor Simmons was not able to replicate the data. He did nested PCR on the N gene and the H gene. The N gene would have been the choice for everyone who wanted to prove that measles is anywhere, because in an acute infection, measles N gene is present in about 30,000 copies per cell whereas F is almost seven or eight fold below, and so we end up in a situation where he tried with the best and most likely gene and he fails to find any samples positive, whereas Unigenetics reported some positive.

I can only say that Dr. Cotter, when he extracted his RNA in his own lab, he did not find any positive data. And there were two possibly borderline positives, and it turned out that those have been RNAs extracted from Unigenetics. So the conclusion that we drew from that was that the Cotter laboratory and the Simmons laboratory were not able to confirm the Unigenetics data, and they were indeed having some modestly weak data to show that contamination had occurred there.

Q At the end of Steve Bustin's testimony, we asked him to identify his top three biggest issues with Unigenetics, and I'll give you that opportunity in a minute, but first I wanted to just go through the

three things he picked out. He picked out that on at

least one occasion, the lab had forgotten to do the RT step and still got a positive result. Clear indication of contamination?

A (Nonverbal response.)

Q Can you say yes or no?

A Pardon?

Q You have to say yes or no, not nod for the purposes of the record.

A Yes.

Q Perfect. He also discussed his observation that there were instances where F gene results from frozen tissue and formalin-fixed tissue had similar CT counts, implying they were both amplifying at the same time. Does this make sense given the different types of tissue?

A No, it doesn't because it's much more difficult to extract RNA from fixed material.

Q And you discussed some of this today, but Steven also observed instances where the housekeeping gene GAPDH wasn't amplifying properly, but Unigenetics still used their results from the F gene?

A Yes.

Q And is it a problem?

A It is, yes.

Q Are these small issues or more substantial

significant ones?

A I think they are extremely substantial issues, and they in my mind indicate as I've already testified here today that the tests that were being done could not be relied upon. And I've indicated that in my report.

Q Do you think these problems were isolated or widespread?

A It's not difficult to find some of the problems that I've identified today. I'm not sure that I would agree with Steve Bustin's ranking in my mind.

Q And what are your top three?

A My top would be this. I cannot understand how you can do a replicate and have 34 copies, 2,400 copies in one and zero in another and then dare to declare that this 2,400 copies is the right figure. That is still my top. And if you look at that, and we might have to go back to this particular slide as well, that is still my top because it is so inconsistent with normal scientific procedure. Nobody does that.

I can only provide you with a statement which the Unigenetics Laboratory made, and that is that it felt that there were no false positives in

this testing regime. It was not possible to have a false positive. And so one ended up in a situation where if there was a positive, then that is in fact your belief, and I can only describe it as a belief because I cannot think that I have seen any test in my life that has no false positives in it.

If you believe that, then maybe you can make what I would consider a very serious error of saying 2,400 and zero, and we're ending up producing a figure of 2,400, not 1,200. What obviously would have been the best way to say is let's do it again. The opportunity existed. They extracted the RNA in 50 microliters. They used 5 microliters per sample, per test, so two replicates of GAPDH and two replicates of measles that they used up 20 microliters.

I would have said if I really wanted to know what that is, I expect another 20 microliters of this in order to make sure that I get it right, but that wasn't done. So that is still my number one.

The fact that they didn't use the N gene and didn't use an optimized assay is a second one. The enzyme that the used in their kits is called Tth enzyme. This is a combined reverse transcriptase DNA polymerase. Most of the other people use an optimized reverse transcriptase to get over the inefficiency of

that first step and then go in with a DNA polymerase, and most of those work quite well.

Using this particular enzyme, which is essentially working in the assay and under sub-optimal conditions for the reverse transcription step as well as sub-optimal conditions for the DNA polymerase step, that in my mind is an error of judgment to use an enzyme like that.

It has two consequences. Your sensitivity isn't as great as it should be, and that's why in any sort of comparative analysis, and I have been involved in a number of attempts like Dr. Oldstone to bring the O'Leary Lab into international comparisons of laboratories that could do measles testing in order to see whether their testing was much more successful or not, and the Kawashima Lab that has been referred to in some of the papers and some of the reports did participate. It turned out to be extremely incapable of detecting measles at, very low sensitivities.

And at the end of the day, I cannot know what the sensitivity of the Taqman RT PCR is, but it was done under suboptimal conditions for reverse transcriptionerase. So that is something that worries me. And I must say that had I been in their position, I would have worked much harder than they did on

trying to find a test that would look at the nucleocapsid genes for these factors that I've already indicated that in normal infections, there's about seven, eight times higher in terms of the copy numbers per cell than we had.

Q Now you've already stated, so I won't ask you this again, but you do not have confidence in Unigenetics' results in general?

A No, I don't, and I think it is that and it is inconsistency. I'm sorry that we didn't develop the last line completely. Maybe I can go to the printed version that you have, because it illustrates the sort of discussion and the sort of general lack of confidence that I have in the data that had been presented from the laboratory.

If you look at the final part of that, there's the following, that yes, 20 microliters was used for the GAPDH and the measles F determination. Samples were set aside for allelic discrimination assays. And what we see in the case of Dr. Bradstreet's paper for Sample No. 490 and 265 is that when the allelic discrimination tests were run a year later, both samples were negative in the CSF.

So this sample, which in one case had 6.1 times 106 copies had become negative as it was used in

the allelic discrimination test. And that's simply Packer's (ph) belief in a sense either you had lessons on the bench for a year, which is probably not what they're describing as standard operating procedure, or alternatively the data are completely destroyed.

So the data for this Child No. 2, and 1 and 2 in Dr. Bradstreet's paper are already essentially -- I have information in my report to indicate that there was no RNA in those CSFs. The only conclusion therefore I can come to is that the original figure was based on contamination in the original test run.

Q So is it fair to say that your conclusions about Unigenetics in general apply specifically to Colten Snyder and Michelle Cedillo?

A They do.

Q And based on your decades of experience and research in the field of measles virus and MMR vaccine specifically, do you have any belief that there's a link between MMR vaccine and autism spectrum disorder?

A I have no belief of that kind at all. I would say that it's not a matter of belief either. It's a matter of well-documented and well-evidenced research that indicates that that link doesn't exist.

Q And that opinion extends specifically to Colten Snyder?

A It does.

Q Now you alluded to this earlier, and I think we sort of hinted at it. There's other things that you've read and know about from the U.K. litigation that you cannot discuss here today?

A That's right.

Q And those items play into your opinion that the MMR vaccine cannot cause ASD?

A They do.

Q But nevertheless, you can reach your opinions here today without the benefit of that additional information?

A I think so. I think I've demonstrated to you why I have doubts about the quality of the data, the quality of the interpretations. I've also indicated to you that both in the Cedillo case and in this case, the case is brought on a single sheet of paper with a headline figure without supporting data and that there is no indication of any evidence having been provided on the presence of measles RNA protein in these samples either.

So I think it is rather flimsy evidence to go by, and I would have expected more in a sense from my experience in the U.K. There would have been other data that I would have liked to have seen before. I

would have wanted the interpretive data that had been provided.

Q And you hold these opinions to a reasonable degree of scientific certainty?

A Certainly.

MS. BABCOCK: I have no further questions.

THE COURT: I would suggest we take our midmorning break at this point then. By my watch, it's about 11:00. Could we reconvene at 11:15?

MR. POWERS: Thank you.

(Whereupon, a short recess was taken.)

THE COURT: We're back on the record then in the case of Colten Snyder. Are you prepared to cross-examine?

MR. POWERS: Yes, I am, Special Master. Thank you.

CROSS-EXAMINATION

BY MR. POWERS:

Q Good afternoon, Doctor.

A Good afternoon.

Q My name is Tom Powers. I know that you've been in the room for at least some of the testimony that you've heard here, but I haven't had a chance to introduce myself. Obviously, I'm one of the attorneys representing the Snyder family in this case and

representing Petitioners at large in the omnibus proceeding. I have a few questions for you, and I first want to go to your Slide No. 2 if you have that still available on your laptop?

A It's not my laptop. Can you switch it back on?

Q If it doesn't come on right away, it's not going to be particularly essential. I know that we have paper copies distributed, and I have just a couple of quick questions.

THE COURT: It's like we just hit the logoff issue. There we go. Okay. Now we just need to go back to Slide 2.

MR. POWERS: And this would be Slide 2. Okay. Now we don't really have to have it up there.

THE COURT: Okay. I have it in front of me, so if you want to go ahead, Mr. Powers, that's fine. We're getting close. There we go. One more. Okay.

BY MR. POWERS:

Q Just a couple of quick questions about this slide. The plotting that's done here, who did these plots?

A This is Professor Simmonds who did these plots.

Q And what data was Professor Simmonds using

to plot the graphs that we see here?

A He would have been using the same data as I would have been seeing.

Q And so the same data that you saw, and the data that he is using here, where did that data come from?

A It came from Unigenetics.

Q And are there any plots like this that you've introduced into evidence that Professor O'Leary or anybody else at Unigenetics did?

A No.

Q Now this plotting or the data that the plotting is based on, do you know whether this data was from any general samples that would have been used to set up assays versus actual patients that were being viewed?

A It would involve patients and controls, so in other words claimants and controls.

Q Claimants and controls. So none of this would have been for an assay as it's set up. And what's your basis for knowing that?

A My basis for knowing that is that I looked at the same data and I've seen the same results.

Q And this is the data that you referred to that is not available?

A (Nonverbal response.)

THE COURT: You nodded. Was that a yes?

THE WITNESS: Yes. Sorry. I mean in terms of I've seen data for about 300 claimants and children.

BY MR. POWERS:

Q So you've seen it, Professor Simmonds has seen it, but certainly none of the attorneys here have seen it and the Special Master hasn't seen it?

A No. But as far as my concerns, I can say that obviously this is the case of a normal experience that I had where essentially I had in my report interpretations of data that I've seen but I can't discuss with you.

Q Now you made mention of contamination, that you've identified contamination issues or claimed to have in the Unigenetics work. I didn't hear you describe contamination in terms of negative controls. Negative controls came up negative when they shouldn't have come up negative, isn't that correct?

A Not in all cases because as you correctly remember from Steven Bustin's report, there are certain indications that sometimes positives were ignored under these circumstances.

Q And that's based again on data that we don't

have available?

A Exactly.

THE COURT: I'm sorry. I didn't hear that.

THE WITNESS: Exactly, yes.

THE COURT: Okay.

THE WITNESS: I'll speak up. Okay.

BY MR. POWERS:

Q Actually, before moving off the slides, Slide 4, if you could turn to that, please?

A This one?

Q Yes, thanks. Now Slide 4 as I understand it, these graphs and these plots, and I should be clear, one is a plot and one is a graph of a standard curve?

A Yes.

Q The plot and the curve are not based on any data that was contained in the O'Leary work, nothing to do with any data or any samples or controls for this litigation, correct?

A I only used this particular curve in my report as well to indicate the problem that there is that a lot of extrapolation was being done and values were determined below the lowest point in the standard curve.

Q And this material is actually marketing

material from a company that sells PCR equipment.

A It is, yes. Yes.

Q I don't know if it's equipment or systems as they call it.

A It sells the kits to do it as well as the machine.

Q Right. And so the lines that they generate here are essentially self-serving. I mean, they're generating lines to say our curve is flatter than the other guy's curve.

A And the competitor, you're right, is not so flat.

Q So this is some marketing material that is illustrative only.

A Sure.

Q It doesn't reflect anything about the data in these cases?

A No. I only use it in order to illustrate a point and that point is made in my report as well that a lot of the data that are provided by Unigenetics involve extrapolations outside the range of standard curve.

Q I want to just for a quick moment here step away from the particulars of the testing methodology and PCR that you spent most of the morning talking

about. Do you believe that the presence of measles virus RNA after an exposure represents continued measles virus replication?

A That depends on under what circumstances you do the testing. We've already inferred that in certain instances, Diane Griffin's (ph) lab has been able to do PCRs and find it positive after 60 or 90 days depending on what particular set of patients you look at. If you do it under those circumstances, you don't actually know exactly what you have because the RNA itself is not that stable. For the virus to maintain a persistent state, it has to replicate. But you don't know whether you're looking at degraded bits of genome or whether there's still a whole replicating system.

Q Exactly. That's what I wanted to get to. So if you find measles virus RNA in a sample postexposure, it's possible that it would represent, I don't mean to use this in a particularly technical term, but an artifact of previous replication, it might not necessarily be replicating, is that right? If it's imbedded in the cell, it's just survived in a cell that has survived?

A Well, to an extent, yes, but it depends entirely on the circumstance that you're looking at.

In this particular case, she was looking at HIV positive children, and she found that it was longer than we normally have seen. But what she doesn't know --

Q Right. And just to make clear for the record, I think we're talking about the same thing. This is Dr. Griffin's 2001 paper on the HIV positive versus HIV negative children?

A That's right. Yes.

Q And I think that was in Cedillo. That was petitioners' Exhibit 112, Tab 1. So in that paper, she determined that through PCR, she identified RNA in the HIV positive children and concluded that 60, maybe even more than that days out, the virus was replicating in the system. The measles virus was replicating in the system of some of those HIV children.

A Yes. My expectation is that she has demonstrated that there is RNA there.

Q So the question is does the demonstration of RNA there, does that suggest that replication has taken place?

A It's a matter of some uncertainty as to how long RNA that is encapsulated in the nucleocapsid protein of the measles virus can survive without

replication, okay? But it is very unlikely that that is a very long period. And I must say that we have relatively few data that suggests to us how long long and not so long is.

It's very clear that RNA by itself as the naked RNA molecule is quite unstable. It is very quickly hydrolyzed by the hydroxyl groups that are present in the cell's water, and that breaks it down very rapidly. So in order for a virus to stay as an entity, a genetic entity that is capable of replicating itself, it is probably requiring constant replication over whatever, for days, maybe even weeks. I can't say that. We have not really got any data to give us an answer in that particular question.

So if you ask me is it necessary for a virus like measles to persist over eight years and that the average is the period between the manifestation of symptoms in SSPE and in the case of the acute infection, then replication must occur. It's not like DNA, which is a very stable molecule.

Q Right.

A But I don't know. If you ask me the specific question, I cannot tell you whether if you find RNA at Day 90 in an HIV positive child whether that means that there was replication until weeks ago

or days ago.

Q And if you had additional evidence in addition to the RNA and identify specific proteins, would that be helpful in determining whether replication had occurred? So if you found proteins that were further down the chain or beyond IV and moving down that chain of proteins, if you found those along with the RNA, would that bolster the case for persistence in that instance?

A It would be helpful, but I don't think that you could ever find that as conclusive evidence.

Q And even if not conclusive, if you did find that evidence, would that be through immunohistochemistry?

A You could do that by immunohistochemistry, yes.

Q And I heard you mention in your direct testimony earlier that the Uhlmann paper did not use immunohistochemistry?

A That's right.

Q I recall a passage in that paper that says that the results were confirmed by immunohistochemistry?

A That's right.

Q So it sounds as if they did do

immunohistochemistry to generate the results in the Uhlmann paper?

A They were not in the Uhlmann paper, and if you read my report, then you'll see that in my redacted report, I posed a large number of questions of the Unigenetics Lab, particularly because it was obviously there for the potential to be used later on in a hearing in the U.K. and to establish what had and what had not been done. And so the important element of that critique that I provided there was that if you confirm something, then please show it to me.

I mean, your case would have been stronger if you had protein data, but you don't have that except where we rely on the statement by Dr. Kennedy and we rely on Dr. Bradstreet's paper, which obviously included Colten Snyder for that particular confirmation. But I have never seen any data, and I have good reasons to doubt whether that was actually done properly, because Unigenetics is not a lab that uses immunocytochemistry.

A lot of the so-called confirmatory data that have been provided in this area come from Andy Wakefield, and in the earlier stories that he had about the link between measles or measles vaccines or measles and mumps with inflammatory bowel disease, he

did try to confirm it through immunocytochemistry. The first case, he used a --

Q Let me interrupt. I was just asking a simple question about whether in the Uhlmann paper they say that their results of PCR were confirmed by immunohistochemistry.

A Yes.

Q And my only question to you is whether you believe, yes or no, that that's a true statement in the Uhlmann paper? Did they in fact confirm their PCR results with immunohistochemistry?

A How could I know it? I've never seen any data. I've never seen any immunocytochemistry data from Uhlmann, from Unigenetics or from Andy Wakefield after the original set of immunocytochemistry data that were based on his theory about inflammatory bowel disease, which was then demonstrated to be wrong in the sense that there is a paper by Iizuka which shows that there is cross-reactivity of the antibody that they had with human antigens.

And secondly, in the first instance, and this is when I referred in my direct already to my collaboration with Andy Wakefield, he used a serum which was a serum generated in a mouse by infecting the mouse with an adenovirus that expressed the

measles nucleocapsid gene.

Q And that would be the N gene?

A The N gene, yes.

Q Now a question about the N gene. The N gene, is that the first gene that's produced in the replication cycle of the measles virus?

A It is, yes. Yes.

Q And a step first in that series?

A Yes.

Q And the N gene is the one that again you described it as being the highest count?

A Copy number, yes.

Q Highest copy number.

A Yes.

Q And that's why I just want to make sure when I say count and copy number, if we're using those terms, are we using the same terms? Does that work for you?

A I mean, I would prefer to use the word "copy number."

Q Copy number. So for the N gene then, that is the gene you would expect to have the highest copy number?

A That's right.

Q And you describe how in the work here they

weren't looking for the N gene, is that correct?

A That's right.

Q And that in fact they were looking for the F gene. In fact, that's what Slide 2 talks about, the search for the F gene.

A Yes.

Q Now the F gene is much further down the chain of genes that are involved for replicating measles virus, is that right?

A In transcription of the virus, yes.

Q In transcribing it. And then presumably the presence of F gene would indicate that the sequencing that preceded the F gene, involving N and everything else in between, if you found the F, that would indicate that everything preceding it was there, is that correct?

A If you had done the proper tests, and obviously I don't believe that the tests were done properly.

Q I'm just talking about the goal.

A But the goal, yes. I mean, that would have been the normal expectation, yes.

Q Right. And then presumably one might do that to establish or at least make a stronger case for replication so that if you have the F gene, you might

be able to make the argument at least as a goal that replication had been taking place in those locations where you found RNA. Does that make sense as a goal approach in a study like this? Looking for the F rather than N if you're looking to find replication? Does that make sense?

A No, it doesn't. I'll tell you why. If you first of all wish to establish whether there is measles in a particular sample, you're not immediately concerned whether the question whether it's replicating or if it's transcribing or how active, how much is there, but you also have to give yourself the best chance of finding that particular virus. Then you would go for the N gene. And the Unigenetics people tried to get results for N, F and H.

Essentially what they then found was that somehow they were not able to establish a good N gene assay. Clearly they would have liked to have seen the confirmation that all these RNAs would have been there. So if you try in the first instance to say well, is it there or not, then you must go for the N gene. You must work very hard to get there. The secondary goal is in terms of looking at whether there's replication or transcription or replication without transcription. That's impossible.

Whether you have transcription without replication, that would all be reasonable to say now I'm starting to look at the other genes. But to take that particular gene as the first target would not be a sensible approach to my mind, and so I know that they tried and they failed.

Q And your knowledge is based again on documents that we don't have available here?

A Let me think. I would have to check. I'm not sure whether the Uhlmann paper makes a reference to the fact that they tried the other genes, but because as you know, the Uhlmann paper also dealt with the solution phase RT PCR, and the fact that they had tried to use priors for the N, the F and the H, and as you know, the Uhlmann paper itself has a list of N, F and H primers.

Q Now you talked towards the end of your testimony about a meeting that happened where a group of people discussed whether they wanted to proceed with taking new samples from children and running tests on those samples to see if the results could be replicated. Do you remember that discussion?

A Yes.

Q And you reported that the upshot of that group's decision was to not go forward with doing

that, and you described the reasons for that. I just want to learn a little bit more about that meeting. That meeting was a group of people that were representing the defendants?

A Sorry. I might have given the wrong impression about the meeting. At some stage, the legal teams asked us is there any value in asking for samples of these children in order to establish whether the Unigenetics data are correct or can we do something.

Q And so I'm really careful here, the legal team that you're describing, you used the word plural, but these weren't legal teams from both sides of the case. This was the legal team that was representing the pharmaceutical companies?

A The respondents, right.

Q So the direction to have this meeting was not by joint agreement of the parties, but the defendant pharmaceutical companies directed you all to have the meeting. Is that fair so far?

A What they asked us was the following question.

Q I just want to establish who the "they" is. Am I correct in saying that the "they" who directed you to have this meeting --

A The people who would be representing the respondents in Court, the barristers asked us.

Q Okay. That's all I was trying to establish. So those are the people that called the meeting?

A Now they didn't call the meeting.

Q Who comes to mind?

A They asked a question, and I said I'm sorry if I misled you about there having been a meeting. The situation was that a number of us were asked by correspondence do you think it's worth testing the children, and then all of us came to the same conclusion that this was not the way forward.

Q And when you say all of us, these would be all retained experts --

A That would be --

Q Let me finish the question, please.

A Sorry.

Q These would all be paid and retained experts exclusively on the side of the pharmaceutical respondents?

A They were.

Q And you all in those discussions, or it sounds like there was some consideration given to the children. Did anybody from your side ever contact the families or the people who were responsible for the

children to get their opinion on whether testing would have been appropriate and whether they would have been willing to undergo that?

A I think those are matters that I cannot discuss.

Q And you cannot discuss these matters because of a seal or confidentiality order imposed?

A There's a confidentiality order on a number of the discussions that obviously we had.

MR. POWERS: I have no further questions. And Special Master, I think, I mean, we've all stated this on the record. We discussed it and it's come up a couple of times. We will be asking for leave to file a supplemental report here in response to some of the information that's been presented, presuming that we can get a hold of some of this underlying documentation from the United Kingdom litigation.

THE COURT: Let me deal with the second part of that first. Are you going to request unsealing of the British litigation, of additional portions of the British litigation?

MR. POWERS: Yes, we are, Special Master.

THE COURT: And when are you going to do that?

MR. POWERS: That process has begun. We

have inquiries to the court in the U.K. and we are initiating that, that proceeding.

THE COURT: Okay. Again, I'm going to ask when, because you were invited, in fact encouraged, in fact all three Special Masters dealing with this litigation in Court said we would join with you back five months ago to get the complete data. We've had five months and it appears that the Petitioners have sat on their hands. So when?

MR. POWERS: I just honestly don't know what the timeline is. I know that in the U.K. system, I mean, it's taken weeks literally just to get a copy of the order.

THE COURT: A copy of which order?

MR. POWERS: The confidentiality order. They don't just send it over. I honestly don't know and cannot represent to you today how long that process will take.

THE COURT: Well, I'm discouraged from the testimony of Dr. Kennedy, who told me that he had not been asked to request disclosure of his report prior to his testimony here in this case from me. The whole discussion of this prior to the start of the Cedillo trial is Mr. Matanoski described the process the government went through to get records unsealed, that

they approached their expert witnesses and asked them to join in the request to unseal that testimony and that the Petitioners have not taken that step.

This is concerning to me because we would like to get a speedy resolution of not only Colten's case and Michelle Cedillo's case and Yates Hazlehurst's case but all of these cases.

MR. POWERS: Understood.

THE COURT: So, while I'm putting you on notice that you've got to move on this, we're not going to tolerate sitting on our hands.

MR. POWERS: Understood.

THE COURT: Okay. You have no other questions for this witness?

MR. POWERS: No other questions for this witness, no, Special Master.

THE COURT: Okay. I have a few, Dr. Rima. Let me ask this question this way. You heard Dr. Kennedy's testimony about Dr. O'Leary's current activities. That is, he's recently published several articles involving RT PCR. I think Dr. Logan is the lead author on those articles. And you've heard that he was recently awarded the St. Luke's Medal by the Royal Academy of Medicine and St. Luke's Hospital and that he is the chair of pathology at Trinity College,

Dublin.

Publications, awards, university chairs don't seem to square to me with the picture you've painted of what happened in the Unigenetics O'Leary Lab. Can you shed any light for this on me?

THE WITNESS: I am not on the award panels that have made these awards. I have not been asked to be an external examiner or a person on the Trinity College appointment panel. So, of course, that particular appointment took place well before Unigenetics started to work, because he was appointed quite a long time ago to his professorship.

THE COURT: The chairmanship?

THE WITNESS: The chairmanship.

THE COURT: Okay.

THE WITNESS: So I have no observations to make. If I was on the St. Luke's award panel, then I could tell you on what basis they made that decision.

THE COURT: Okay. Well, let me phrase the question this way. We've heard that contamination is not unusual in labs doing PCR, is that correct?

THE WITNESS: It is correct, and I certainly have experienced it myself, as I identified in my report.

THE COURT: Can you square the problems in

the O'Leary lab that you discussed and Dr. Simmonds and Dr. Bustin have discussed in testimony and reports with mere contamination or mere carelessness?

THE WITNESS: What I provided evidence of is carelessness in certain instances. I provided you this morning with evidence where I found some practices are unacceptable as a scientist. And that's all I can say.

THE COURT: I think that answers my question, Dr. Rima. At the time Colten's samples or Michelle Cedillo's samples were sent to the O'Leary Lab, were there other labs doing PCR of cerebrospinal fluid, whole blood for a measles virus or was this the only lab doing it at the time?

THE WITNESS: It was the only lab. Let me explain this. I mean, if the technology had been validated, then Dr. O'Leary would have found me and Oldstone and several other people interested in measles virus at his door saying, can you help us resolve issues about not only this disease. I can give you other diseases where there is a question about the formation of measles virus in -- disease, in otosclerosis. And I'm involved in several of these instances where people are struggling to try to find a link or an etiology for a disease which has no known

etiology.

And so, if indeed that technology had been validated, if that indeed had been the circumstance, a lot of people would have knocked on O'Leary's lab and said you can do something which we can't do. And there would have been a flood of people coming to him independent of the litigation of some.

But that flood hasn't taken place for the very simple reason that everyone who has looked at it said, no, actually, this technology does not work. What he claims he can do he cannot do. What he claims, he simply has not been able to give us the sort of confidence in his technology that would allow us to start looking at it from a research perspective. That's a research perspective. That is a very different perspective even from the perspective of a diagnostic lab that is going to test children for pathological conditions that there are.

So I would have said I would have been the first at his door. I mean, he is only 100 miles down the line from me and it would have been great. I'd like to work with this person. But it was clear that the company that was set up by Unigenetics had only one trading activity and that was to test measles presence in samples from the litigants in the U.K.

And so essentially when people started to look at it and when experts came in, measles experts came into the field, we tried to get as many people involved. On both sides, attempts were made to involve people. We came quickly to the conclusion that some of the practices that I described here, some of the sloppiness, some of the inconsistencies in the data were there and they led us to the conclusion that this simply does not work.

THE COURT: You've characterized the reports of measles virus in Colten s headline reports.

THE WITNESS: Yes.

THE COURT: And in the ordinary course of my work, I rely on headline reports. I mean, I don't ask the lab at whatever institution has tested blood for the presence of whatever we might be looking for, a virus, a bacteria, whatever might be at issue in our case. I mean, I look at headline reports routinely. As I understand what you just told me, it is the nature of or the purpose for which this lab was established as well as the practices of the lab that leads you to question the reliability of the results in Colten's case?

THE WITNESS: Yes.

THE COURT: And that you would not routinely question a headline report.

THE WITNESS: Well, I'm obviously not in your position and so I don't know what I would question. I mean, I'm a scientist. I question everything that comes on my desk and --

THE COURT: Okay.

THE WITNESS: -- in the first instance do not believe it until I'm convinced that I can. And in that sense, it was clear experience that we had once we started to look at that. It was clear that we couldn't rely on what was made available to us.

But why I call it a headline is because that is based on two figures, a numerator and a denominator, which could be both small and both -- and multiply up, one small figure divided by an even smaller figure gives you quite a large figure, leads to a completely and utterly biologically implausible situation where as I said, if you come forward with a situation where you have two times 10 to the second copies per nanogram, that means that that whole cell is stuffed with measles F messenger RNA, let alone the fact that Mr. Powers has already indicated that actually it also had N and P and H and L as well. And so essentially what we are seeing is something that is

biologically, that's all I'll say, implausible.

A cell normally has about 200,000 copies of message. So, if you say to me that this sample contains two times 10 to the second per nanogram, that is 200,000 copies of measles F. There is no space, no availability for the housekeeping gene that needs to be there, for the other genes of measles that need to be there. So it is simply impossible to have these figures. And that is where when figures like that came out in the Uhlmann paper, I said this is nonsense.

THE COURT: So, when you say "these figures," you're referring to the figures in some the papers and in some of the data you have seen and the graphs.

THE WITNESS: That's right. And I gave you the example of the Uhlmann paper and the Bradstreet paper where figures like that became very implausible.

THE COURT: But in Colten's specific case, are the figures beyond plausibility?

THE WITNESS: Well, he has 34,000 copies per nanogram of RNA in his CSF. If I calculate that on a cellular basis, and I have already indicated why I do that, because I have no indication that free virus is there, if we do that, then he has about 3,400 copies

of measles F per cell.

THE COURT: Of the 200,000 that are available in the cell?

THE WITNESS: Of the 200,000, yes. In order to put that in context, I refer you to the fact that there's a paper by Catanial (ph), which is in my report which actually has measured copy numbers by other technologies than Taqman, and they come to a conclusion that in circumstances where I take my best virus, the lab adapted Edmonston strains, which grow much better than the wild type, in vero cells, which is a cell that has no innate immunity and therefore is capable of allowing the replication of a virus to occur, in those conditions, I can get up to about 4,000 copies of measles F.

THE COURT: So we have a factor of seven?

THE WITNESS: No, we have 3,400 in Colten Snyder. I had 4,000 in my best case of growing. So I would say if that's the case, we have no difficulty in saying take those cells, grow up the virus and look at immunocytochemistry, because this would be analogous to my best, to what I could grow best in the cell.

THE COURT: Okay. So this is just too high?

THE WITNESS: Too high.

THE COURT: Too high to be believed?

THE WITNESS: Indeed.

THE COURT: Okay. Questions?

MS. BABCOCK: A few.

REDIRECT EXAMINATION

BY MS. BABCOCK:

Q Dr. Rima, to your knowledge, have any of Professor O'Leary's recent publications or awards dealt with his measles PCR research?

A No, they haven't. They have done some publications on DNA viruses, which I've already indicated PCR is extremely sensitive and there is no question that you can pick up one copy. And the latest paper has dealt with the diagnosis of a number of viruses in stools of patients, and these viruses are present in immense copy numbers in the stools. These are noroviruses and also viruses where essentially you have 10 to the 11th, 10 to the 12th copies of free virus in the stools. And therefore, it is not surprising that you can use this technology to make that diagnosis.

THE COURT: Just a second. By "free virus," you mean not present in a cell?

THE WITNESS: Not replicating, simply "free virus."

THE COURT: Okay.

THE WITNESS: If you look at stool samples

of patients with that type of diarrhea, you only see virus practically. It's very infectious, as all of us know who go on cruises on the wrong ship.

THE COURT: Just ensuring I understood the distinction between free virus and cellular virus.

THE WITNESS: Yes.

THE COURT: Okay. Go ahead.

BY MS. BABCOCK:

Q Now there was some discussion on cross of the meeting that you mentioned on direct, and you sort of cut it off because your really didn't want to go into much more detail. But am I correct, on your direct examination, in talking about this inquiry into whether you were going to try and replicate the tests on the claimants themselves that part of the reason, a big part of the reason was because you didn't think it was medically or ethically justified?

A Uh-huh.

Q That's correct. And that was already your testimony here today?

A Well, it is also I think I don't know to what extent it was part of the record, but a number of CSF samples were sought after because the claimants then wished to start to find evidence for their conjecture that there was direct brain infection. And

so similar to the U.S. cases where CSF samples were available, they were not in the original cases in the U.K. And essentially people having looked at that found that no laboratory in the U.K. was willing to take CSF samples from these children because they did not feel that there was sufficient ethical background to validate or to justify taking those samples. And the children had to travel to the U.S., and I don't know where the sample was taken.

Q Now Mr. Powers also asked you about the immunohistochemistry in Uhlmann, and I wanted to make sure, is there anything else you wanted to add about why you're not confident in the immunohistochemistry done here?

A Well, I mean, the Bradstreet paper is sort of referring to the fact that there might be immunocytochemistry done, but --

Q And let me be clear, it sounds sort of like immunohistochemistry and immunocytochemistry are interchangeable?

A They're the same.

Q Okay.

A So, no, it hasn't been done. And it's surprising to me. This is why I come back to the question of the headline figure being the only thing

available. If you had data on the presence of measles protein being in the CSF of these children, then I think it should have been presented to courts.

Q Now your report and your testimony today accurately summarize your concerns about Unigenetics, correct?

A Uh-huh.

THE COURT: And that was a yes?

THE WITNESS: Yes, sorry.

THE COURT: Okay.

MS. BABCOCK: Thank you. Sorry.

THE WITNESS: I'm sorry. I'm learning slowly.

BY MS. BABCOCK:

Q And this additional data that keeps getting referenced and that you can't talk about, this just provides more support for your opinions?

A On the basis of my redacted report, I hope to convince the Court that there were a number of questions about practices, consistency of the data and questions of contamination, et cetera, that would say to me there is a question about the quality of the material that has been provided in addition to the fact that there is not the sort of background information that we have seen available to us from the

other claimants in the U.K. That would have specified the cycle number for GAPDH in that run, what the standards were doing in that run, what the standards for measles F were doing on that plate where the sample was, how many positives were there on that particular plate on that particular day, and the actual copy numbers, which would have given rise to the headline figure.

So this is where I think first of all I question the plausibility of these figures. Secondly, I then question the basis on which that figure has been derived. I think I simply don't have the data. Part of being a scientist is trying to get confidence in the tests that are being presented to you, and all I have been able to say is that I from my experience in that U.K. litigation without having to disclose any confidential data say that I have no confidence in what I saw, and therefore, I said that by extension, I simply cannot take on good faith value the data that we have seen in the cases of Cedillo and Colten Snyder.

MS. BABCOCK: I have no further questions.

MR. POWERS: Just one quick one to follow up on there.

THE COURT: Certainly.

RECROSS-EXAMINATION

BY MR. POWERS:

Q Based on what Ms. Babcock was describing, again without commenting specifically on content, is it your testimony that Dr. Cotter, without revealing any details of his report, is it your opinion that Dr. Cotter failed to replicate the work of the Unigenetics Lab?

A It is. And that is well-documented in Professor Simmons' redacted report as well as in Professor Bustin's report.

(Witness excused.)

THE COURT: All right. It appears that we are ready for our lunch recess, and by my watch, it's a little after 12, so let's reconvene at about five after 1.

(Whereupon, the hearing in the above-entitled matter was recessed, to reconvene at 1:05 p.m. this same day, Thursday, November 8, 2007.)

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A F T E R N O O N S E S S I O N

(1:10 p.m.)

THE COURT: We are back on the record in the case of Snyder v. Secretary of HHS. I see Dr. Ward advancing toward the witness chair, so apparently he's your next witness.

MS. BABCOCK: No need for Respondent to do it.

(Laughter.)

THE COURT: All right. Would you raise your right hand, Dr. Ward?

Whereupon,

BRIAN WARD, MD

having been duly sworn, was called as a witness and was examined and testified as follows:

THE COURT: All right. You may proceed, Ms. Babcock.

DIRECT EXAMINATION

BY MS. BABCOCK:

Q Dr. Ward, could you please state and spell your name for the record?

A I'm Brian Ward, W-A-R-D.

Q And Brian with an I?

A B--R-I-A-N, yes.

Q Okay. And you testified during the Cedillo

trial, correct?

A I did.

Q So we're not going to go through any extensive rediscussion of your qualifications, but could you just tell the Court where you are currently employed?

A I'm currently at McGill University in the Divisions of Infectious Diseases and Microbiology.

Q And you've also published and studied the measles virus?

A I have.

Q Including book chapters, articles?

A Yes.

Q And have you also seen patients with measles virus infections?

A Yes, many.

Q About how many do you estimate over the course of your medical career?

A I haven't kept notches on my belt, but probably many hundreds, perhaps low thousands.

Q What materials did you review in preparation for your testimony today?

A I reviewed the medical records that were sent to me, the expert opinions that were sent to me and resorted to the medical literature when necessary.

Q And you've of course also reviewed the medical records and materials in Cedillo?

A Yes.

Q And I should say as Mr. Powers did earlier, do you incorporate your opinion in Cedillo by reference in this testimony as well?

A Yes, of course.

Q And therefore, we're going to attempt not to replicate that testimony again. But here in this case, again, there's been some effort to use SSPE and MIBE as models for Colten Snyder. I even think at one point in Colten's medical records, they were working him up for SSPE. What is the clinical picture of someone with SSPE?

A Well, as Dr. Rima said, the most common clinical picture is a period of confusing clinical presentation, typically at least five to seven years after wild-type measles, and often a diagnosis is not immediately entertained. But after a period of progressive clinical deterioration, then somebody thinks of the diagnosis and the diagnosis is made. And so far the individuals with SSPE progress and actually lead to death.

Q And is there inflammation in the brains of people with SSPE?

A Well, there's surprisingly little inflammation. That's one of the things that people don't really understand why there is so little inflammation in the brains of these individuals. But it's not extensive inflammation that you would see from an acute viral encephalitis or bacterial meningitis, for example.

Q Now ADEM or PIEM, can they be associated with measles virus?

A Yes. They are also reported to occur after wild-type measles virus and may very rarely occur following vaccine exposures.

Q Is Colten Snyder's clinical picture consistent with ADEM?

A Not at all.

Q Now Dr. Kinsbourne discussed a 2004 editorial by Paul Dyken discussing a condition called MINE, which I believe is measles-induced neuroautistic encephalopathy. It's a paper that was actually introduced on the last day of the Cedillo trial, actually during Diane Griffin's cross if I recall, and hadn't been previously referenced by any of the experts. Do you think this theory as offered in the editorial by Dr. Dyken is scientifically sound?

A No. It's quite an amusing acronym because

it's sort of laying claim to an acronym that seems quite possessive. But in this particular instance, it seems that Dr. Dyken simply took articles that were in the literature in a completely noncritical way and said, well, if this is true and this is true and this is true, then there might be this new thing that I'm going to call MINE. And it was only subsequent to that publication, which was in a fairly obscure medical journal, that many of the problems with the hypothesis became apparent, and Dr. Dyken hasn't said anything else about this since then.

Q And sort of following up on that, to your own knowledge, was this editorial written before information came out in the U.K. MMR litigation that caused funding to be withdrawn?

A Yes, it was. I'm not sure. I don't recall when it was submitted, but it was certainly published prior to the suspension of the U.K. litigation.

Q Now, switching topics, is IVIG a treatment commonly used for wild measles virus infection?

A Almost never except in the very unusual circumstance of a baby, a newborn baby, who is exposed to a mother who develops measles either in the last few days of the pregnancy or in the first weeks to months after delivery of the child. And the reason

that it's used in those circumstances is because the maternal antibody generally protects the child during the first four to eight months of life, and if the mother develops acute measles, then she obviously could not have transmitted any of those protective antibodies to her child.

Also, the mother is in close contact with the baby and so there is a virtual certainty of transmission to the child. In that case, IVIG is occasionally used to give the baby a better chance, because the mortality from natural disease is very, very high in very young infants.

Q So when it's used there, does IVIG contain measles neutralizing antibodies?

A Yes, it does. In North America and I think also in Europe but certainly for North America, the FDA requires that IVIG formulations of different lots have a minimal amount of antibodies directed against common childhood exanthems.

Q Do these levels fluctuate depending on the batch or source of the IVIG?

A Oh, absolutely. That's why the FDA made that requirement of minimal amounts, because people were using these products assuming that they all have lots of measles or varicella or other antibodies. And

when it was discovered that in fact they didn't, in some cases, some lots had very low measles antibodies, the FDA required that there be a certain minimal level. But there's wide variability above that minimal level so that some lots have much more anti-measles antibodies than other lots.

Q So, because of that, if you were using IVIG to treat a purportedly persistent measles virus infection, would it be important to take titer levels before you administer the IVIG?

A Sure. Well if you've got a choice of lots. It would be I would think a very reasonable precaution to take to use the lot that had the highest titers and make sure that you had enough of it to treat the individual for a period of time. Basically buy as much of it as you thought you would need.

Q Now is IVIG ever used to treat MIBE?

A No, because most people don't believe that that's an active measles -- oh, measles inclusion body encephalitis, yes, sorry. Yes, rarely. Not really. In the case of individuals with MIBE, they might actually use it as a temporizing measure to see if they could actually protect the individual for a long enough period of time for their immune system to come back.

Q And even with the use of IVIG, what is the usual course for someone with MIBE?

A Well, most individuals with MIBE will die. And IVIG can temporize for a while and if the immunosuppression that allowed them to be susceptible to that manifestation cannot be reversed, then even in the presence of IVIG, the most likely outcome is that they will probably die as well.

Q Is there evidence that wild-type measles virus actually cures some autoimmune diseases?

A Yes, that's one of the sort of interesting little things about measles is that there's limited but some quite consistent literature of children who have well-defined autoimmune conditions prior to the development of wild-type measles, and then after wild-type measles, the disease is either suppressed for a long period of time or goes away. They're permanently cured.

Q Now, in his original opinion, and I realize he's been put forth as the treating doctor, not as an official expert, but certainly he wrote several expert opinions. Dr. Bradstreet cites to Dr. Singh, several papers by Dr. Singh. We certainly know that Dr. Singh gave some testimony on Colten Snyder here. Are the tests that Dr. Singh did on Colten Snyder consistent

with what you understand Petitioners theory to be in this case?

A Well, I said many times that I'm often not really sure what the Petitioners' theories are. There seem to be many of them in Dr. Bradstreet's written statements. But if the simplified position is that you have a persisting measles virus infection that somehow causes autistic spectrum disorder, then I don't see any support for this hypothesis in Dr. Singh's work or in Dr. Bradstreet's arguments.

Q Did Dr. Singh test Colten's CSF for measles virus antibodies?

A Yes, he did.

Q And what were the results?

A That result was negative.

Q Now Dr. Bradstreet's explanation for the negative tests is that Colten received IVIG treatment not long before the sample was drawn. Is this explanation persuasive to you?

A Well, not at all, because the half-life of antibodies is typically stated to be four weeks and certainly if they're made by the individual. And so if you are making antibodies, you wouldn't expect them just to disappear. The mother gives a child IgG just prior to delivery, and those antibodies last typically

eight to nine months. And so, if Colten had antibodies in his brain, in his CSF rather, one wouldn't expect them simply to turn on or off like a switch with IVIG administration.

Q Now Dr. Kinsbourne cited to work by Dr. Pardo particularly on page 17 of his report. And in the middle there, he discusses it as evidence that some scientists may believe that environmental toxins or infections in the presence of genetic susceptibility can lead to neuroinflammation and autism. Is Dr. Pardo's laboratory actively studying potential environmental causes of autism?

A Yes.

Q And are Dr. Pardo or his colleague, I believe Dr. Swado (ph), considering the MMR vaccine or measles virus in their research?

A No, they're not. They're not testing for measles virus.

Q Now is the theory being proposed here that measles virus persists in the human and eventually results in autism consistent with any condition associated with wild or vaccine strain measles virus?

A Sorry. Could you repeat the question?

Q The theory being proposed here that measles virus persists in the system and eventually results in

autism consistent with any condition associated with wild or vaccine strain measles?

A Not that I'm aware of. To my knowledge, there's no convincing evidence whatsoever that exposure to wild-type measles is associated with autism at all. Given the number of children who experience wild-type measles in the world still half a million cases, and certainly it's assumed that virtually everybody in the world prior to the introduction of the vaccine experienced wild-type disease, the silence in the medical literature on any association between wild-type measles and autism is striking.

It's not an association that would have been missed because wild-type measles came in waves, and normally, for example, the east coast of the U.S. had an outbreak of measles with thousands of cases in the 1990s. The eastern province of Canada had a similar outbreak at that time. Many children were infected with measles in a relatively short period of time, and there wasn't a sudden burst in autism in either Canada or the States following those very well-defined outbreaks of measles in societies that certainly had the tools to do surveillance for things like autism.

Q Now moving on to the Unigenetics testing,

and again, you testified about a lot of this in Cedillo. We're not going to duplicate that here. But talking about Colten Snyder specifically, I believe that even Petitioners' experts concede that at best, Colten Snyder's gut biopsy is borderline positive, or I think Dr. Kennedy actually stated he wouldn't have confidence that measles virus was actually in Colten's gut. Do you agree?

A Well, I mean, I think with what Dr. Rima just explained to the Court, it's impossible to have confidence in either of those results because it's entirely plausible that the very high titers that one saw in what were reported in the CSF were simply the result of very, very low copy numbers that were then multiplied enormously by a very low GAPDH copy number value. So I would say that if Dr. Kennedy has difficulty believing the gut results, I would hope that after the testimony of Dr. Rima, he has a similar level of concerns about the CSF reported values.

Q Now Dr. Rima talked about this this morning, that with the positive, markedly positive, what were reported to very highly positive CSF and negative whole blood results, there might be a logical inconsistency there. Do you agree?

A Sure. Measles is essentially a completely

cell-associated virus. There is very little evidence of virus living outside of the cells. Obviously, it has to move from cell to cell at some point, but it does that with enormous efficiency, almost frightening efficiency. And so a virus that's released by a cell breaking would enter into another cell essentially instantaneously. And so, when people have looked to isolate virus from, for example, blood, you can't isolate the virus from the plasma. You can only isolate the virus from the cells.

In an individual with some degree of neuroinflammation or even without any inflammation, the only cells that are floating around in the cerebrospinal fluid are the lymphoid cells, the white blood cells, and, yes, those are the same white blood cells that are in the blood. So, if you have extremely high copy numbers in the white blood cells in the brain, it is completely logically inconsistent that you would not see those have the same virus in the white blood cells in the peripheral circulation.

Q Now is it accurate to say that PCR can be useful as a diagnostic tool and a research tool?

A Sure.

Q What was Unigenetics using its testing for in this circumstance?

A Well, I think quite clearly they were using it as a diagnostic tool. They were reporting results that were specific to an individual child.

Q When you're using something as a diagnostic tool, what's an acceptable rate of false positives?

A Well, I could turn that question around to the Court, but really if it's me being diagnosed with a serious condition, I'd like it to be as close to 100 percent sensitive and specific as possible. Very few tests actually achieve that rate of sensitivity and specificity, but all competent labs strive to make their tests that sensitive and that specific. And some of them come remarkably close.

I think if you imagine if a test gave out 10 percent false positive results, on the one hand, you'd say, well, gosh, they got it right 90 percent of the time. But, on the other hand, if that test is HIV and it's you, that's a completely unacceptable rate of false positives, because one in ten individuals would be falsely informed that they have HIV, for example.

Q Have you recently had occasion to speak with Michael Oldstone about Unigenetics?

A Well, yes, I did with some fear and trepidation in fact, because as a graduate student and also as a postdoctoral fellow working in Diane

Griffin's lab, I had occasion to witness Michael Oldstone taking apart a fellow trainee in a session in Philadelphia in fact. And I came out of the session and asked in a loud whisper, is Michael Oldstone always such a blank, deleted for the purposes of the transcript, and it turned out my friend went like this and he was standing right behind the door.

So he has quite a reputation for remembering things like that and taking people's heads off. So I was a little hesitant to call him, but I decided to call him and ask because I thought he might be interested in knowing the extent to which some of the experts in the Snyder case were using his work to support their hypothesis.

Q And I believe it's been noted it was also used quite extensively in Cedillo, correct?

A It was used extensively in Cedillo. So I plucked up my courage and I was both reassured and a little humbled by the fact that of course he'd completely forgotten who I was. And so my comment after the meeting was I guess not very memorable for him. It was memorable for me. But I asked him if he was aware of how his data was being used and I thought misinterpreted. And then he told me about his interaction with Dr. O'Leary and Wakefield in the

early 2000s.

Q I guess you should maybe even explain what exactly happened.

A Well, I only know what Dr. Wakefield told me over the phone, which was --

Q Dr. Oldstone?

A Sorry, Dr. Oldstone.

Q You said Dr. Wakefield.

A Oh, right. Dr. Oldstone, sorry. I only know what he told me over the phone. I took notes during the meeting, during the telephone conversation. And essentially he was approached by a politician, a California politician, Mr. Rollins I believe, who was associated with the MIND Institute, and at the behest of Andrew Wakefield, they wanted to encourage Dr. Oldstone to work with Drs. O'Leary and Wakefield to assess the hypothesis of the persistence of measles virus in individuals with autistic spectrum disorder.

Q So was this testing funded by the MIND Institute?

A Yes. What Dr. Oldstone said was probably what all researchers say: if you want me to do something, can you fund me to do this. And what he asked specifically was for funding for a postdoctoral fellow to work in his lab for a period of time to

prepare samples and send them to Dr. O'Leary's laboratory in a coded, blended fashion.

Q What were the results of this exercise?

A Again, according to Dr. Oldstone, a number of samples were prepared from different tissues and also different in vitro infected cell lines so that uninfected cell lines and uninfected tissues -- the tissues that were used here were from -- transgenic mouse model where he put the gene for one of the receptors for the virus into a mouse so he could infect some tissues in the mouse. And so he was able to send, for example, some gut tissue, some brain tissue.

But he used measles virus to infect some of the mouse tissues and some of the in vitro cell cultures at different levels of infection, and these blinded samples were sent to Dr. O'Leary's lab. And then both Dr. O'Leary and Dr. Oldstone together unblinded the set of specimens to find out how well the O'Leary Lab had done.

Q And how well had they done?

A About 80 percent accuracy. About 80 percent of the samples were correctly identified as being either positive or negative, but about 10 percent were found to be false positive, so there was no virus

present, but O'Leary Lab reported that there was. And others which had virus, in some cases high titer virus, were reported as negative. Dr. Oldstone's recollection was that it was 50-50. About half of the incorrectly classified samples were false positive and the other half were false negative.

Q Now, as a scientist and someone who performs PCR, is this an acceptable rate? Is 20 percent acceptable in doing testing for the purposes Unigenetics was doing it?

A Well, it's not even acceptable in a research lab. If one had an assay that was giving you both false positives and false negatives, you'd fix the assay as opposed to continuing to do research with it, because you're going to have a guaranteed 20 percent inaccuracy in whatever you're doing. It's wildly inappropriate for a diagnostic lab, any lab, let me rephrase that if the only test availbale to you is this test.

Then under certain circumstances, you could justify doing that test. But the results of that test that were only 80 percent accurate would have to be sent out with a big red warning saying be aware that this test is wrong 20 percent of the time. And then the clinicians can make a decision based on what

they're getting and based on the reliability of the assay. Of course, that was never done by the O'Leary Lab.

Q Did Dr. Oldstone try to publish the results?

A Well, actually the story wasn't finished, because after the first round of testing, Dr. Oldstone and Dr. O'Leary, neither of them was happy. And so according to Dr. Oldstone, there was an agreement again between the two them that they should do it again, that Dr. O'Leary was going to try to make the assays work better. And so another set of samples was prepared by the postdoctoral fellow. Again, they were sent to Dr. O'Leary's laboratory. And again, the results were jointly unblinded by Dr. O'Leary and Dr. Oldstone, and once again, the samples were found to be only about 80 percent accurately diagnosed. And again, there was about 50-50 false positive and false negative.

If this wasn't troubling enough, Dr. Oldstone did something that was I think quite careful. He took some of the samples that had been called false positive or false negative in the first go-around, the same identical samples, these were not new samples, but the same identical samples were given new code numbers and sent back. So the same identical samples were sent back, and in several instances, samples that had been false positive now became false negative and others that had been false negative now became false

positive. And at that point, Dr. Oldstone said that he was no longer interested in collaborating and suggested that the results should be published.

Q And was Dr. Oldstone successful in that effort?

A He was not. He made a fundamental error I think of trust in not having a pregranting agreement, which is fairly standard actually, where the investigator has the right to publish the results even if the sponsor doesn't like them. He did not have that agreement with the MIND Institute and he was unable to publish these results.

Q Is it fair to say that officials, Dr. O'Leary and people in his camp, were unhappy with the results?

A I'm not sure how anyone could possibly be happy with the results.

Q Now, in his testimony on Tuesday, Dr. Kennedy suggested that some of the problems might have actually been because of contamination in Dr. Oldstone's lab. What's your reaction?

A I'm sure Dr. Oldstone has had contamination in his lab. As Dr. Rima said, we all have. Anybody who works with PCR has to deal with contamination. It happens all the time. The quality of the lab is not

in whether you have contamination or not, but it's how

respond to that contamination. If you respond by ignoring negative controls that go positive, that is not a responsible reaction. If you try to figure out where the contamination is coming from and fix it, then of course it's entirely possible that there may have been some contamination in Dr. Oldstone's laboratory at some point. But he is one of the I think most meticulous scientists I know, know of, I don't even know him, and has a track record of more than 50 years of high-quality, high-impact publication in this area using a huge variety of technologies, including PCR. So, if there was contamination in Dr. Oldstone's laboratory, I would have I think very close to complete confidence that he would do whatever he could to fix it.

Q And given the purpose of the exercise, which is in fact to see if Dr. O'Leary could properly identify positive and negative samples, do you think Dr. Oldstone would have taken extra care to ensure that what he was sending was in fact what he thought he was sending?

A Absolutely. It's also I think quite relevant that the issue of contamination in Dr. Oldstone's laboratory did not come up in the conversation between Dr. O'Leary and Dr. Oldstone

between the first and the second round of testing. It was only when the O'Leary Lab failed to achieve a reasonable rate of sensitivity and specificity that any concerns were raised about Dr. Oldstone's competence to prepare samples and send them to O'Leary, Dr. O'Leary's laboratory.

Q Now Dr. Kennedy also suggested on Tuesday that one of the reasons Dr. O'Leary might have missed some of the positive tests from Dr. Oldstone's lab was because the copy numbers were very low. It was low detectable limits. Does that make sense given what actually happened in the attempt to replicate?

A Well, sure. I think, to be a good test, I mean, my daughter is now trying to get into high school. I keep telling her to be a good test, it has to be hard. And so I'm sure that Dr. Oldstone sent Dr. O'Leary some slam-dunk easy samples and some really low copy number samples. I think Dr. Rima pointed out very clearly that a large number of labs around the world would have beaten a path to his door had he really been able to do this in order to initiate collaborations with Dr. O'Leary, because he was claiming to do something that nobody had actually done yet.

And so I'm sure that it's plausible that

some of the low, low positive samples that Dr. Oldstone sent to Dr. O'Leary's lab might be missed because of lack of sensitivity. However, that doesn't explain how a test can be false positive. That's not an issue of sensitivity. That's an issue of specificity. And it certainly doesn't explain how a false positive can become false negative or a false negative can become false positive. It's impossible that that would occur because a low copy number was there.

Q Now did Dr. Oldstone also discuss or comment on the hypothesized link between MMR and ASD?

A Yes. He said that he was quite willing to believe that there could be such an association when he entered into this agreement with Dr. O'Leary with funding from the MIND Institute. Dr. Oldstone is a curmudgeon. He's a tough old guy and there's no way that he would waste his time setting up a series of things if he didn't think it was possible that Dr. O'Leary had actually done this. He would have just said no, I'm not going to be involved with this at all.

So, by entering into this agreement, he was showing a willingness to believe. It's just that as Dr. Rima said, for a good scientist, it's really not a

question of belief, it's a question of what you can prove to be true. And in this case, he was willing to believe but only until proof could not be supplied.

Q And just for the sake of the transcript, did he put all of this into a letter which he then sent to you?

A Yes. What happened was I was taking notes as he was talking, and so after our conversation, I asked him if he would be willing to put this into a letter, and he basically said send me your notes. And so I sent him my notes and he wrote the letter and the letter was submitted to the Court.

Q Yes. Respondent's Exhibit AA. Now switching gears a little bit, did you read the rebuttal opinions from Dr. Kennedy and Dr. Hepner concerning Unigenetics and PCR?

A I did.

Q Now Dr. Hepner goes into some detail about the work you did and suggests that SYBR Green is an inadequate tool for comparing results from Taqman PCR testing. Do you agree?

A No, not at all.

Q Why not?

A Well, certainly in terms of the generation of amplicons, that really doesn't depend upon your

detection system. You can detect PCR results with a wide range of the agents with probes, as was pointed out last time, or with dyes that intercolate into the DNA. And so really what is amplified in a PCR reaction is driven by the primers. And if the primers amplify something that is picked up either by a probe or by SYBR Green, it still is amplified by the primers.

SYBR Green is actually a good first step to determining whether or not your primers are amplifying what you want. And so, in this case, we chose to use the primers and SYBR Green, knowing full well that we were going to take any products that were amplified out to the stage of sequencing to know exactly what we were dealing with. And so we weren't going to rely on a probe to give us the specificity. We were actually going to take it all the way to the stage of sequencing.

And so the detection system is irrelevant in terms of the major observation, which is that O'Leary or the Uhlmann primers result in the amplification of things that in this case look like a duck, walk like a duck but aren't ducks. They are human genes.

So, in the multilayered evaluation of the amplification products, we looked at melt curve

analysis. We looked at the size of the amplicons produced. And then we did sequencing on the results. And some of the samples yielded things that have the correct melting temperature, had the right size on gel but were nonetheless human gene products as opposed to viral gene products.

Q Now on the topic of the primers, Dr. Hepner also suggested the southern blot and Taqman PCR results ensured that the primers from Dr. O'Leary and Dr. Uhlmann were basically doing what they're supposed to do, amplifying measles virus. You suggested, do you agree?

A Well, I think that the Uhlmann primers on a positive control specimen can probably amplify the correct sequence and it can be confirmed on a western blot or a southern blot. So it's not the fact that the Uhlmann primers are so bad that they never amplify measles. It's just that they don't only amplify measles. That's really the distinction. They amplify measles. And so, yes, in this case, there's sort of no contest. They're both true. It's just that Dr. Hepner doesn't acknowledge that the primers amplify more than just measles.

Q And can this amplification problem affect data interpretation?

A Well, of course, because if your primers are amplifying, are capable of amplifying both the measles gene, message or measles genes and human genes and human messages, then if you get a product, if you get a signal, you really don't know if it's the human gene that's been amplified or the measles gene that's been amplified.

Q Now Dr. Rima testified about this at some length this morning, but because you also have expertise in PCR, I want to give you the opportunity to comment on this point of the rebuttals, what Drs. Kennedy and Hepner are saying that high copy numbers eliminate concerns about contamination assay inefficiency in threshold cycle. Do you agree? Do you care to briefly comment?

A Well, I think with the caveat that Dr. Rima has pointed out that in fact we have no idea what the actual copy number that was amplified was. All we know is the end product that's the result of in some cases huge multiplication. The fact that one has a high copy number does not at all rule out that you have contamination. I could show you some students' work in my lab where they have extraordinarily high contamination and therefore have extraordinarily high rates of copy numbers.

So simply to say we have a high copy number, therefore, there can't be contamination doesn't make any sense at all but it can simply mean that you had gross contamination rather than low-level contamination, although I have to say low-level contamination is much more common, but gross contamination certainly can occur.

Q Now Dr. Bradstreet in his report and his testimony on Monday discussed a number of test results for Colten Snyder, implying that they would be indicative of measles virus persistence. I want to go through a few of them and just see to the extent they haven't been covered by our other experts. What's the significance of an elevated rheumatoid factor?

A In isolation, almost nothing.

Q What sort of conditions can it be associated with?

A A whole range of autoimmune, inflammatory, neoplastic and infectious conditions. Many, many different conditions can give you an elevated rheumatoid factor. It's a fairly nonspecific measure.

Q Now does this similar statement apply to the anti-myelin basic protein tites?

A Yes, I would think so. In a single result in isolation or pulled from a very thick chart where

hundreds of tests have been ordered, an isolated result needs to be interpreted in light of that clinical presentation and all of the other results.

Q So would this also apply to the serum vitamin A and elevated IgE?

A Absolutely. One of the axioms in clinical medicine, and Dr. Rima sort of deferred a little bit because he has experience with measles but not so much clinical experience, but one of the axioms in clinical medicine is if somebody comes to you with a result, and I'll give you an example, an extremist.

If a medical student comes to you with a result like a potassium value of 1, now they're going to come to you in a panic because that is not compatible with life. And you smile because you've been there before and you say, did you stop and look at the patient? And the student says, well, yes. Were they breathing? Yes. The lab result is a mistake. It was probably drawn from the arm where somebody was running in an intravenous solution that has no potassium in it. And so, in isolation, any given value is almost, almost, not completely, but almost useless.

You also have to realize that all lab values are based on -- normal ranges are based on 95 percent

confidence intervals. That means that the normal range is determined by the population average value. By definition, that means that 2.5 percent of the values will be abnormally high or abnormally low.

And so the statistical argument then becomes if you do 100 tests on any of us in this courtroom right now, statistically, 5 percent of them will be abnormal, half abnormally low, half abnormally high. And this would be if all of us in the room are completely healthy.

What seems to have happened with some of these lab results is that Dr. Bradstreet would look at a very big chart with lots of lab results and say, look at that one, look at that one, that's abnormal and then try to figure out a hypothesis that would explain that lab result in the context of the case that he was trying to build.

I call that cherry-picking data. So one of the expert witnesses yesterday was asked about the high IgE, and the answer was, well, gosh, you really should pursue parasites. But that doesn't make a whole lot of sense unless there's a clear epidemiologic exposure to parasites. So, if an individual comes from a developing world country, has high eosinophilias, high eosinophils and high IgE, it

would be completely logical to look for parasites.

Even if they go to a daycare. They're in daycare. We see kids like this all the time. Daycares are filthy places. If you see a child like that, you would logically look for parasites. But in isolation, without any other explanation, it just doesn't make sense to incorporate that into this larger theory based on a single report. What you should really do is say was there a clinical picture that is logical, coherent and explainable on the basis of normal biology.

THE COURT: A parasite like pinworms?

THE WITNESS: Absolutely. Eosinophilia and elevated IGE is very rare in pinworm infection.

THE COURT: Okay.

THE WITNESS: But certainly there are other parasites that are spread in daycares that can cause elevated IgE and eosinophilia.

BY MS. BABCOCK:

Q I wanted to switch a little bit to Colten Snyder and some specific MMR questions. Is the MMR vaccine known to cause an increase in secondary infections?

A No. So far as I'm aware, there's never been any report of clinically relevant immune compromise in

any way involving that vaccine.

Q And are the symptoms Colten presented with between his MMR vaccination and his May 26, 1998, hospitalization consistent with measles virus infection?

A No, not that I can see.

Q Now, on direct examination on Monday, Dr. Bradstreet suggested that the small white patchy exudates on April 6, 1999, might have been -- actually that was probably May 6, 1999, I correct myself -- might have been Koplik's spots. Do you agree?

A I don't. Remind me how many days after the MMR that was. Day 14? 14, 13? That seems to be very, very late. I've looked for a lot of Koplik's spots because I've been involved in several outbreaks, including the one in Philadelphia in 1990. And Koplik's spots are part of the prodrome of natural measles, so they occur very early at the time that individual, whether they be adult or children, have conjunctivitis or red eyes, runny nose. Those individuals have no sore throat.

But if you look carefully on the buccal mucosa, under just the right light, you have to be quite careful, occasionally you can see Koplik's spots in the two to three days before the development of the

rash. But it's a very subtle, very transient phenomenon except in children who are severely malnourished. So I've seen them in the developing world as well. And then those Koplik's spots can actually coalesce and result in sloughing of the buccal mucosa, sometimes with bleeding.

But in recently nourished individuals, they are a very fleeting observation that you have to look hard. And the reason we spend so much time looking is that they're one of the very few things in medicine that are called pathognomonic, which is if you find it, you have the diagnosis. It's a guarantee. There's nothing else that causes Koplik's spots. And so it's one of those things that older staff people like to do, because if you can find it, you can show it to all of your students and say, look at this, this is pathognomonic measles. It doesn't occur in vaccine-strain disease.

Q Now backing up to again the symptoms Colten had between April 23 and May 26, the time he was hospitalized, do you think they're consistent with measles encephalitis ADEM or PIEM?

A There's no way that you can stretch the observations enough to make them fit even reasonably into any of those diagnostic criteria.

Q Are they consistent with any other condition known to be associated with measles virus?

A Not that I'm aware of, no.

Q Now you mentioned in your first report that there was evidence that Colten Snyder had a bacterial infection at the time of his May 26, 1998, hospitalization.

A Yes.

Q What do you rely upon to make that statement?

A Well, the fact that he was sick, that he had an exudative pharyngitis and that he had an elevated white count with a marked left shift.

Q What does that mean?

A Most of the elevation of his white count was attributable to an elevation of his neutrophils, so polymorphonucleocytes. And those are the classic white blood cells that respond to bacterial infections. But he also had a very marked left shift, which is where the neutrophils which are normal in multisegmented cells, the nucleus of the neutrophil typically has four, five, anywhere up to 12 lobes in its nucleus. But those lobes like wrinkles on those of us who are passing 50 accumulate with age of the cell.

And so a young neutrophil doesn't have very many lobes to its nucleus. And a white blood cell that's just released from the bone marrow, it often has no lobes. It's just a single big nucleus. It's just a band for a nucleus. And so those are actually called band neutrophils or bands.

And in fact he had a very elevated, what doctors call bandamia. He had an elevated level of neutrophils with this band form. And that's almost pathognomonic of an active, ongoing bacterial infection. That's again one of those things that when you find it, you bring all of your students and trainees over and say, look at this, remember it, because it can really help you when you're trying to figure out if this is a viral or a bacterial process.

Q So is it fair to say that this was a laboratory finding that was consistent with the clinical picture?

A Absolutely.

Q Is it consistent with a viral infection?

A I would say almost, almost impossible. I'm not aware of any viral infection that gives you an elevated band count. Furthermore, this relatively small number of lymphocytes, which are typically elevated in viral infections, when you have an active

viral infection, many of those lymphocytes are what are called atypical lymphocytes. They are big. They are often angular.

Most resting lymphocytes are little round things with dark nuclei and have very pale blue cytoplasm, using the typical stains. Atypical lymphocytes have a much larger nucleus, a more active looking cytoplasm that tends to be a different shade of blue. And so competent technologists can readily say this is typical and this is an atypical lymphocyte. And a high lymphocyte count with lots of atypical lymphocytes would be standard for many acute viral illnesses. And at that time, Colten had relatively few lymphocytes, with only I think two or three percent atypical lymphocytes, so very compatible with a bacterial process, not at all compatible with a viral process.

Q And is this left shift that you've just described evidence of a functioning immune system?

A Oh, sure. It's the kind of response that you don't see in individuals who have just had a bone marrow transplant or who are immunocompromised because of chemotherapy. That's precisely the response that they can't make.

Q So overall, based on your own medical

experience and practice, review of the medical records, expert reports, listening to testimony in this case, do you place any reliance on the Unigenetics results for Colten Snyder?

A No. I have no confidence whatsoever in the results.

Q Do you think there's any evidence to show that the MMR vaccine more probably than not caused Colten Snyder's ASD?

A No, I do not.

Q Do you think the MMR part of this hypothesis is biologically plausible?

A At some point in time, it may have been biologically plausible. Hypotheses have lives. And I think that this was a hypothesis that had someone as prominent as Michael Oldstone willing to consider it at one point. We embarked on our own study, in part because we were interested to know if there was any truth to this hypothesis. But it stops being credible after a certain point as evidence builds up against the hypothesis.

I mean, there are many hypotheses that people consider to be too weird to be true. The one that comes to mind immediately is Stanley Prusiner's insistence that prions existed, and he was roundly

criticized for a number of years because nobody believed his data. His hypothesis at that point was just that, it was a hypothesis. But over time, he stuck with it. He convinced other competent scientists to work with him, and he demonstrated in fact that prions were an entirely new biology. And he I think quite rightly won a Nobel Prize not only for his science but for his stubbornness.

I think in this case, so biologically plausible? Yes, the hypothesis was biologically plausible at some point in some ways. But no longer, because the evidence that has accumulated in the time since the introduction of the hypothesis is just overwhelmingly against it. It was a hypothesis that was biologically plausible but is no longer. It no longer deserves that recognition.

Q Any you hold these opinions to a reasonable degree of medical certainty?

A Absolutely.

MS. BABCOCK: I have no further questions.

THE COURT: Mr. Powers, do you want to recess or do you want to launch?

MR. POWERS: We're going to go ahead and do the recess. I don't think that we'll go long enough for me to take another recess later, so we should do

it now.

THE COURT: All right. Well, it's 5 after 2 by my watch, so let's reconvene at 20 after.

MR. POWERS: Thank you.

(Whereupon, a short recess was taken.)

THE COURT: All right. We're back on the record in the Snyder case. Dr. Ward remains on the witness stand. Mr. Powers, feel free to cross-examine.

MR. POWERS: Thank you, Special Master.

CROSS-EXAMINATION

BY MR. POWERS:

Q Good afternoon, Dr. Ward.

A Good afternoon.

Q I wanted to ask you a few questions primarily about the direct testimony that you gave here related to a couple of issues that came up in your most recent of a series of expert reports that you filed in this case. In the latest iteration of the expert report, I believe you use a term, "neurovirulence," in describing why the Petitioners can't make out their case. That is, there is no evidence that the measles attenuated strength in neurovirulence. Do you remember using that terminology?

A Not really.

Q I believe the symptoms --

A I don't remember that specific word in that specific instance.

Q Well, I just wanted to raise the issue because my understanding of the whole idea of an attenuated virus is to make it less virulent, that is, to reduce its virulence so that it can still invoke an immune response but not kill or enter the host, is that right?

A Sure, that's the whole idea.

Q And so that's the whole idea of it. And as you work through that process of altenuating a wild virus, it's a multistep process, going through various cell passages, isn't that correct?

A Yes, that's right.

Q And if I recall Dr. Rima's testimony, he said that as you work through that attenuation process, what happens with the virus is a series of mutations at each step of the way, is that correct?

A We presume that to be the mechanism of attenuation, yep.

Q And what does it mean when you say you presume that to be as opposed to simply saying yes, that's the mechanism of attenuation?

A Well, Dr. Rima also pointed out that even though he knows there are lots of mutations, we don't know which ones of those mutations have resulted in a change in biological character of the virus. So there are many things that are different about vaccine strain and the wild-type virus.

Q And certainly there are many things that are different about them. It's just that the underlying, the mechanism, the underlying series of mutations, the details of how that results in attenuated virus is a mystery to this day from what I've heard?

A In my lectures, I call it a black box virus. We put a wild-type virus in, we package it a bunch of times and quite amazingly we take it out at certain points and give it to our children. And it worked.

Q And the fact that it's a black box and that the process and the model inside that box is opaque and nontransparent, you still have an end product and you are confident in the end product even though you didn't know exactly what happened inside that box and when I say confident I mean you know what the end product is.

A Right. I think where we have more than 40 years of experience with this particular family of vaccines so that we have great competence now, I think

that the first few kids they gave it to, the people were probably pretty nervous.

Q And in describing the attenuation as a black box, that implies that there are other mutations and other changes going on there that (a) you don't know that they're happening and (b) might not be able to explain the significance or the consequence of, correct?

A I think with any living thing, you can't predict what's going to happen. You can do your best to minimize the change from a certain viral strain, but absolutely you don't know what's going to happen.

Q You've also said in your report and in your testimony that the measles virus is known to cause -- the neurological injuries caused by measles virus are limited I think to two, the SSPE and the MIBE, is that correct?

A Those are the two principal known manifestations of wild-type disease.

Q And when you say "principal known manifestations," are there other known manifestations that you would add to the mix of those two?

A There is the presumed autoimmune process called postinfectious encephalomyelitis or ADEM. So, in fact, we know a great deal about the neurologic

complications of wild-type measles. That's why it's so implausible in some ways that suddenly there would be something so different as what's being proposed here.

Q Is there anything about the properties or the structure of the measles virus that would make it impossible for it to cause any outcomes other than the ones that you've already described?

A Of course not. There's nothing that would make it impossible.

Q So there's not anything about its structure, its replication, its life cycle that would biologically rule out something like the injuries that are claimed here?

A Something like the injuries? So you're asking me is it in the realm of -- I think Dr. Rima has also reacted by saying you can't prove a negative. There's no way that anybody could credibly answer it can never happen. The fact is there's no evidence that it does happen.

Q Now you discuss in your direct, I would say it's seen in the report, I think I heard it on direct for the first time, that wild-type measles virus can actually cure some autoimmune diseases.

A Yes. There are a couple of case reports

where that appears to have occurred, either a cure or for a period of time made better.

Q When was that discovered? You're relying on case reports. Where were the case reports?

A This is the literature from the late '60s and early '70s where individuals with different conditions like idiopathic thrombacytopenic purpura where you have an immune disruption of your platelets or a couple of kids with juvenile rheumatoid arthritis would get quite remarkably better right around the time that they had the natural measles.

And the presumption has always been that the virus would target actively replicating cells and that might actually delete enough of them or kill enough of them that these T-cell autoimmune-mediated processes might actually be resolved following measles, although I'm not sure that anybody would recommend measles therapy if you had JRA or any of these other conditions.

Q So, at the time that it became discovered that this was in fact a result of wild measles virus exposure, at that point, it was new and it was pretty novel?

A Pretty new and pretty novel? Yes, it was novel enough to be interesting and be published, yes.

Q Now you spent a significant amount of time in your testimony discussing conversations that -- well, I don't know if it was a conversation or multiple conversations.

A Single conversations.

Q Single conversation with Dr. Oldstone. And in that conversation --

A Lots of conversations with his secretary.

Q In order to get the one conversation with Dr. Oldstone, okay.

A That's right.

Q Now Dr. Oldstone has not appeared as far as you know in any case in the vaccine program or in the civil system involving the debate about MMR and autism, is that correct?

A I didn't ask him that, so I don't know.

Q That's all right. Just based on as far as you know.

A As far as I know, I don't know, yes.

Q And he did not appear, for example, to testify in Cedillo, nor did he submit an expert report in the Cedillo matter?

A That's correct.

Q Didn't appear or submit an expert report in this matter?

A That's correct.

Q And in the letter where he does make a note that he sees no evidence to support a link between measles virus and autism, we don't have any record of what he was reading or reviewing or relied on to make that statement. We don't have any indication of that here in front of the Court or on the record, do we?

A I certainly don't.

Q So all we know is what his conclusion is based on a telephone conversation with you but not really knowing what the basis in fact and in the evidence of that opinion was, correct?

A Well, no. I think as I say, I don't know Dr. Oldstone, but I think that this is an area of enormous interest to Dr. Oldstone. If this hypothesis that's being forward is true, it would be of enormous interest scientifically to Dr. Oldstone. And I think that the fact that Dr. Oldstone has not referenced, has not cited any of the publications that have been produced in support of this hypothesis in any of his writings in the last two decades suggests that it's not that he's not aware of the hypothesis, it's that he is voting with his pen to understand he actually voted against the hypothesis. He doesn't believe it.

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Q So I understand that. That's been expressed in the letter, so I'm not asking you to speculate on what he might have been thinking or what his motives are. I'm just trying to determine is there anything that you're aware of in notes, in material that you might have exchanged after the phone call, anything that you can point to that tells us what he relied on in order to come to the conclusion that is expressed in this letter?

A Only the facts that he related to me in the telephone conversation.

Q Okay. That's all I was trying to get to. Now the letter itself talks about what sounds like some conclusions or a summary that Dr. Oldstone is making of a process of back-and-forth that went on for a fair amount of time between himself and Dr. O'Leary and the staff at Dr. O'Leary's lab. Is that a fair statement?

A I don't know the exact period of time. I don't know the exact period of time, but I would assume it would be over a period of at least a year.

Q Okay. And what we have here summarizes a period of at least a year's back and forth with sort of the headline numbers, the headline numbers being the 20 percent samples in two rounds of testing that

were allegedly misidentified. We don't have in front of us and I'm curious as to whether you have access to it or have seen it, any documentation from Dr. Oldstone's lab describing the methods and the procedures that were used to generate the samples that he sent to Dr. O'Leary? Do you have any of that?

A I have none of that.

Q Have you reviewed any of that?

A No.

Q Do you know of anybody who has reviewed that material aside from apparently Dr. Oldstone in making the presentation in this letter?

A I think that if Dr. Oldstone had been allowed to publish the data, then the entire world could have reviewed the methods and the data.

Q But we don't know, so we don't know what he was doing about contamination in his laboratory, do we?

A No, we do not, but that reasonably would have been contained in any publication that he was allowed to produce.

Q Yes. So I'm not asking about what presumably might have happened. I'm asking about what we know now today based on a letter that now today is in front of the Special Master. I'm just trying to

focus on that and not speculate about what might be out there. So we do not know today what methodology was used to generate the samples in Dr. Oldstone's lab?

A No, we do not.

Q We don't know what controls were there to make sure that he had confidence before they left the door that the samples that were labeled positive were in fact positive and the samples labeled negative were in fact negative. We don't have any information that would illuminate that, do we?

A We do not.

Q We don't have any information to illuminate it on either the first round of the sample exchange or the second round, correct?

A That's correct.

Q We don't have any information about how Dr. Oldstone might or might not have handled contamination at his lab, do we?

A You asked me that before. No, we do not.

Q And we do know that that lab handled a fair amount of measles virus. That was a central focus of his investigations, correct?

A Yes.

Q Now was your testimony that the possibility

that Dr. Oldstone's samples might have been contaminated, was it your testimony that that didn't come up until after the second round of samples were exchanged?

A I'm responding simply to Dr. Kennedy's testimony where he raised the possibility that the contamination may have been in Dr. Oldstone's laboratory. If in fact there had been a concern by the O'Leary Lab about contamination from Dr. Oldstone's laboratory, it seems logical to me that Dr. O'Leary would not have continued the collaboration because he would not have had confidence in Dr. Oldstone's laboratory.

By entering into the second round of testing, I think that it is a pretty reasonable assumption that at that time, Dr. O'Leary believed Dr. Oldstone's lab to be free of contamination. It would have been scientifically very foolish for him to continue to work with what he believed might have been contaminated specimens.

Q Or it might have been reasonable since they were looking forward to working in a collaborative nature to see if at both ends there might ne contamination, and perhaps together they could resolve the contamination issue if in fact that was the issue.

That seems like a reasonable conclusion to reach about people collaborating.

A In a situation where your laboratory is being tested, all of us who run reference labs deal with this all the time. We get test samples sent from outside. It's a requirement in the U.S. and Canada to have your lab undergo external evaluation to see how well you're doing. Even though we try to blind those specimens as best as we can, when those specimens come in, the technologists know what they are and they do their very, very best to make sure that those samples are treated in the very, very best way possible.

I think it's a reasonable assumption that Dr. O'Leary's laboratory was on high alert when receiving specimens from Dr. Oldstone, and they still couldn't do it right.

Q And we still don't know because we don't have the data in front of us whether Dr. Oldstone's lab did it right either?

A Your own experts appear to hold Dr. Oldstone in fairly high regard, as do I. I think his reputation is pretty good.

Q I understand that, and this is not to impugn his reputation. All I'm saying is that I think it was Dr. Rima on the stand who said particularly when it

comes to headline numbers, his instinct is to distrust or to disbelieve the things that land on his desk, and this is what's landed on the desk here. I'm just raising the issue that we don't know because we don't have evidence, and we can't go beyond that lack of evidence.

A If Dr. Oldstone had been allowed to publish the data, we would have that evidence.

Q Or perhaps if Dr. Oldstone was here to testify and was willing to bring materials here with him to support his testimony, that might provide an answer. But that hasn't happened at this point, has it?

A Perhaps petitioning the MIND Institute to permit him to publish the data would be a scientifically valid way of getting this into the public domain.

Q Or again, you've made that point a couple of times. Just without being contentious, I want to make sure that you understood the question and get an answer to the specific question. The question is the debate about the facts in this process between Dr. Oldstone and Dr. O'Leary could be illuminated if Dr. Oldstone was here to testify about it and provide the Special Masters and the parties with the underlying

information, isn't that correct?

A I believe that either Dr. O'Leary or Dr. Oldstone would be able to provide the Court with that information.

Q Now you mentioned again towards the end of your testimony a couple of issues that you were raising with Dr. Bradstreet and the tests that he did and the possibility that parasites might be involved came out. I know that the Special Master had a comment about parasites, and I think it was based on things that you were saying that the immune labworks indicated there might be parasites that were involved here. Do you remember that back-and-forth?

A Sure.

Q Did you review Colten Snyder's medical records before you testified today?

A Yes, I did.

Q In reviewing those records, do you recall that on his admission to the hospital, he was tested for parasites and came up negative?

A Yes.

Q Okay.

A I also run a reference lab for parasitology and I know the limits of those tests.

Q I understand that, but I don't want to get

in a collateral debate about the quality of the lab work at the Ormond Beach Hospital.

A That's fine.

Q All I want to do is say, you understand that he was tested at a hospital, no parasites?

A By a stool examination, and they found no parasites in the stool examination.

Q You also mentioned in talking about Dr. Bradstreet that he was cherry-picking data to support the case he was trying to build. Do you recall making that statement on direct testimony?

A Yes, I do.

Q Is it your understanding that he was reviewing data to provide what he believed was reasonable medical care for a very sick child?

A I have to believe that Dr. Bradstreet was acting in good faith for a patient.

Q To provide clinical care and medical treatment he felt was indicated for that child, correct?

A It's my understanding that the clinical care of this child was Dr. Bradstreet's responsibility, yes.

MR. POWERS: I have no further questions.

THE COURT: I do not have any questions for

Dr. Ward.

MS. BABCOCK: I just have one.

THE COURT: Followup?

MS. BABCOCK: Just one.

REDIRECT EXAMINATION

BY MS. BABCOCK:

Q Dr. Ward, though we don't understand exactly how the measles virus becomes attenuated, do we understand what adverse effects are associated with the MMR vaccine?

A We have hundreds of millions of children immunized with that product. So, yes, we have a very good idea what the side effects are.

Q And is ASD one of those adverse effects?

A It is so far as I am aware, and the Institute of Medicine is aware it is, and the British authorities it -- is not a known side effect of MMR or measles vaccine.

MS. BABCOCK: Nothing further.

THE COURT: Mr. Powers, anything further?

MR. POWERS: I have nothing further.

THE COURT: All right. Dr. Ward, you may step down.

(Witness excused.)

THE COURT: Okay. Do we need to have

anything off the record or are you prepared to let me

know, Petitioners, what you plan on doing insofar as rebuttal?

MR. POWERS: Yes, we do, Special Master. We anticipate a very brief rebuttal from Dr. Kennedy tomorrow morning.

THE COURT: Is there any reason since it's only a quarter to 3 today we could not proceed with his rebuttal today? I'm happy to give you an hour if you think an hour is necessary.

MR. POWERS: We can do that, Special Master.

THE COURT: All right. Do you need an hour? If you want an hour, you've got it. If you want more, you've got it.

MR. POWERS: Could I step away? I don't want to be conferring on the record. If I could go off the record to confer?

THE COURT: You certainly may. We'll go off the record.

MR. POWERS: Okay.

(Whereupon, a short recess was taken.)

THE COURT: We're back on the record.

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Whereupon,

RONALD KENNEDY

having been previously duly sworn, was recalled as a witness herein and was examined and testified further as follows:

DIRECT EXAMINATION

BY MR. POWERS:

Q Obviously, you have already testified on direct and have been cross-examined in this matter. You've been called in rebuttal because there are some specific issues that arise in the expert report and in the direct testimony of Respondent's expert, Dr. Rima. Is that your understanding?

A That's correct.

Q And you're taking the stand here so we can briefly deal with a handful of issues that you want to talk on rebuttal for in terms of statements of fact and discussions of your relevant experience to testify in this matter, is that correct?

A That's correct.

Q So the first matter is if we can look initially to Dr. Rima's expert report itself, and this is Respondent's Exhibit V. And the first place I'd like to draw folks' attention to is on page 4 of Exhibit V. I see people turning pages, so I will

pause and let folks get to where they need to be.

THE COURT: Okay.

BY MR. POWERS:

Q So, Dr. Kennedy, do you have that opened to page 4?

A Yes, I do.

Q If you look down at the second to last full paragraph on that page, there's a paragraph that begins "On page 6." Do you see where I'm referring to?

A Yes.

Q And in Dr. Rima's report, he describes that you expressed the relationship between two different measles strains, the Schwarz and the Moraten, as being closely related. Do you see that reference?

A Correct.

Q He then says that they are actually genetically identical. Do you see that?

A Correct.

Q When you read that under the heading "Discussion of Dr. Kennedy's relevant experience," what significance did you attach to that mention of the two different measles strains by Dr. Rima?

A Well, I thought that perhaps it was unclear on how that was cited in my expert report and there

was some confusion relative to where the statement came from.

Q Where in fact did the statement come from? Is this something that you just came up with on your own?

A No. This statement is from the Virology, Fields, a chapter by Dr. Diane Griffin. It's chapter 44. And if you look on page 127 --

Q Or would that be --

A 1427, I'm sorry. 1427, and I apologize, I highlighted stuff in pink and your copies are coming out dark. But if you see, there's a comment on page 1427 under "attenuated live virus vaccines," that section, and if you see a No. 1 --

THE COURT: Yes.

THE WITNESS: -- near the bottom of the page, it says, and I quote, "The Moraten strain used in the United States was licensed in 1968 and is closely related to Schwarz."

BY MR. POWERS:

Q Was that the source of the comment in your own expert report that Dr. Rima then takes issue with here?

A Yes.

Q Another issue that we want to address on

rebuttal is if we go back to Exhibit V, which is Dr. Rima's report, and turn to page 2, and at page 2 in the last full paragraph, there's a discussion of a subject that also came up on direct testimony about the high titer measles virus vaccine work that was done. And if you continue over to page 3, Dr. Rima made some statements about that study and about your comments on that study. Can you describe that, please?

A Yes. Dr. Rima was concerned about some confusion and it was in light of a statement that I made on page 8, paragraph three of my report, which was not clear. And I would like to essentially cite where the clarification came as it relates to the high titer measles vaccine and whether or not immunosuppression did occur.

Q And where would you direct the Special Master's attention?

A On page 1428, the first column, lines 9 to 14, and it should be label number 2, and I'll go ahead and just read that paragraph. "The pathogenisis" --

THE COURT: Please don't read it to me.

THE WITNESS: Okay.

THE COURT: I can read it.

THE WITNESS: Got it. Okay. So anyway, I

use that to support my claim.

BY MR. POWERS:

Q And the claim specifically is a claim that Dr. Rima describes as representing an improper analysis of the literature?

A Correct.

Q Okay. And then what we want to address is back on page 4 of Dr. Rima's report, which again is Respondent's Exhibit V, the second full paragraph. This is a paragraph that he makes comments about your description of the immunosuppression and immunodeficiency being contraindications for the MMR. I take it that in rebuttal, you take issue with Dr. Rima's statements there?

A Yes. The source of that statement you can find on page 3 of my expert report in the second paragraph, the first and second line. And I cite the Physicians Desk Reference, Volume 51, in support of that statement. And that was also cited and should have been provided as an exhibit in the Cedillo case. And I was specifically referring to the Merck MMR vaccine product. And if you look under contraindications, immunosuppression and immunodeficiency are contraindicated as stated in the Physicians Desk Reference.

Q And is it your understanding that the PDR both in its authority and its literal weight is the Bible that guides medical care providers in the use of biological products?

A Yes, it's my understanding.

Q And that any language describing contraindications for any product would be PDR's language that was submitted to and approved by the U.S. Food and Drug Administration?

A Correct.

Q Anything else on this point that you wanted to address?

A I think I understand Dr. Rima's area of confusion, because the MMR vaccine is recommended for HIV-1 seropositive children, and he cites that in his expert report. But there are some caveats to that, and you can find one of the caveats that's mentioned by Dr. Griffin in her textbook. If we want to go there, that is specifically on page 1427, second column, second paragraph, lines 3 to 6, and it starts with "Progressive fatal."

Q And it's that statement by Dr. Griffin that you believe lends support to the statement that you made in your own expert report?

A In addition to the citation of the

Physicians Desk Reference. And then also below that, she states that it is not recommended for vaccination in children with low CD-4 T-cell counts.

THE COURT: For the clinically or the serologically immunosuppressed children?

THE WITNESS: Correct. So I just wanted to clarify that point. I understand where the confusion came in, and I apologize to Dr. Rima for that.

BY MR. POWERS:

Q All right. The next point to talk about again is in Respondent's Exhibit V, Dr. Rima's report, still on page 4. This is an issue that also did come up on direct testimony by Dr. Rima today I believe. If you bring your attention to the third full paragraph down on page 4 of Dr. Rima's report, that's the paragraph that discusses Dr. Kennedy's reference to the measles virus receptor as being a molecule called CD-46. Dr. Kennedy, do you see what I'm referring to here?

A Yes.

Q And you recall that issue was mentioned briefly in Dr. Rima's direct testimony?

A Yes.

Q Something that you were cross-examined about also?

A Yes.

Q Why do you take issue with particularly the direct testimony of Dr. Rima?

A Well, I agree with Dr. Rima, that CD-150 is indeed a receptor for measles virus. In fact, in my single publication on measles virus, it's clearly stated that CD-150 or SLAM is a receptor for measles virus. The point in my expert testimony for the Snyder case was that I got pretty beat up with the Cedillo Court from the standpoint of mixing wild-type measles virus versus vaccine measles virus, and C-46 preferentially is recognized by tissue culture adapted in vaccine strain measles virus whereas CD-150 is primarily for wild-type. So I again apologize. That was an omission on my part, and I do cite my single publication. But CD-150 is the primary receptor.

Q So just to clarify that, by talking about CD-46, in no way did you mean to even imply that CD-150 or the SLAM wasn't the appropriate preferred receptor?

A That's correct.

Q And then one last point. I don't think it's in Dr. Rima's expert report, but it did come up during his direct testimony today. I should mention you were here for his direct testimony, is that correct?

A Yes.

Q In his direct testimony, do you recall he mentioned an issue about the R protein in measles virus?

A Correct.

Q What is your recollection of his testimony?

A That he was not aware that an R protein had been identified.

Q And what is your response to that in rebuttal?

A If you turn to the Griffin chapter on page 1404 and if you look at the schematic, Figure 4, you'll see that the P gene is divided into P, V, C and R such that the P gene product is a multicistronic gene which encodes those four proteins. Then if you go to the next page, 1405, schematic Figure 6 again talks about P, C, V and R proteins. And then if you go to the second column, lines 9 to 12, and I believe I have those bracketed, it describes the fourth protein from the P gene product, the R protein, that it is a ribosomal frameshifting product.

Q So based on what you see here and the text that you refer to both in the tables and the narrative chapter underneath that, what is your opinion about the existence of the R gene in measles virus?

A That it is present and that it's the result of ribosomal frameshifting.

MR. POWERS: I have no further questions, Special Master.

THE COURT: Okay. Cross-examination? Do you need a minute?

MS. BABCOCK: No.

THE COURT: Okay.

(Pause.)

THE WITNESS: Glad I highlighted all my evidence just to help you out.

MS. BABCOCK: Just a few.

THE COURT: Go ahead.

CROSS-EXAMINATION

BY MS. BABCOCK:

Q Is there a more recent edition of Fields' Virology?

A Yes, there is several more recent editions.

Q Okay. And there's also a 2006 edition?

A There's actually one that just came out. I thought it was 2007, but I think they're up to Volume 7.

Q And let me just clarify, Diane Griffin wrote all of these chapters?

A Yes.

Q Now I just want to note, we talked briefly about the high titer measles vaccine for explaining where your language in your report came from, and I just wanted to make sure that our conversation on cross-examination hasn't changed, because this language clearly says it may be related to long-term suppression of immune responses?

A Correct.

Q So we don't know?

A No, we don't know. And my inference was that it may be related.

Q Okay. Now you were talking about the PDR. Actually, I apologize. I have the current edition of the PDR for MMR, and I believe the language the language is the same because I looked at the 51st edition as well. On the issue of HIV, and I know this is just a very small point here, but I'm just going to read the outline because we don't have it filed.

"Primary and acquired immonodeficiency states, including patients who are immunosuppressed in association with AIDS there are other clinical manifestations of infection with human immunodeficiency viruses." So, by this, they mean it's contraindicated for patients that have some

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pretty clear symptoms?

A Correct.

Q Or full-blown AIDS?

A Correct.

MS. BABCOCK: Nothing further.

THE COURT: Okay. Anything else?

(No response.)

THE COURT: I have no questions. I think I understood all the testimony at this time. Thank you much, Dr. Kennedy. You may return to your seat.

(Witness excused.)

MR. MATANOSKI: Ma'am, if we may have five minutes to determine if there's going to be any surrebuttal?

THE COURT: Certainly.

MR. MATANOSKI: Thank you.

THE COURT: We're in recess.

(Whereupon, a short recess was taken.)

THE COURT: One moment. I'm just trying to make sure we're recording. Okay, we are. We're back on the record then in the Snyder case. Ms. Babcock?

MS. BABCOCK: Respondent calls Dr. Rima for very brief surrebuttal.

THE COURT: Okay. Dr. Rima, if you'll resume your seat on the witness stand. And I remind

you that you are still under oath.

Whereupon,

BERTUS KAREL RIMA, PhD

having been previously duly sworn, was recalled as a witness herein and was examined and testified further as follows:

THE COURT: Ms. Babcock, you may proceed.

DIRECT EXAMINATION

BY MS. BABCOCK:

Q Dr. Rima, you were sitting in the room when Dr. Kennedy came up to clarify a few points?

A I did.

Q What's your response?

A Well, there's a number of points that he raised, and on a number of points, he obviously indicated that he was sorry for creating some confusion and I appreciate that.

In terms of the more substantial points that he made, there is a difficulty with the R protein in the sense that nobody has ever demonstrated it. It was based on a single publication by Darryl Briedis a long time ago. It has never been quoted. It has never been shown. And essentially it is in the textbooks, yes, but as far as people who are working in the field are concerned, it is of no particular

discussion point anymore because there is no evidence that it exists. And so, in that sense, that's a statement that I make in relation to that point.

In terms of the receptors, in terms of the Schwarz and Moraten vaccine, in the 2001 edition of Diane, she might have written that and it was clearly there. But in the field, we know there are papers by Chris Parcks at the time which actually provide --

Q Can you spell the last name?

A Parcks, P-A-R-C-K-S, in the Journal of Virology, and I unfortunately haven't got the reference at hand, which shows very clearly that two strains are genetically identical and cannot be separated and hence was my point.

So what it demonstrates is this, that there's obviously a number of statements taken out of this version of Diane Griffin's chapter in Fields' Virology, but in the field, we discount the R protein completely because no evidence has ever been produced for its existence. And a mechanism of frameshifting is actually one which is difficult to rhyme with the further information that we have about the various proteins that are generated.

And secondly, as I said, the Parcks paper shows the point that I was making. In terms of the

receptors, my main reaction in Dr. Kennedy's direct evidence was that we call it a primary receptor for measles. SLAM is the receptor that is actually preferred both by the vaccine strain and by the wild-type strains, and that is something that it is not easy to make a complete and utter determination of which of the two receptors is the most preferred one. But certainly the vaccine strain can use SLAM as well as CD-46.

And I refer back to my direct testimony this morning where I said that even in the case of this child that we are studying at the moment, and this is unpublished and therefore, you could say that -- and certainly it would be difficult for Dr. Kennedy to know about that. But even in the case of the child that has the Schwarz vaccine and was immunocomprised, had -- we see that virus in that particular child. Even though there's a vaccine strain which can use CD-46, it still goes to cells which express SLAM and not CD-46.

So that is where I took issue with the particular thing that may well appear in the textbook, but the folks in the field know that this no longer current knowledge.

Q So is it fair to say that the statements you

made in your report were based on your own experience, knowledge and expertise in specifically studying the measles virus?

A That's right.

MS. BABCOCK: I have nothing further.

THE COURT: Cross?

MR. POWERS: Nothing further.

THE COURT: And I just have one followup question and that is, as you talked about the Parck paper and someone from Live Labs, that involves actually sequencing both strains?

THE WITNESS: That sequenced the whole. That sequenced the Schwarz and Moraten, the wild-type strain that we have, a reference which isn't the complete wild type because it had already been passed eight times in the original Edmonston as it's called. He also sequenced the Edmonston and I think one other vaccine strain.

THE COURT: Okay. Questions based on mine?

MR. POWERS: No, Special Master.

THE COURT: All right. Then it would appear we can recess until 9:00 tomorrow morning. But do we need to do something else in the record?

MR. WICKERSHAM: If I might?

THE COURT: Go ahead. Certainly, Mr.

Wickersham.

MR. WICKERSHAM: May it please the Special Master. I took to heart your comment earlier about the U.K. and the reports from the U.K. and the need to obtain those. Admittedly I'm here representing the Snyders and we're the last in the series and to some degree the new kids on the block if you'll excuse the expression.

I'm very concerned about obtaining those reports. The experts in our case are perfectly willing to waive any confidentialities, but that doesn't create standing in a British court for the other issues. What I'm interested in is the standing issue that I will need to have access to a British court to have a judge there reconsider either his order or another judge to overturn his order. And in that regard, I would like to ask this Court to issue a subpoena that I then can domesticate in the U.K. and then I would have standing to attack that order. We don't have standing --

THE COURT: Mr. Wickersham, I understand. There are very specific procedures for subpoenaing things from foreign jurisdictions that involve the Hague Convention.

MR. WICKERSHAM: Correct.

THE COURT: And we'll have to delve into that more. But ordinarily we don't use a subpoena to get them, get things that are under seal in particular from a foreign court.

MR. WICKERSHAM: I'm just concerned about the standing issue and with the briefing times that I know that you're very interested in turning out a fair opinion as soon and as expeditiously as possible, and I don't want to leave any stone unturned that's going to create a delay.

THE COURT: I certainly sympathize with you and we'll do everything possible to assist you, as I know that the government will, in this regard. Okay?

MR. WICKERSHAM: Thank you.

MR. MATANOSKI: Yes, ma'am. If I could just follow up on that?

THE COURT: Please, please, Mr. Matanoski.

MR. MATANOSKI: Mr. Wickersham and I had a discussion during one of the breaks about that very topic and we have offered the contact points that we've made. Admittedly, this was very hurried up for us and sort of recreating our steps might be difficult to find some of the things that we want to. But we'd be happy to share whatever we can, because we came in in the same way as he expressed. We did not have

standing. We found a law that allowed us to go in and file.

THE COURT: And it was not a law that involved your government-to-government procedure as I understood it.

MR. MATANOSKI: No. No, ma'am. This is certainly not sovereign to sovereign as it has been portrayed. It was, we came in, yes, our identity is a sovereign, but we came into the court with no different process than any other third party would.

THE COURT: Okay.

MR. MATANOSKI: Thank you.

THE COURT: All right. And I have not yet established a briefing schedule in this case. I would ask that all of the parties give some thought to that this evening and that we be prepared to discuss that tomorrow at the conclusion of the closing arguments. Are there any other matters we can take up today?

MR. POWERS: Not for the Petitioners.

MR. MATANOSKI: Nor for the government.

THE COURT: All right. The Court's in recess until 9 tomorrow morning.

(Whereupon, at 4:30 p.m., the hearing in the above-entitled matter was recessed, to reconvene at 9:00 a.m. on Friday, November 9, 2007.)

REPORTER'S CERTIFICATE

DOCKET NO.: 01-162V

CASE TITLE: Colten Snyder by and through Katherine Snyder and Joseph Snyder, his natural guardians vs. Secretary of Health and Human Services

HEARING DATE: November 8, 2007

LOCATION: Orlando, Florida

I hereby certify that the proceedings and evidence are contained fully and accurately on the tapes and notes reported by me at the hearing in the above case before the Department of Health and Human Services.

Date: November 8, 2007

Ron LeGrand, Sr.
Official Reporter
Heritage Reporting Corporation
Suite 600
1220 L Street, N. W.
Washington, D. C. 20005-4018