

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

THERESA CEDILLO AND MICHAEL)
 CEDILLO, AS PARENTS AND)
 NATURAL GUARDIANS OF)
 MICHELLE CEDILLO,)
)
 Petitioners,)
)
 v.) Docket No.: 98-916V
)
 SECRETARY OF HEALTH AND)
 HUMAN SERVICES,)
)
 Respondent.)

Ceremonial Courtroom
 National Courts Building
 717 Madison Place NW
 Washington, D.C.

Friday,
 June 22, 2007

The parties met, pursuant to notice of the
 Court, at 9:00 a.m.

BEFORE: HONORABLE GEORGE L. HASTINGS, JR.
 HONORABLE PATRICIA CAMPBELL-SMITH
 HONORABLE DENISE VOWELL
 Special Masters

APPEARANCES:

For the Petitioners:

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2279

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C O N T E N T S

WITNESSES:	DIRECT	CROSS	REDIRECT	RECROSS	VOIR DIRE
For the Respondent:					
Nicholas Chadwick	2282	2290	--	--	--
Jeffrey Brent	2295	2372	2491	--	--
	--	2438			

1 P R O C E E D I N G S

2 (9:00 a.m.)

3 SPECIAL MASTER HASTINGS: Good morning to
4 all in the courtroom and if there are any of you
5 listening in at home.

6 We had a technical breakthrough in the last
7 few hours, and we were able to work the system so that
8 we can be on phone conferencing this morning for the
9 testimony of the witness coming in by telephone from
10 England, Dr. Chadwick.

11 I apologize for the information I gave out
12 yesterday that the phone conferencing wouldn't be
13 available, but I'm glad that it is for those who are
14 able to listen.

15 With that, we've got Dr. Chadwick on the
16 line. Dr. Chadwick, can you hear me? Dr. Chadwick,
17 can you hear me?

18 DR. CHADWICK: I can, yes.

19 SPECIAL MASTER HASTINGS: Yes. This is
20 Special Master Hastings.

21 DR. CHADWICK: Hi.

22 SPECIAL MASTER HASTINGS: Hello. Good
23 morning to you.

24 DR. CHADWICK: Good morning.

25 SPECIAL MASTER HASTINGS: Or afternoon

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CHADWICK - DIRECT

1 perhaps where you are.

2 DR. CHADWICK: Yes.

3 SPECIAL MASTER HASTINGS: I'm going to ask
4 you, please. We're going to give you the oath for
5 testifying here. I'm going to ask you to raise your
6 right hand.

7 Whereupon,

8 NICHOLAS C. CHADWICK

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

11 SPECIAL MASTER HASTINGS: All right. Who
12 will be doing the questioning?

13 MS. PATTON: I will be.

14 SPECIAL MASTER HASTINGS: Ms. Patton will be
15 doing the initial questioning.

16 DIRECT EXAMINATION

17 BY MS. PATTON:

18 Q Good afternoon, Dr. Chadwick.

19 A Hi.

20 Q Can you please state your name for the
21 record?

22 A Yes. Nicholas Chadwick. Nicholas Charles
23 Chadwick.

24 Q And do you recall writing a declaration for
25 this case, which you signed on May 23, 2007?

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1 A Yes, I do.

2 MS. PATTON: For the record, we'll be
3 referring to Respondent's Exhibit QQ, which was filed
4 on May 25, 2007.

5 BY MS. PATTON:

6 Q Dr. Chadwick, do you swear under penalty of
7 perjury that the contents in that declaration are true
8 to the best of your knowledge?

9 A Yes, I do.

10 Q We're not going to go through the entirety
11 of your declaration, but I'm going to ask you a couple
12 questions about several portions of that declaration
13 that we'd like the Court to pay particular attention
14 to.

15 A Okay.

16 Q You stated in there that you began working
17 in Dr. Wakefield's lab at the Royal Free in 1994. Is
18 that right?

19 A Yes, that's right.

20 Q And the lab started focusing on samples and
21 testing from autistic patients in 1996?

22 A Yes. Yes.

23 Q In your affidavit you state that you were
24 present in the operating room -- I think the operating
25 theater is what it's called over there -- during

CHADWICK - DIRECT

1 collection of gut biopsy material and cerebral spinal
2 fluid. Is that right?

3 A Yes, that's right. It was an endoscopy
4 suite rather than an operating theater.

5 Q And what was your role in the collection of
6 the material?

7 A My role was to take the material, bring it
8 to the lab and process it by extract RNA and then look
9 for evidence of measles RNA.

10 Q Okay. Did you personally test the gut
11 biopsy samples for measles RNA?

12 A Yes.

13 Q What tests did you perform?

14 A A PCR test, a polymerase chain reaction.

15 Q What results did you receive from the gut
16 biopsy materials for measles RNA?

17 A They were all negative.

18 Q They were always negative?

19 A Yes. There were a few cases of false
20 positive results, which I used a method to see whether
21 they were real positive results or false positive, and
22 in every case they turned out to be false positive
23 results. Essentially all the samples tested were
24 negative.

25 Q So when you say you got a positive and it

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CHADWICK - DIRECT

1 ended up being a false positive, what further testing
2 or what did you do to determine that those positives
3 were actually false positives?

4 A Well, we could sequence the products of the
5 PCR reaction and could find out whereabouts the virus
6 came from, and in every case it was a lab strain virus
7 based on the sequence and didn't match up with any
8 known wild-type or vaccine strains.

9 Q You sequenced wild-type that's in the lab
10 for control or to make sure your testing worked?

11 A Yes, that's right. It was just to validate
12 any positive samples. If we had a positive sample we
13 would have to sequence it to make sure it was a real
14 positive rather than a false positive.

15 Q Did you personally test CSF samples from
16 autistic children in the lab?

17 A Yes, I did. Again, they were all negative.
18 I can't recall how many I tested, but they were
19 definitely negative, the ones I did test.

20 Q Did you personally test peripheral blood
21 mononuclear cells, the PBMCs?

22 A Yes, that's right. I tested PBMC samples
23 from the blood of the autistic patients and also
24 cultured some of those blood cells in the lab to
25 enable any measles virus present to replicate and

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1 become detectible, but in every case again the samples
2 proved to be negative.

3 Q So you personally tested while you were in
4 Dr. Wakefield's lab gut biopsy material, CSF and
5 PBMCs?

6 A Yes, that's right.

7 Q And all the results were either negative, or
8 if they were positive it always turned out that they
9 were false positives?

10 A Yes, that's correct.

11 Q Did you inform Dr. Wakefield of the negative
12 results?

13 A Yes. Yes.

14 Q You state in your affidavit that you sent
15 samples of RNA to Dr. Kawashima.

16 A Yes, that's right. Dr. Kawashima had been
17 working on the detection of measles virus in a
18 different disease, and Dr. Wakefield thought it would
19 be a good idea to use his methodology to see if any of
20 our samples proved positive using his methods.

21 Q Dr. Chadwick, what was your role in sending
22 the samples to Dr. Kawashima?

23 A My role was just to put the samples in test
24 tubes and randomize them, code them and randomize them
25 so that only we would know which samples were which

CHADWICK - DIRECT

1 and Dr. Kawashima wouldn't know which samples he was
2 testing.

3 Q What were the results of Dr. Kawashima's
4 testing?

5 A Well, some of the samples we sent over as
6 duplicate samples so if one of them was to come up
7 positive then we would expect the other sample to come
8 up positive as well. In every case where he did have
9 a positive result then the duplicate didn't match
10 that, which led us to question his results or led me
11 to question his results.

12 When he told us that he had some positive
13 results he sent us the sequencing data back, but the
14 sequencing data matched up with the positive control
15 samples that we sent out to him, which indicated to me
16 that he had contaminated his samples and they were
17 false positive samples.

18 Q Based on the coding that you had done
19 beforehand, you knew that all of the positives that he
20 was reporting were false positives?

21 A Yes, that's right. I was pretty sure based
22 on, you know, how I'd coded the samples.

23 Q Did you tell Dr. Wakefield about the
24 problems with Dr. Kawashima's results?

25 A Yes, I did.

CHADWICK - DIRECT

1 Q You state in the affidavit that during your
2 time on your Ph.D. research in Dr. Wakefield's lab you
3 only obtained nine positive PCR results for measles.
4 Every time you did that you sequenced them?

5 A That's correct, yes. We sent it off to a
6 sequencing lab to be sequenced, and the data that came
7 back showed that they were all false positive results.

8 Q Every positive result you got was a false
9 positive?

10 A Yes. Yes, apart from the case of the
11 positive control samples which we had, which were a
12 measles infection, a brain disease. We were able to
13 detect measles virus in those cases, so I was
14 confident that the methods were working fine.

15 Q Towards the end of your affidavit you state
16 that you had reservations about the
17 immunohistochemistry done to detect measles virus,
18 specifically the use of an antibody from Porton Down?

19 A Yes, that's right. The antibody seemed to
20 cross-react.

21 Experiments we did in the lab seemed to show
22 that the antibody cross-reacted with bacterial
23 proteins, which I think is an artifact of how the
24 antibody was made, and that led us or led me to think
25 that it may have been cross-reacting with bacteria in

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CHADWICK - DIRECT

1 the guts of patients rather than measles virus.

2 Q Now, that would lead to contamination?

3 A Well, it would lead to a false positive
4 result. Say for instance if the antibody was binding
5 to something in the guts of these patients, it may
6 well have been a bacteria rather than the measles
7 virus.

8 Q Okay. Producing the false positives in
9 those?

10 A Yes, that's correct.

11 Q You also state in your affidavit that you
12 believe Dr. Wakefield was aware of all of your
13 negative results when he submitted his paper, "Ileal
14 Lymphonodular Hyperplasia, Nonspecific Colitis and
15 Pervasive Developmental Disorder," which was published
16 in 1998 to the Lancet.

17 A Yes, that's correct.

18 Q You were working at the lab at that time,
19 and you had actually published some articles with Dr.
20 Wakefield on other subjects, hadn't you?

21 A Yes. Yes.

22 Q Why isn't your name on the paper I just
23 referenced?

24 A Well, my name isn't on that because none of
25 my data went into that paper.

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CHADWICK - CROSS

1 A I'm not aware of that.

2 Q Are you aware that the Kawashima Lab is also
3 not the lab in question here?

4 A Well, I don't know the details of the case,
5 to be honest.

6 Q When you were approached to testify in this
7 matter, what were you asked to do?

8 A I was asked to provide a statement regarding
9 the work I did for Dr. Wakefield relating to the
10 autistic patients.

11 Q And did you ask why?

12 A Sorry. I couldn't hear that last question.

13 Q Did you ask why?

14 A Did I ask why? Because it was a case
15 regarding the safety of the vaccine.

16 Q Now, you testified that you worked with
17 in-situ PCR. Is that it?

18 A Yes. This was a few years before any of the
19 autistic work was being undertaken. I did a few
20 months of working on this methodology.

21 Q In-situ PCR?

22 A Yes. I did a few months at the beginning of
23 my project with Dr. Wakefield, and I did a few months
24 at the very end as well on in-situ PCR.

25 Q So this was all on in-situ PCR? Is that

CHADWICK - CROSS

1 correct?

2 A The work that was in my thesis relating to
3 autistic patients was using normal PCR, not in-situ
4 PCR. The in-situ PCR work I performed was never
5 written up.

6 Q I see. So the in-situ PCR is more specific
7 than the regular PCR, isn't it?

8 A No, that's not the case.

9 Q It's not?

10 A No, it's not specific. Because of the
11 methodology it's actually less specific so there's
12 less way of being certain about what is being
13 detected.

14 Q Okay. Doctor, did you at any time use
15 TaqMan PCR?

16 A No. TaqMan PCR wasn't really available
17 while I was doing the Ph.D. It was something which
18 came afterwards.

19 Q I see. Are you aware that the case that
20 we're dealing with involves TaqMan PCR?

21 A I'm not aware, no. No.

22 Q Are you aware that the lab that we're
23 dealing with involves the O'Leary Lab in Dublin,
24 Ireland?

25 A Okay. I've heard of that lab, but I didn't

CHADWICK - CROSS

1 know that that was the lab that you were using in this
2 case.

3 Q And you've had no relationship with the
4 Dublin lab, have you?

5 A No.

6 Q You have no knowledge of their procedures or
7 the testing that was done there, do you?

8 A No. I mean, I'm aware of TaqMan PCR, but
9 that's all I know about the O'Leary Lab.

10 Q And as of the date that you left Dr.
11 Wakefield's lab, you had not utilized TaqMan PCR in an
12 experiment, had you?

13 A No.

14 Q Doctor, is there anybody with you?

15 A No.

16 Q No? You're by yourself?

17 A Yes.

18 MS. CHIN-CAPLAN: Okay. I have no further
19 questions.

20 SPECIAL MASTER HASTINGS: Any redirect?

21 MS. PATTON: No, sir.

22 SPECIAL MASTER HASTINGS: Dr. Chadwick,
23 again this is Special Master Hastings with the Court
24 in Washington. I want to thank you again for taking
25 the time to be with us. You're excused at this time.

CHADWICK - CROSS

1 THE WITNESS: Okay. Thanks so much.

2 SPECIAL MASTER HASTINGS: Thank you, sir.

3 (Witness excused.)

4 SPECIAL MASTER HASTINGS: So, Mr. Matanoski,
5 we'll be taking Dr. Brent's testimony next?

6 MR. MATANOSKI: That's correct, sir.

7 SPECIAL MASTER HASTINGS: All right. Maybe
8 while we're getting the phone out of the way Dr. Brent
9 could take the witness stand.

10 DR. BRENT: Yes, sir.

11 (Pause.)

12 MS. RENZI: Special Master, may I?

13 SPECIAL MASTER HASTINGS: Yes, please. We
14 have now Dr. Brent in the witness chair, and Ms. Renzi
15 will be doing the examination for the government.

16 Dr. Brent, I'm going to ask you to raise
17 your right hand.

18 Whereupon,

19 JEFFREY BRENT

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

22 SPECIAL MASTER HASTINGS: All right. Ms.
23 Renzi, when you're ready go ahead.

24 //

25 //

BRENT - DIRECT

1 DIRECT EXAMINATION

2 BY MS. RENZI:

3 Q Good morning, Dr. Brent.

4 A Good morning, Ms. Renzi.

5 Q Could you please state your name for the

6 Court?

7 A Sure. It is Jeffrey Brent, B-R-E-N-T, M.D.

8 Q And what are your professional titles?

9 SPECIAL MASTER HASTINGS: Please speak up.

10 MS. RENZI: Okay. I will speak up.

11 BY MS. RENZI:

12 Q What are your professional titles?

13 A I am presently a full clinical Professor of

14 Pediatrics and Internal Medicine at the University of

15 Colorado Health Sciences Center in Denver.

16 Q And do you also maintain a private practice?

17 A Yes. I have a private practice which is a

18 group practice. It's a single specialty practice that

19 deals solely with issues related to medical

20 toxicology. The name of the practice is called

21 Toxicology Associates.

22 Q And could you briefly go through your

23 education and training?

24 A Okay. How far back do you want me to go?

25 Q Start with your undergraduate degree.

BRENT - DIRECT

1 A Okay. You may have listened to me long
2 enough to realize my undergraduate was obtained in New
3 York where I went to college and subsequent to that
4 did a Master's and subsequently a Ph.D. in
5 Biochemistry at the Mount Sinai School of Medicine in
6 New York.

7 Following that I went to Columbia University
8 College of Physicians and Surgeons as a postdoctoral
9 fellow there. After completion of my postdoctoral
10 fellowship I attended medical school at the State
11 University of New York School of Medicine at Buffalo,
12 New York, and then went to Harvard where I served as
13 an intern and subsequently ended up completing my
14 primary residency at Emory University School of
15 Medicine in Atlanta.

16 Once I graduated from that I moved to
17 Colorado to pursue a subspecialty fellowship in
18 medical toxicology. That was a two-year fellowship.
19 I did that fellowship from 1987 to 1989, and upon
20 completion of the fellowship I got offered a faculty
21 appointment to stay on.

22 It was a very attractive offer and I stayed
23 on, and I've remained basically in Denver on faculty
24 and in practice ever since.

25 Q Could you briefly list some of the honors

BRENT - DIRECT

1 you have received?

2 A I could. I mean, you know, they're listed
3 on my curriculum vitae. I assume everybody has a
4 copy. I can give you one or two examples without
5 going into any detail.

6 It's interesting when you think of honors.
7 There are ones that are the most prestigious and there
8 are the ones that are the most important to you, and
9 they're not always the same.

10 For example, the one that to me is the most
11 important to me was when I was given the Excellence in
12 Teaching Award from the second year medical students.
13 Not a big thing in the world, but I was touched by
14 that.

15 Probably the most prestigious was last year
16 I received what's called the Louis Roche Award from
17 the European Association of Poison Control Centers and
18 Clinical Toxicologists. I guess it's the year before
19 last now.

20 They award the Louis Roche Award to one
21 person each year as an acknowledgement of their
22 contributions in the field, and associated with that I
23 had to go and give what they call a Louis Roche
24 lecture, which is a big lecture that is at a meeting.
25 That was in Berlin.

BRENT - DIRECT

1 Q Have you had occasion to deliver to
2 professional groups lectures on toxicology?

3 A Quite often, yes. That is something that I
4 do quite a bit. I get invited to lecture not
5 infrequently both in the United States and abroad.

6 I've given multiple lectures -- I think most
7 of them are listed in my curriculum vitae -- on
8 various aspects of toxicology, including mercury
9 toxicity.

10 Q And what professional organizations and
11 honorary societies are you a member of?

12 A A whole group of them. The American Academy
13 of Clinical Toxicology, the American College of
14 Medical Toxicology, the American Medical Association,
15 the American College of Occupational Environmental
16 Medicine, European associations. I think that's most
17 of them. There might be one or two others.

18 Q And do you currently serve as a peer
19 reviewer for any medical journals?

20 A Yes. Oh, yes.

21 Q Could you list a few?

22 A Sure. I end up spending a lot of time being
23 a peer reviewer. I'm senior editor of one journal, so
24 I obviously peer review quite a bit for that, and
25 that's for the journal called Clinical Toxicology.

BRENT - DIRECT

1 Clinical Toxicology is the largest circulation peer
2 reviewed journal in the world devoted to clinical
3 toxicology.

4 I also routinely peer review for a number of
5 other toxicology journals plus general medical
6 journals. I review quite a bit for New England
7 Journal of Medicine, Journal of the American Medical
8 Association, some occupational medicine journals,
9 environmental medicine journals.

10 Q And you have published over 200 peer
11 reviewed articles relating to toxicology? Is that
12 correct?

13 A Well, my publication lists over 200
14 publications. That includes peer reviewed articles,
15 books, book chapters, letters, abstracts and so on,
16 reviews of various kinds.

17 Q Have you ever received funding from a
18 pharmaceutical company for a speaking engagement?

19 A I recall back it was in the vicinity --
20 don't hold me to this year, but I think it was maybe
21 in the vicinity of 1991. It was shortly after I
22 finished my fellowship.

23 I gave a lecture for which a pharmaceutical
24 company paid me with an honorarium for giving that
25 lecture. I don't recall any subsequent to that.

2300

BRENT - DIRECT

1 Q And have you ever received money from a
2 pharmaceutical company for research?

3 A Back once again in the early 1990s I had
4 some grants when I was a fellow. I had just passed my
5 fellowship. I had a very, very small grant from a
6 pharmaceutical company, which I had a couple of other
7 grants from pharmaceutical companies.

8 I have not taken a grant -- I have not taken
9 pharmaceutical company research money -- probably in
10 15 years. However, I was an investigator on an FDA
11 grant. The money came from the FDA for a clinical
12 trial of a new antidote. A pharmaceutical company was
13 sort of my partner in that grant. I was the principal
14 investigator, but they were on the grant as well.

15 Q And other than your testimony today, have
16 you ever testified as an expert witness in a legal
17 case?

18 A Yes, I have.

19 Q Approximately how many times?

20 A Oh, boy. I don't know. Since graduating
21 from my fellowship in 1989, several dozen times
22 usually.

23 Q Have you ever testified as an expert witness
24 on behalf of a pharmaceutical company?

25 A I have.

BRENT - DIRECT

1 Q Can you recall the circumstances?

2 A I probably have over the years at least a
3 half a dozen times. One on behalf of Pfizer
4 Pharmaceuticals with regard to a medication that
5 caused hepatotoxicity and has subsequently been taken
6 off the market called Rezulin.

7 I gave testimony once on behalf of Merck
8 Pharmaceuticals. Another example, I think probably
9 the most relevant example, is I gave testimony once in
10 a case where the allegation was autism induced by
11 thimerosal.

12 Q And do you recall the name of that case?

13 A Yes. That was the Easter case.

14 Q And were you an expert for the
15 pharmaceutical company or the defendant? For the
16 defendant pharmaceutical company?

17 A For the defendant, GlaxoSmithKline, yes.

18 Q And did you testify at a trial in that case?

19 A No. I testified at deposition in that case.
20 There was ultimately no trial because the case was
21 dismissed on the basis of a Daubert motion.

22 Q Have you ever testified as a legal expert on
23 behalf of a medical device company?

24 A Yes, I have.

25 Q Could you describe that, please?

BRENT - DIRECT

1 A Sure. In the early 1990s I was chair of a
2 national panel which was assessing the issues of
3 potential health effects in terms of systemic disease
4 related to silicone breast implants.

5 There was a lot of concern about it at the
6 time, and we had concluded that the data was very
7 anecdotal and didn't support systemic effects. I
8 think subsequently everybody has come to that same
9 conclusion.

10 However, during that time period of the
11 1990s there was a good deal of litigation going on
12 regarding silicone breast implants, and manufacturers
13 came to me and said would you testify regarding your
14 work that you did on silicone breast implants. I said
15 I would, time permitting, and I testified in a number
16 of those trials over the 1990s.

17 Q I'd like to move on now to your experience.
18 Could you describe your position as a clinical
19 professor at the University of Colorado Health
20 Sciences Center?

21 A Right. My duties at the University of
22 Colorado Health Sciences Center involve three things.
23 It involves some patient care, it involves teaching,
24 and it involves maintaining my academic activities.
25 Those academic activities are reviewed annually.

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BRENT - DIRECT

1 The teaching is both my direct teaching in
2 the medical school by way of lectures and other
3 similar forms of teaching and bedside teaching. We
4 have a service which is called the clinical
5 pharmacology and toxicology consultation service where
6 we do consultations regarding adverse effects,
7 toxicology consultations regarding adverse effects of
8 drugs or chemicals, adverse drug reactions, whatever,
9 on people in the hospital.

10 Those consultations, because it's a teaching
11 hospital, are generally primarily done by the group on
12 the toxicology service, which generally involves
13 probably about five or six people, including a medical
14 toxicology fellow in training, maybe one or two
15 residents, a couple of medical students.

16 They do the initial assessment and then I
17 round with the patients at the bedside with them and
18 go over their assessment, go over their examination
19 and see how it concurs with my examination, go over
20 the laboratories, and then we discuss a plan of what
21 to do next, what our impressions are, and then the
22 house staff usually writes up a consultation note,
23 which I generally co-sign.

24 Q And could you describe the nature of your
25 private practice?

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BRENT - DIRECT

1 A My private practice is Toxicology
2 Associates, and at Toxicology Associates we have three
3 major missions and that is patient care, teaching and
4 research in the area of medical toxicology.

5 Our patient care component, we actually have
6 two components to the patient care component, an
7 inpatient and an outpatient one. Our inpatient
8 component involves admitting patients directly to our
9 hospital. They're generally admitted directly to us.
10 Most often our hospitalized patients are intensive
11 care unit patients. I do a good deal of intensive
12 care medicine.

13 These are patients who have been acutely
14 poisoned for one reason or another. It could be a
15 drug overdose. It could be a child with an accidental
16 poisoning. In Denver at this time of the year we
17 treat a lot of rattlesnake bites. A couple of months
18 from now it starts getting a little cooler. We start
19 treating a lot of black widow spider bites. In the
20 winter we treat a lot of carbon monoxide poisoning
21 from heating systems.

22 We have patients who have adverse drug
23 reactions that can make them very sick, so there's a
24 number of ways that patients can end up coming to our
25 toxicology service and being admitted to our inpatient

BRENT - DIRECT

1 service.

2 We also have an outpatient service, a
3 clinic, and in the clinic we see patients who have
4 concerns about occupational or environmental
5 exposures.

6 We will sometimes follow up patients that
7 we've seen in the hospital, and we also do a good deal
8 of following workers who are exposed to hazardous
9 material in their work where OSHA mandates that these
10 workers get followed periodically and evaluated, so we
11 do a lot of that as well.

12 Q Have you ever treated a patient with mercury
13 toxicity?

14 A Quite a number of times. Yes, I have.

15 Q Could you describe some of the circumstances
16 in which you've treated a patient?

17 A Sure. Absolutely.

18 SPECIAL MASTER HASTINGS: Before we go into
19 that question, let me interrupt.

20 Just for the benefit of those who may just
21 be coming on line within the last few minutes to
22 listen in on the phone conferencing, I wanted to let
23 you know that right now we have the testimony of Dr.
24 Brent, an expert witness for the Respondent, a
25 toxicologist from the University of Colorado. We have

BRENT - DIRECT

1 just gone through his credentials and background.

2 I wanted to let the folks know that we
3 finished with the testimony of Dr. Chadwick earlier.
4 I told you yesterday the best information we had at
5 that point was we would not be able to put Dr.
6 Chadwick's testimony -- Dr. Chadwick was the witness
7 who was going to be coming in by telephone. We
8 wouldn't be able to put him on the phone conferencing.

9 It turned out at a last minute breakthrough
10 here we were able to put Dr. Chadwick's testimony on
11 this morning. I apologize to anyone who tuned in
12 after that. He gave very brief testimony, about 15 to
13 20 minutes. That testimony will be available by
14 downloading the audio from our website or by viewing
15 the transcript on our website.

16 I apologize to those who missed that
17 testimony, but now we've got Dr. Brent testifying for
18 the government with Ms. Renzi questioning him.

19 Mr. Renzi, why don't you ask that last
20 question again?

21 BY MS. RENZI:

22 Q Could you describe some of the patients
23 you've treated with mercury toxicity?

24 A Well, mercury toxicity is distinctly unusual
25 to see, so most of the time when we see it it's a very

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1 unusual circumstance.

2 I've seen some workers who were overexposed
3 to mercury. I have had a patient not too long ago who
4 was a dentist and bought a dental practice from
5 another dentist who was apparently rather sloppy and
6 had spilled mercury from fillings on the floor. It
7 was a rug floor, and apparently there was mercury in
8 the rug.

9 Now, what this dentist who was my patient
10 did -- it was a woman -- is she not only ran the
11 practice, but she would also clean it. She used the
12 vacuum cleaner on the rug. Never use a vacuum cleaner
13 on a mercury contaminated rug because it vaporizes all
14 the mercury. She developed a neurological syndrome
15 and was found to have very high levels of mercury. We
16 ended up chelating her.

17 I had a patient who we believe her husband
18 tried to kill her by putting large amounts of liquid
19 mercury in her study in an area where it wouldn't be
20 seen and allowing it to vaporize in the air.

21 Probably my most colorful patient was a
22 gentleman we took care of -- we actually published the
23 case -- about a year or so ago who had a form of
24 Munchausen syndrome where they like to make themselves
25 sick and get medical care. He injected mercury

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1 intravenously, liquid mercury intravenously, and then
2 came to my hospital.

3 Q Have you ever treated or examined a child
4 diagnosed with autism?

5 A Oh, yes.

6 Q Under what circumstances?

7 SPECIAL MASTER HASTINGS: Do speak up, Ms.
8 Renzi.

9 THE WITNESS: Well, under a number of
10 circumstances. One is that autistic children, just
11 like any other child, can end up accidentally
12 overdosing, and in fact it's a little bit more common
13 in autism because they have a tendency towards pica.
14 They have a tendency to put lots of stuff in their
15 mouth.

16 So we have had patients on our service who
17 were autistic who had overdose on various things. It
18 happens occasionally. It's unusual, but we do see it
19 from time to time.

20 When all this stuff about mercury toxicity
21 and autism spectrum disorder found its way into the
22 blogosphere and websites we started to get a number of
23 calls from mothers primarily asking about and wanting
24 to know if their child should be chelated with a
25 mercury toxic. We've seen a number of those as well.

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1 BY MS. RENZI:

2 Q I want to move on to your opinions today.
3 Do you have an opinion whether Michelle Cedillo's
4 autism is causally related to the receipt of
5 thimerosal-containing vaccines in conjunction with an
6 MMR vaccine?

7 A Yes, I do have an opinion about that.

8 Q What is that?

9 A Well, I've looked at the medical records
10 quite extensively. I've reviewed the literature in a
11 great deal of detail, and I think it's clear there's
12 no relationship between thimerosal administration and
13 the development of autism or ASD.

14 Q And do you have an opinion whether it is
15 more likely than not that the thimerosal-containing
16 vaccines that Michelle Cedillo received caused
17 an immune suppression that was ongoing at the time she
18 received her MMR vaccine?

19 A There's absolutely no evidence that I saw
20 that would suggest that thimerosal in the doses
21 administered in vaccines would cause
22 immunosuppression.

23 Q Doctor, you discussed in your credentials
24 that you're a medical toxicologist. Could you just
25 describe medical toxicology and how that differs from

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1 toxicology?

2 A Sure, I would be glad to.

3 SPECIAL MASTER HASTINGS: Now, we just got a
4 slide on the screen so let me interrupt again.

5 It looks like we've got a set of slides that
6 Dr. Brent is going to be showing, and we have a paper
7 copy of those slides so let's mark that paper copy as
8 Respondent's Trial Exhibit No. 17.

9 We've just put on the screen page 1 of that
10 presentation, so go ahead, Dr. Brent.

11 THE WITNESS: Sure. Well, it's important
12 before I tell you what a medical toxicologist is, it's
13 important to understand what a toxicologist is.

14 Toxicology is simply the science of the
15 adverse effects of chemical substances on living
16 systems. There's no formal requirement to being
17 called a toxicologist. Anybody can tell you I've
18 studied the stuff and therefore, you know, I'm a
19 toxicologist.

20 In contrast, the use of the term medical
21 toxicology is a specific term that has attached to it
22 a whole series of very formal and official
23 requirements, and that comes from the fact that in
24 medicine we have a number of specialties -- you know,
25 we have pediatrics, internal medicine, surgery, so on,

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1 radiology -- and a number of subspecialties under
2 those specialties, and all of those, all of the
3 recognized specialties and subspecialties, are under
4 the purview of what's called the American Board of
5 Medical Specialties.

6 Medical toxicology is a subspecialty. It's
7 a recognized subspecialty by the American Board of
8 Medical Specialties, and therefore to call yourself a
9 medical toxicologist you have to complete their
10 requirements and get certified as a medical
11 toxicologist, much like if you were going to call
12 yourself a cardiologist or if you were going to call
13 yourself a thoracic surgeon. You know, you'd have
14 specific requirements you'd have to meet under ABMS.

15 For medical toxicology you have to complete
16 a primary residency in a clinical field. Following
17 that you do a two-year full-time medical toxicology
18 subspecialty fellowship in an accredited program after
19 which you are then eligible to take the medical
20 toxicology certifying examination, and if you
21 successfully complete that certifying examination then
22 you are certified as a subspecialty, a board certified
23 medical toxicologist.

24 BY MS. RENZI:

25 Q And you are one of approximately 250 board

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1 certified medical toxicologists in the United States?

2 A Yes. It's fascinating. You know, as
3 interesting as this field is, there's a very small
4 number of us that are actually medical toxicologists.
5 About 250 I think, 260 certified ones in the United
6 States today.

7 Q Dr. Brent, is it your understanding of this
8 case that the receipt of thimerosal-containing
9 vaccines by Michelle Cedillo caused an
10 immunosuppression that was ongoing at the time she
11 received her MMR vaccine?

12 A No. I think there's no evidence to support
13 that.

14 Q Okay. We'll move on to Slide 2. What is
15 thimerosal?

16 A Thimerosal is a preservative. It was a
17 preservative that was in vaccines and still is in some
18 vaccines and other medications that are given to
19 patients. It's been widely used as a pharmaceutical
20 since the 1920s.

21 In 1931, Powell and Jamieson published a
22 major study, which for its time was a state-of-the-art
23 safety study, which established its safety based on
24 current standards, and it continued to be used.

25 Actually its use blossomed incredibly during

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1 World War II because what happened during World War II
2 is the military surgeons learned that where there is
3 penetrating trauma associated with blood loss, i.e.,
4 gunshot wounds, that there would be a significant
5 beneficial effect on outcome, saved lives, if the
6 blood volume that was lost from bleeding was
7 aggressively replaced with blood plasma.

8 The blood plasma was preserved with
9 thimerosal, a great deal of use of very, very large
10 quantities of thimerosal during that period, with
11 clearly an excellent safety profile.

12 Q And how is thimerosal different from ethyl
13 mercury?

14 A There's a very important difference between
15 thimerosal and ethyl mercury.

16 Q And we're on Slide 3 now.

17 A What you can see, if I may just switch
18 around here for a minute. I'll try to bring the mic
19 over. What you can see here on the screen is the
20 thimerosal molecule. Thimerosal is chemically ethyl
21 mercury thiosalicylate.

22 Now, here you see this Hg atom. That's a
23 mercury atom. You see it's right here in the middle
24 of the molecule. This part of the molecule to the
25 left is the thiosalicylate part of the molecule, and

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1 this part to the right is the ethyl mercury part of
2 the molecule.

3 As soon as this gets into the body, this
4 bond, which is a relatively weak bond, breaks and
5 hence you end up simply with ethyl mercury as opposed
6 to the whole thimerosal molecule, so thimerosal
7 becomes ethyl mercury plus thiosalicylate.

8 There's probably even some disassociation of
9 this bond in the vial before it even gets to the body,
10 so clearly ethyl mercury is a very different molecule
11 from thimerosal.

12 Q Doctor, on page 3 of Dr. Aposhian's report,
13 and that's Petitioners' Exhibit 55, he states that it
14 is an enigma that thimerosal was included in childhood
15 vaccines, and I'll quote, "because there is no bona
16 fide evidence for either thimerosal's presumed
17 bacteriostatic activity or presumed safety."

18 Have you read that?

19 A Yes. Yes, I have read that.

20 Q There's also a footnote cited by Dr.
21 Aposhian that relies on two government rulings for
22 that statement, and I'd like to show those.

23 A Right.

24 Q The first one is a 1982 FDA ruling that's 47
25 Federal Register 436. Have you read this ruling?

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1 A Well, actually, Ms. Renzi, it wasn't a
2 ruling. It was a notice of proposed rulemaking and
3 request for comments, and I have read it, yes.

4 MS. RENZI: And I also have passed out a
5 copy to the Court and to Petitioners' counsel of the
6 actual rulings cited by Dr. Aposhian.

7 SPECIAL MASTER HASTINGS: Right.

8 MS. RENZI: I think that would be Exhibit
9 18.

10 SPECIAL MASTER HASTINGS: Let's make that
11 Respondent's Trial Exhibit 18.

12 BY MS. RENZI:

13 Q I'm sorry, Dr. Brent. Please continue.

14 A Yes, I have read it, and what it was was an
15 assessment by an FDA panel of the use of a series of
16 mercurial compounds as over-the-counter sort of
17 disinfectants.

18 We probably all remember growing up that
19 we've had merthiolate put on our wounds. Thimerosal.
20 There were a whole series of these organic mercurial
21 disinfectants, and the panel that was assessing the
22 safety and efficacy of those disinfectants had
23 expressed three areas of concern.

24 One is that if you in an unregulated fashion
25 just pour all the stuff directly on a wound -- you

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1 know, you buy it over the counter. You just pour it
2 on the wound. You can get a very high concentration
3 on the wound, and therefore you can get a
4 concentration that could be potentially tissue toxic.

5 The second concern was that wounds have
6 associated with them some blood and pus and so on, and
7 they cited data that shows that thimerosal loses its
8 efficacy as a bacteria static agent when it comes in
9 contact with pus and therefore may not be a good thing
10 to use on a wound.

11 The third concern they expressed was one of
12 potential allergy.

13 Q Is this proposed rule in any way relevant to
14 demonstrate the doses of thimerosal contained in
15 thimerosal-containing vaccines are unsafe?

16 A No. No. It just dealt with that unique
17 circumstance of putting it on. You're buying it over-
18 the-counter and just pouring it on wounds.

19 It had nothing to do with its potential use
20 as a preservative in vaccines where these various
21 concerns wouldn't apply.

22 Q And is it relevant to demonstrate that the
23 doses of thimerosal contained in thimerosal-containing
24 vaccines cause immunosuppression?

25 A No. There's nothing about that.

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1 MS. RENZI: The second ruling that Dr.
2 Aposhian refers to us 21 C.F.R. 310.545. We can pull
3 that up on the screen as Slide 4, and I've also passed
4 out the actual ruling to the Court and Petitioners'
5 counsel

6 SPECIAL MASTER HASTINGS: So let's mark that
7 as Respondent's Trial Exhibit No. 19.

8 BY MS. RENZI:

9 Q And are you familiar with this ruling?

10 A I am.

11 Q Could you describe it, please?

12 A Sure. Thimerosal, like so many substances
13 that have been sort of used for many, many, many years
14 since the FDA evolved, ended up being sort of
15 grandfathered in and was used, did not go through the
16 typical new drug application process which right now
17 is a very, very complex process that the FDA requires
18 of new drugs to certify that they're appropriately
19 safe and effective for use.

20 What they did is they listed here
21 approximately 700 substances that had been used
22 medicinally over the years and had just sort of ended
23 up going through this grandfather process of being
24 used without the FDA doing a formal assessment of
25 their safety.

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1 Yes, thimerosal was on that list. A number
2 of interesting substances were on that list if you
3 look. For example, aspirin is on that list;
4 lidocaine, which you might get if you go to a dentist
5 and get an injection to numb your gums; honey in cough
6 syrup, in cough drops is on that list. I was very
7 disappointed to see caffeine was on the list. I maybe
8 wonder if I should give up Starbucks.

9 The calcium salts which we give now to women
10 particularly who have bone loss to prevent that from
11 happening; the iron salts that we give to treat iron
12 deficiency anemia, or pregnant women very often need
13 iron salt; codeine. Almost all the vitamins in your
14 daily vitamin pill are on that list.

15 We could go on quite a bit with what's on
16 that list. You'll find wheat germ on that list,
17 garlic and thimerosal.

18 Q Is this regulation in any way relevant to
19 demonstrate that the doses of thimerosal and
20 thimerosal-containing vaccine are unsafe?

21 A There's nothing in this regulation that says
22 that.

23 Q Or that they cause autism?

24 A No. There's nothing that says that.

25 Q As a medical toxicologist, how do you

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1 determine whether a person's exposure to a certain
2 chemical has caused a particular outcome?

3 A Well, in medical toxicology we have a very
4 formal set of criteria that we go through to determine
5 when we see a patient whether a chemical to which the
6 patient was exposed may have caused the condition that
7 we're treating or that that patient has.

8 Although it's rather a complicated
9 formalism, it can be really boiled down to three very
10 basic and simple steps.

11 SPECIAL MASTER HASTINGS: We've got Slide 5
12 on the screen now?

13 MS. RENZI: Yes.

14 SPECIAL MASTER HASTINGS: Go ahead.

15 THE WITNESS: We just ask three simple
16 questions, and the first and very important one is
17 what was the patient exposed to. I have to know what
18 chemicals the patient was exposed to to know whether
19 that chemical caused the adverse effects. To what was
20 the patient exposed?

21 Then we ask the question can that exposure
22 to that chemical under any circumstance cause that
23 patient's disease. I put there, and I hope I've got
24 this right. I believe that's your legal concept of
25 general causation.

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1 If the answer is no, that this chemical is
2 not associated with that disease, then we really don't
3 have to look any further. If the answer is yes,
4 however, then the next question becomes did that
5 chemical in this particular patient under these
6 circumstances cause this disease.

7 In other words, did the patient get a
8 sufficient dose of the chemical under the right
9 circumstances that's been shown to be associated with
10 that disease, and I think you call that -- correct me
11 if I'm wrong -- specific causation.

12 We always tell students all you have to
13 remember is three words: what, can, did. That
14 embodies this formalism, which if you apply it it can
15 be a quite complex exercise, but this is essentially
16 the formalism that you have to go through to reach
17 conclusions about whether a chemical can cause a
18 disease in general and whether it may happen in a
19 particular patient.

20 BY MS. RENZI:

21 Q I'd like to move on now to in vitro studies.
22 Doctor, what is an in vitro study? We're going to
23 pull up Slide No. 6.

24 A We talk about two different kinds of
25 studies, and they are referred in the scientific

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1 literature to in vitro studies and in vivo studies.
2 An in vivo study or an in life study is a study that
3 is done in an intact animal or an intact human being.

4 On the other hand, many scientific studies
5 are done in the laboratory where we might work with
6 just cells that are taken from an animal or cells that
7 are taken from a human being, grown typically in
8 what's called a petri dish, and treated in some way
9 under experimental conditions. That's an in vitro
10 study. That's an in vitro study.

11 Q And if a chemical causes an adverse reaction
12 in vitro can you extrapolate that the same results
13 will occur in a human? We'll turn to Slide 7.

14 A Absolutely not. I'd like to make a couple
15 of points. Actually, if we could go back to Slide 6
16 for a minute?

17 It's important to realize that when you have
18 some cells growing, and I'll show you some pictures of
19 this in a bit. When you have some cells growing in a
20 petri dish in the laboratory they are in such a
21 dramatically different environment than when they are
22 in a whole animal or a whole human that they become
23 highly susceptible to all kinds of perturbations and
24 to all kinds of insults that would really never happen
25 when all the defenses that are present in the intact

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1 animal or the intact human are there.

2 Now we can go to the next slide. Let's
3 take, for example, so we don't get too abstract, let's
4 take mercurial compounds like ethyl mercury. If you
5 were to do an experiment where you just take some
6 cells from an animal and grow them in a petri dish and
7 then put ethyl mercury on them, that is completely
8 different from administering ethyl mercury to an
9 intact animal.

10 Because when the cells are in an intact
11 animal there are all kinds of protective systems that
12 the body has against foreign substances. In the case
13 of mercury compounds, for example, there's a protein
14 called metallothionein which binds and inactivates
15 mercury. There's glutathione which inactivates
16 mercury. There's cysteine which inactivates mercury.
17 There's a variety of other proteins to which mercury
18 binds and is inactivated.

19 If you look at the mercury, organic mercury
20 like ethyl mercury in the blood which is going out to
21 the tissues, almost all of it is in red blood cells.
22 Those red blood cells aren't present when you just put
23 the ethyl mercury on the cells.

24 So for that reason the cells become so
25 vulnerable and things that could kill cells in vitro

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1 at very low levels are harmless in vivo. Water. If
2 you put too much water on the cells you will kill
3 them.

4 The in vitro environment is a highly
5 vulnerable environment. Cells are very susceptible in
6 ways that they would not be in vivo, so you can never
7 make the assumption that affects you see in vitro
8 occur in vivo.

9 I was here actually when Dr. Aposhian
10 testified about that, and he himself said if you just
11 show in vitro results nobody will believe that it
12 occurs unless you can show it in an intact animal.

13 Q And has the IOM commented on the use of in
14 vitro studies?

15 A As a matter of fact they have specifically
16 even in this context. We see here the 2004 IOM report
17 about thimerosal and vaccines, and it discusses the
18 various in vitro studies.

19 As you can see, they say, "Demonstration of
20 an adverse effect of mercury in vitro does not readily
21 translate into a physiologic argument." I think this
22 is a well accepted concept in science.

23 MS. RENZI: And that's Respondent's Exhibit
24 JJ at page 140.

25 SPECIAL MASTER HASTINGS: Thank you.

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1 BY MS. RENZI:

2 Q Are in vitro studies ever useful?

3 A Oh, yes. They're used all the time.

4 Q When are they useful?

5 A Well, they're useful in a number of
6 circumstances. Number one, they're useful for what we
7 call hypothesis generation.

8 If I want to know if a compound causes some
9 potential effect before I go to the very large expense
10 of an animal study, for example, I might want to see
11 what happens in vitro. If it doesn't do anything in
12 vitro it's not going to happen in the animal.

13 If I know there is an effect in a human,
14 let's say, or in an animal and I want to study what
15 happens on the subcellular level I can do that by
16 studying the cells in vitro, but you can never say
17 that's exactly what's happening in the animal, in the
18 animal or the human, until you test the animal or the
19 human.

20 Q Both Drs. Aposhian and Byers rely on in
21 vitro studies to form their opinions that thimerosal-
22 containing vaccines cause immune suppression.

23 Specifically they rely on two studies that
24 I'd like to discuss with you now. One is the Goth
25 study, which is Petitioners' Exhibit 55 at Q, and the

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1 other one is the Agrawal study, which is Petitioners'
2 Exhibit 55 at Tab A.

3 In your opinion, is it reliable science to
4 extrapolate the results of these studies to conclude
5 that immunosuppression will occur in humans following
6 the receipt of thimerosal-containing vaccines?

7 A I think there's no reasonable way anybody
8 could conclude from the Goth and Agrawal studies that
9 the thimerosal from the vaccine would cause
10 immunosuppression.

11 Q We have the Goth study up on the screen as
12 Slide 8. Could you summarize the Goth study, please?

13 A Sure. It's an in vitro study, and it
14 studied a rare cell type in mice called the dendritic
15 cell. The dendritic cell plays a role in the
16 immunological response. They presented some data with
17 ethyl mercury and some data with thimerosal, but
18 really most of the meat of their experiments were done
19 with thimerosal.

20 Now, I'm not exactly sure why they did it
21 with thimerosal because if you'll recall cells in the
22 body are not exposed to thimerosal. They're exposed
23 to ethyl mercury following a thimerosal injection.
24 Thimerosal disassociates very quickly into ethyl
25 mercury.

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1 So they were looking at effects of
2 thimerosal, and we don't know to what extent, if any,
3 any of this translates into what would happen with
4 ethyl mercury. What they primarily studied were some
5 calcium influxes, which are part of the physiology of
6 these dendritic cells.

7 Q Dr. Aposhian testified that he found this
8 study compelling because the concentrations of
9 thimerosal that were used in this experiment was
10 almost equal to the concentration of thimerosal used
11 in thimerosal-containing vaccines. Is that correct?

12 A No. That is absolutely wrong.

13 Q Is the 100 nanomolars of thimerosal used in
14 the Goth study equivalent to the amount of thimerosal
15 that these cells would have been exposed to following
16 the administration of the thimerosal-containing
17 vaccine?

18 A Well, first of all you have to back up and
19 realize that following the administration of a
20 thimerosal-containing vaccine these cells would not be
21 exposed to any thimerosal at all. They would be
22 exposed to ethyl mercury, a different compound.

23 But let's put that part aside for a minute.
24 You know, we have to look at what the cells would
25 actually experience following the administration of

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1 the vaccine, the dose that they would get.

2 Now, the Goth study reported effects of
3 about 100 nanomolars when thimerosal was in the medium
4 in which the cells were incubated. Forgetting for a
5 minute that in the blood there is no thimerosal, let's
6 just put that aside. That amount, however, would be
7 equivalent to a mercury concentration of about 20
8 micrograms per liter. We convert 100 nanomolars over
9 to 20 micrograms per liter.

10 Now, it's critically important to realize
11 that we're talking about here's an example of how
12 dramatically different an in vitro and an in vivo
13 study can be. In the body when the cells are exposed
14 to mercury for a cell to be exposed to mercury the
15 mercury has to be free and available to interact with
16 that cell.

17 Now let me show you. We go to the next
18 slide, the little diagram.

19 Q And this is Slide 10.

20 A Here we have an example. Here we have a
21 picture of how cells experience substances that are in
22 the blood, and what you can see is that we have the
23 blood vessel and the blood is in the blood vessel.
24 The blood contains two things. It contains plasma and
25 cells. So we have the plasma, and we're not showing

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1 here red blood cells.

2 Now, here is the tissue. Tissues lie
3 outside of the blood vessels. So material from the
4 blood diffuses in and out of the tissues through these
5 little pores in the blood vessels, and if they're
6 small enough to get through these pores it will go
7 through and interact with the cells. This is, for
8 example, how cells would experience ethyl mercury if
9 they were exposed to ethyl mercury, if there's ethyl
10 mercury in the blood.

11 Now let's look at what happens when there's
12 ethyl mercury in the blood. We know --

13 SPECIAL MASTER HASTINGS: Now we've gone to
14 Slide No. 11.

15 THE WITNESS: We know that for
16 organomercurials, greater than 90 percent of the
17 organomercurial is actually in the red blood cell. We
18 see here we have most of the mercury here in the red
19 blood cells. Ten percent would be in the plasma.

20 A lot of that 10 percent, by the way, and
21 I'm going to put this aside for a minute, but a lot of
22 that 10 percent would be bound to these proteins we
23 talked about, so the amount that's free and that can
24 get through these pores is probably a much smaller
25 percentage.

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1 Let's just use that 10 percent figure worst
2 case scenario. So what we see of the total mercury in
3 the blood, only this fraction of less than 10 percent
4 is actually free to interact with the cells.

5 Thus, when the Goth study has a mercury
6 concentration of 20 micrograms per liter from the
7 thimerosal in the medium and so the cells were
8 directly exposed to 20 micrograms per liter, that's
9 equivalent to 20 micrograms per liter in the plasma.

10 In order to get 20 micrograms per liter in
11 the plasma, we need a whole blood level of 200
12 micrograms per liter because 90 percent of it is in
13 the red cells. Two hundred micrograms per liter is an
14 incredibly high blood level. Most people in this
15 country are walking around with blood mercury levels
16 less than five micrograms per liter.

17 If you look at the Pichichero data after
18 vaccination, total blood levels are one to 1.6
19 micrograms per liter, and here we have an exposure
20 essentially equivalent to 200 micrograms per liter.

21 BY MS. RENZI:

22 Q Is this study scientifically reliable to
23 determine what will happen in humans following the
24 receipt of the thimerosal-containing vaccine?

25 A No. No, of course not. First of all --

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1 Q And we're on Slide 12 now.

2 A First of all, they used thimerosal, and
3 these cells aren't even exposed to thimerosal in the
4 body. As we just saw, the concentrations that they
5 used were unrealistically high. You never get these
6 kinds of concentrations from vaccines.

7 It's also important to remember that let's
8 just put all that aside. Let's just put all that
9 aside and say yes, they used ethyl mercury. They used
10 reasonable doses. Let's even say that. This study
11 still says nothing about the duration of effect.

12 You would expect that any effects they saw
13 would happen while the ethyl mercury was there and
14 then would go away once the ethyl mercury was gone. I
15 mean, you wouldn't expect anything they reported to be
16 a long-lasting or clinically significant effect.

17 Now, I looked at Michelle Cedillo's medical
18 records. Just as an example of the case here, her
19 last thimerosal exposure was approximately nine months
20 prior to receiving her MMR. Now, thimerosal in the
21 blood has about a eight day half-life, so that
22 thimerosal within about a month is essentially gone or
23 five weeks essentially gone.

24 So this thimerosal could not possibly have
25 been exerting any kind of effect nine months hence

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1 when she got her MMR vaccination.

2 Q Drs. Byers and Aposhian also rely on the
3 Agrawal study, and I'd like to go over that as well.

4 A Sure.

5 Q That's Slide No. 13. Could you describe the
6 Agrawal study?

7 A The Agrawal study was in many ways similar
8 to the Goth study. It also studied dendritic cells in
9 vitro, but these were human dendritic cells. They
10 too, like Goth, studied thimerosal, but not ethyl
11 mercury.

12 They found that at 50 nanomolars thimerosal
13 there was a shift in dendritic cell function towards
14 what we call a TH2 or a pro antibody production and
15 anti-inflammatory posture of the immune system. They
16 saw this at 50 nanomolars. They did not see this when
17 they went down to 10 nanomolars thimerosal.

18 Q And like with the Goth study, is the 50
19 nanomolars of thimerosal that was used in Agrawal
20 equivalent to the amount of thimerosal that these
21 types of cells would have been exposed to following
22 the administration of a thimerosal-containing vaccine?

23 A No. It's exactly the same thing. First of
24 all, they used thimerosal, and these cells would never
25 be exposed to thimerosal, but let's just put that

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1 matter aside for a minute.

2 The simple math tells us that 50 nanomolars
3 of thimerosal is equivalent to a blood mercury level
4 of 10 micrograms per liter. Now, once again this is
5 not whole blood. There's no red cells, so it's all
6 pure 10 micrograms per liter in the medium, just like
7 10 micrograms per liter in the plasma.

8 In order to get the 10 micrograms per liter
9 in the plasma you'd have to get a whole blood mercury
10 level of 100 micrograms per liter or actually probably
11 more for any interaction at this level in the cells,
12 so clearly these cells were overdosed with thimerosal.

13 Q And is this study scientifically reliable to
14 extrapolate what will happen in humans following
15 receipt of a thimerosal-containing vaccine?

16 A No. That would be a tremendous leap of
17 faith. First of all, it's an in vitro study so you
18 can never conclude that this is what is going to
19 happen in humans for all the reasons that we talked
20 about.

21 Secondly, once again they exposed these
22 cells to ethyl mercury. That's not even the right
23 substance.

24 Q Do you mean thimerosal?

25 A Yes, to thimerosal. That's not even the

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1 right substance. Thank you.

2 You know, additionally they studied
3 dendritic cells from normal individuals, not ones with
4 ASD. They did not study anything about the response
5 of these cells to measles virus. They did not study
6 anything, for that matter, about ASD.

7 Like the Goth study, there's no implications
8 in this study about any long-lasting effect so here,
9 for example, once again to take us back down to
10 reality to the case that we're discussing here,
11 there's no reason to think even if these results
12 applied that they would possibly be applicable at the
13 time that Michelle Cedillo received her MMR vaccine.

14 Q Are in vitro animal studies scientifically
15 appropriate to extrapolate what will happen in humans?

16 A No. You can never conclude from an animal
17 study that exactly the same thing will happen with
18 humans. You could never get a drug approved through
19 the FDA just on the basis of animal studies because if
20 you want to know what happens in humans you have to
21 study humans.

22 Animal studies once again are very good for
23 hypothesis generation to see what happens and to ask
24 the question does it happen in humans, but the
25 scientific landscape is too replete with examples

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1 where results in animals, even primates, don't
2 translate into what happens in humans.

3 I put a couple of examples here, the famous
4 saccharin example that caused a great deal of stir a
5 number of years ago where rats were getting bladder
6 cancer from saccharin and there was great concern
7 because that was all the diabetics had to avoid sugar
8 at the time. It turns out that doesn't happen in
9 humans. There's no relationship.

10 You know, everybody here I'm sure in this
11 courtroom takes Tylenol from time to time. It's a
12 very safe drug. Just a very tiny dose of Tylenol, a
13 subtherapeutic dose of Tylenol, is actually lethal to
14 cats.

15 I could just go on forever about these
16 various examples, but I won't. The bottom line is you
17 can never infer human causation only by animal
18 studies.

19 Q And is there any evidence that thimerosal in
20 the doses contained in thimerosal-containing vaccines
21 adversely affect immunological function in humans?

22 A There's not a single study. I believe
23 there's already been testimony here from Dr. Aposhian
24 that there's not a single study that would suggest or
25 that demonstrates that the dose of thimerosal in

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1 vaccine causes adverse effects on the immune system in
2 humans.

3 Q And is there any evidence that Michelle
4 Cedillo's immune system was adversely affected by
5 receipt of thimerosal-containing vaccines?

6 A No. If we go back to looking at the timing
7 of her vaccination, between the time of her last
8 thimerosal-containing vaccine before the MMR, the time
9 she received her MMR, that was the time period of
10 about nine months between March of 1995 when she got
11 vaccinated with a thimerosal-containing vaccine to
12 December when she got her MMR.

13 There's nothing in the medical records that
14 suggests that she was immunosuppressed, that she had
15 increased infections, doctor visits for infections
16 during that time period. There's no indication that
17 she was immunosuppressed, nor would you expect her to
18 be.

19 Q Doctor, I'd like to move on to dose.

20 A Okay.

21 Q As a medical toxicologist, is it possible to
22 assess the toxicity of a substance without considering
23 dose?

24 A No, absolutely not. Dose is the most
25 fundamental concept that we deal with as a medical

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1 toxicologist.

2 I know there's been discussion about dose
3 here earlier. I was here for some of that discussion.
4 I think there may have been some confusion about the
5 importance of dose so I'd like to just say a couple of
6 words about this.

7 You know, this concept really goes back to
8 Paracelsus and the famous saying, "Poison is
9 everything. Nothing is without poison." The dosage
10 makes it either a poison or a remedy. He was actually
11 talking about mercury compound at the time.

12 SPECIAL MASTER HASTINGS: We're on Slide 19
13 now. Go ahead.

14 THE WITNESS: And as you see here on Slide
15 20, the bottom line we take from Paracelsus and is
16 still quoted in every toxicology textbook today as a
17 fundamental principle is that there is no such thing
18 as a poisonous substance. There are only poisonous
19 doses.

20 There is no substance that at low enough
21 doses will not hurt you, and there is no substance
22 that at high enough doses can be toxic. Water. I've
23 had patients die from water, from drinking too much
24 water. Psychogenic polydipsia it's called.

25 Almost any medication which can be very

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1 beneficial at certain doses, if you get the high doses
2 obviously as a medical toxicologist I can tell you can
3 cause significant adverse effects.

4 We think of things like cyanide as being a
5 pretty dangerous molecule, but in fact the bad news is
6 that as we're sitting here today we are breathing in a
7 couple molecules of cyanide with every breath we take,
8 but it's such low doses that it absolutely can't hurt
9 you. The same is true of mercury or virtually any
10 other substance.

11 BY MS. RENZI:

12 Q And this principle is accepted by the
13 scientific community? Is that correct?

14 A This principle is accepted as the most
15 fundamental principle of toxicology by the scientific
16 community.

17 Here you have a book called Casarett &
18 Doull. This was a book, by the way, that was endorsed
19 by Dr. Aposhian. It's probably the most widely used
20 basic scientific text in the world, and if you just go
21 to one of the first chapters, Principles of
22 Toxicology, you see here that they point this out very
23 clearly.

24 "One could define a poison as any agent
25 capable of producing a deleterious response in a

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1 biological system, seriously injuring function or
2 producing death. This is not, however, a useful
3 working definition for the very simple reason that
4 virtually every known chemical has the potential to
5 produce injury or death if it is present in a
6 sufficient amount.

7 "Paracelsus phrased this when he noted,
8 'What is there that is not a poison? All things are
9 poison, and nothing is without poison.' Solely the
10 dose determines that the thing is not a poison."

11 If you go further in that chapter,
12 Principles of Toxicology, you see once again this is
13 emphasized. "The characteristics of exposure and the
14 spectrum of effects come together in a correlative
15 relationship customarily referred to as the dose/
16 response relationship. This relationship is the most
17 fundamental and pervasive concept in toxicology.
18 Indeed, an understanding of this relationship is
19 essential to the study of toxic materials."

20 Now, I know there's been testimony here that
21 dose is an outmoded concept, but I think that
22 testimony is probably incorrect in terms of the
23 mainstream thinking in toxicology.

24 SPECIAL MASTER HASTINGS: Now, for the
25 record here I note that Dr. Brent has just read a

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1 couple excerpts from the toxicology textbook that he
2 mentioned in his slides and in his testimony.

3 You've given us a copy, a paper copy, of
4 those excerpts. Let's mark that as Respondent's Trial
5 Exhibit No. 20.

6 Go ahead, Ms. Renzi.

7 BY MS. RENZI:

8 Q Doctor, I know you have one more example of
9 the fundamental concept.

10 A Yes. Let me show you one more very
11 important example, and you'll see why it's an
12 important example in a minute.

13 This is a well respected text on toxicology
14 by Sullivan and Krieger, and I want to draw your
15 attention to the chapter called Principles of
16 Toxicology.

17 SPECIAL MASTER HASTINGS: So now this is
18 going to be page 3 of our Trial Exhibit No. 20.

19 THE WITNESS: And the senior author of that
20 chapter, as you notice there, is Dr. Glen Sipes. Let
21 me just point out what Dr. Sipes has to say about
22 dose.

23 "One of the most important concepts in
24 toxicology is the dose/response relationship. The
25 underlying premise is that any compound can be toxic

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1 if it is encountered in large enough doses. No matter
2 what the compound's potency or how little compound is
3 necessary to produce an effect, its respected toxic
4 dose threshold must be surpassed to produce toxicity."

5 Now, that chapter was written, as you saw,
6 by Glen Sipes. Glen Sipes is Professor of Medicine in
7 the Department of Pharmacology at the University of
8 Arizona, which is Dr. Aposhian's institution, and is
9 actually head of Pharmacology and Toxicology there.

10 And, as a matter of fact, if you look at the
11 Sullivan book, John Sullivan, the senior editor of the
12 book, is a dean at the University of Arizona.

13 BY MS. RENZI:

14 Q To discuss more about those, Dr. Aposhian's
15 report contained several examples of mercury toxicity
16 in humans, and I'd like to pull up Slide 24. We have
17 a comparison chart.

18 Can any comparison be drawn from these case
19 reports about the toxicity of low doses of ethyl
20 mercury in thimerosal-containing vaccines?

21 A No. No, clearly not. It's a very profound
22 chart that I think makes the point clearly. These are
23 the cases that were cited by Dr. Aposhian in his
24 report where there was information about dose or
25 exposure. It's basically three papers, Opitz,

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1 Nierenberg and Fagan.

2 The Opitz paper, that was a totally
3 different kind of mercury. It dealt with elemental
4 mercury vapor, and, yes, there was toxicity. The
5 calculated blood level that this person has from that
6 exposure was almost 500,000 micrograms per liter.

7 Now, a typical blood level we see in the
8 United States is one, two, three, maybe five
9 micrograms per liter depending on how much seafood you
10 eat. It could be 10 if you're a big sushi eater.
11 This is almost 500,000 micrograms per liter, and it's
12 elemental mercury vapor. Clearly this has nothing to
13 do with very low dose exposures to thimerosal or ethyl
14 mercury.

15 The Nierenberg paper is a case report about
16 the chemistry professor at Dartmouth, which I think
17 everybody here has heard about. She was using a very
18 scary form of mercury that has nothing to do with
19 anything in this case called dimethyl mercury, and her
20 dose was over a million micrograms of mercury. A
21 million micrograms. Look at her blood level. Almost
22 150,000 micrograms per liter.

23 The next one that Dr. Aposhian cited was the
24 Fagan report where thimerosal at high concentrations
25 was repeatedly applied to an individual's what's

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1 called amphalocole, part of the remnant of the
2 umbilical cord. We don't know the dose, but we know
3 the blood level, which gives an assessment of those,
4 and here too -- look at this -- over 1,000 micrograms
5 per liter.

6 Now, by contrast -- by contrast -- if we
7 look at the Pichichero data on vaccination where
8 individuals got up to 62.5 micrograms of mercury, this
9 gives blood levels in the one to 1.6 micrograms per
10 liter range.

11 Clearly here we're seeing that the dosage to
12 cause these adverse effects are overwhelmingly higher
13 than anything that can possibly occur related to
14 vaccination.

15 Q Dr. Brent, what are the different species of
16 mercury?

17 A There are certainly different species of
18 mercury. There are many different kinds of mercury,
19 and it's important to remember that they are all
20 toxicologically different.

21 Here we have another quote from that
22 Casarett & Doull book. It says, "No other metals
23 better illustrate the diversity of effect caused by
24 different chemical species than does mercury." That
25 is true. The different forms of mercury have very,

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1 very different chemicals.

2 In fact, I think there's already been
3 testimony by Dr. Aposhian in that regard as well. I
4 believe he agreed with that.

5 Q And which type of mercury exposure has been
6 the most extensively studied by scientists?

7 A It depends on the timeframe that you're
8 talking about. In the past it was probably mercury
9 vapor and organic mercury because of industrial
10 exposures. More recently it's probably been methyl
11 mercury.

12 Q And why is that?

13 A The reason for that is because of the fact
14 that we all get significant exposures to methyl
15 mercury via our diet through seafood. As physicians
16 we're always telling our patients back off on the red
17 meat, eat more seafood, and yet seafood is the source
18 of methyl mercury.

19 So it's important to remember that when we
20 talk about mercury compounds they're all different.
21 There is the organic. We divide them into two major
22 categories, the organic and the inorganic. The
23 inorganic can be mercury vapor or mercury salts.

24 There are a number of different organic
25 mercuries. One of them is methyl mercury, which is

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1 the kind that you'd find in seafood, and I think there
2 has been some discussion here about Minamata disease
3 where the fish in Minamata Bay in Japan became highly
4 contaminated because of industrial release, became
5 highly contaminated with methyl mercury.

6 The individuals that were eating off those
7 fish -- there were lots of fishermen families -- got
8 very, very high doses of methyl mercury, and that
9 caused the condition called Minamata's disease. It
10 primarily affected individuals who were in utero at
11 the time of the exposure. That's methyl mercury.

12 It's very important to remember that methyl
13 mercury is a different compound from ethyl mercury,
14 and here you see an example of the significance of the
15 difference between methyl mercury and ethyl mercury.

16 Why is methyl mercury called methyl mercury?
17 Let me point this out. Here you see the structure of
18 methyl mercury, and it is a carbon and three
19 hydrogens, and that is what we refer to chemically as
20 a methyl group, so it is a methyl group attached to a
21 mercury atom, so it is methyl mercury.

22 On the other hand, where we have a carbon
23 and three hydrogens and then a carbon and two
24 hydrogens, that's what we call an ethyl group. So we
25 have an ethyl group attached to a mercury atom. That

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1 is what we call ethyl mercury. This can have
2 unbelievable consequences in terms of the differences
3 in the properties of the compound.

4 Let me show you an example that is virtually
5 identical. Here we see a methyl group, just like a
6 methyl mercury. A methyl group attached to an oxygen
7 hydrogen group. An oxygen hydrogen group is an
8 alcohol group, so this is methyl alcohol.

9 Here we see an ethyl group attached to an
10 alcohol group, so this is ethyl alcohol. Ethyl
11 alcohol is what is in spirits. Ethyl alcohol is what
12 is in beer or wine. Ethyl alcohol is probably what
13 everybody is going to go drink at the end of the day
14 today.

15 Methyl alcohol, on the other hand, instead
16 of having an ethyl group and just having a methyl
17 group, it is also referred to as methanol or wood
18 alcohol, which is one of the more dangerous substances
19 known to mankind. Just small sips of methanol can
20 kill you, and for those people who survive the serious
21 illness that you get from methanol, they will almost
22 uniformly end up blind.

23 You can see here that there is a huge
24 difference between a methyl group and an ethyl group
25 when it's attached to a molecule.

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1 SPECIAL MASTER HASTINGS: And he was just
2 looking at Slide No. 27. Go ahead.

3 BY MS. RENZI:

4 Q So is it scientifically valid then to use
5 the toxicological properties of methyl mercury
6 exposure to determine what the effects of ethyl
7 mercury exposure will be?

8 A Of course not.

9 Q I'd like to turn now to reference dose. Up
10 on the screen we're going to show Dr. Aposhian's slide
11 that showed how the doses of mercury that Michelle
12 Cedillo received through her thimerosal-containing
13 vaccines relate to the Environmental Protection
14 Agency's reference dose for methyl mercury.

15 SPECIAL MASTER HASTINGS: Was that Slide 39?

16 MS. RENZI: No. Actually it's not a slide.

17 SPECIAL MASTER HASTINGS: Okay. No?

18 MS. RENZI: It's Petitioners' Trial Exhibit
19 1, page 39. It's Dr. Aposhian's slide presentation at
20 page 39.

21 SPECIAL MASTER HASTINGS: Okay.

22 BY MS. RENZI:

23 Q What is a reference dose?

24 A Okay. A reference dose is, if you'd go to
25 the next slide --

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1 Q Let's go to Slide 28.

2 A Yes. A reference dose is a concept used by
3 the Environmental Protection Agency, the U.S. EPA, and
4 what it is is a designation for that dose of a
5 substance when averaged over a lifetime of use would
6 not be expected to cause an adverse effect, would be
7 safe.

8 Now, it's important to remember that there
9 is no reference dose for thimerosal, and there is no
10 reference dose for ethyl mercury. What we just saw
11 shown on Dr. Aposhian's slide, which he took the
12 reference to those from methyl mercury and applied it
13 to ethyl mercury. That can't be done. They are
14 different compounds.

15 There's no scientific basis for applying one
16 reference dose for one compound to a dose of a
17 different compound, although I should point out that
18 even if we accept the reference dose -- remember, the
19 reference dose, it's not a dose you can't ever exceed
20 on any given day. I mean, we could easily exceed it
21 every time we have a seafood meal. It is just over a
22 lifetime. It's just an average dose over a lifetime.

23 If you were to figure out Michelle Cedillo's
24 mercury exposure, unless she had some other unusual
25 exposures from other sources she would be under the

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1 reference dose even at this point in her life.

2 Q A reference dose is not a threshold amount
3 above which toxicity will occur. Is that correct?

4 A No, it is clearly not a threshold amount
5 above which toxicity occurs. There is a big
6 difference between the reference dose and the dose in
7 which toxicity will occur, as I'll show you in a
8 minute.

9 It's also important to remember that Dr.
10 Aposhian, when you talk about the EPA reference dose
11 for methyl mercury, there are other agencies that have
12 reference dose like the FDA and the Centers for
13 Disease Control, and really those don't get exceeded
14 by vaccinations. It's very rare for that to happen.

15 But, it's important to remember that you
16 cannot apply the reference dose as a daily limit. It
17 is an average over a lifetime. You have expected
18 exceedences over the course of days.

19 Q What was the basis for the EPA's reference
20 dose regarding methyl mercury? We're on Slide 30.

21 A The EPA's reference dose for methyl mercury
22 is based on events that happened initially in Iraq a
23 number of years ago when there was methyl mercury
24 contamination of grain that people ate.

25 And then there was data from the Faroe

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1 Islands which more updated our database with regard to
2 methyl mercury and was used in the reference dose
3 analysis. It dealt with prenatal exposure. It was
4 based on prenatal exposure to methyl mercury and
5 effects that were found related to prenatal exposure.

6 Now, it's important to remember. Reference
7 dose has nothing to do with risk of autism or ASD or
8 immunosuppression. None of that is implicit in the
9 reference dose.

10 What the reference dose is based on, and now
11 they use the Faroe Islands study. What the reference
12 dose is based on is looking at prenatal exposure and
13 then as you follow children out in time they are
14 clinically normal children, but if you do sensitive
15 testing on them you can find subtle subclinical
16 deficits based in learning memory and language in
17 children who are otherwise clinically normal. That's
18 the basis for the reference dose.

19 Now, it's important to remember. You had
20 asked the question, Mr. Renzi, about whether exceeding
21 the reference dose means there's a threshold for
22 toxicity. It's important to remember it's clearly not
23 because the technique used by the EPA to determine
24 this reference dose is called benchmark method.

25 What they do is they look at the population.

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1 They look at the effects of the population and through
2 the benchmark method come to a conclusion about dose
3 that is very, very unlikely to affect anybody in that
4 population.

5 They take that dose, and then they take just
6 a safety back just to be on the safe side. Of course,
7 that's EPA's job. Just to be on the safe side we'll
8 drop it down another tenfold below that, and that's
9 where the reference dose comes in, so there's a big
10 safety margin implicit in the reference dose.

11 Q So if we go back to Dr. Aposhian's chart,
12 and I think you've already said this. Would the
13 amount of mercury contained in Michelle Cedillo's
14 thimerosal-containing vaccines cause her to exceed the
15 EPA reference dose?

16 A Well, as you can see on individual days,
17 yes, she has exceeded the reference dose. In fact,
18 over the period of time that she was being vaccinated
19 she exceeded the reference dose.

20 If you go out, however -- remember, this is
21 something you average over a lifetime. If you go out
22 over a period of time you find that, no, she would no
23 longer be over the reference dose.

24 Once again, remember the reference dose
25 isn't even about the ethyl mercury or the thimerosal

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1 from vaccines. It's about methyl mercury, so it's not
2 even applicable. It's not even applicable in this
3 instance.

4 Q Dr. Aposhian stated in his testimony that
5 autistic children have a mercury efflux disorder. Are
6 you familiar with the term mercury efflux?

7 A I've heard the term.

8 Q What is it? We'll look at Slide 31.

9 A Well, it's this hypothetical disorder that
10 is based on the belief that children with ASD somehow
11 cannot properly excrete mercury and hence become
12 mercury toxic. They have adverse effects of mercury.

13 This efflux disorder hypothesis is really
14 based on two studies. It's based on a study of Amy
15 Holmes, and it's based on a study of Bradstreet and
16 the Geiers.

17 This study I know was discussed here. It's
18 important to note that much better studies from other
19 investigators could not replicate the results of
20 either the Holmes study or the Bradstreet/Geier study.

21 Q Could we go over the Holmes study, please?
22 We'll start with Slide 32.

23 A Okay.

24 Q If you could describe that study, please?

25 A What the Holmes study purported to do was to

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1 measure hair levels of mercury in autistics and
2 compare them to normal controls.

3 Here you see the data summarized. If you
4 look at the autistics, the hair levels were reported
5 out at about 0.47 parts per million. If you look at
6 the normal control, the hair levels averaged about 3.6
7 parts per million.

8 They therefore saw this difference and
9 concluded, and this is the conclusion of their paper,
10 hair excretion patterns among autistic infants were
11 significantly reduced relative to control.

12 Now, if you look at this data you're
13 immediately struck by the fact that something must be
14 very, very wrong here because there's a very
15 excellent, huge study, a United States Government
16 funded study called the NHANES study, National Health
17 and Nutrition Exposure Survey, and what the NHANES
18 study did was went out and surveyed randomly many
19 people in the U.S. population, and among things that
20 they looked at were hair levels of mercury.

21 If you look at what you expect from the
22 NHANES study of hair levels of mercury in the U.S.
23 population in children, you see that the average is
24 about 0.22 parts per million, remarkably close to what
25 was reported in the Holmes study for the autistics.

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1 But if you look at the normal control, they
2 have very, very, very elevated hair levels. This
3 suggests that there is something clearly wrong with
4 this data in that their controls are so highly
5 nonrepresentative of the general population in the
6 United States, and that's what you would think the
7 controls would be.

8 Q Does this study provide a reliable
9 scientific basis to conclude that autistic children
10 are not able to excrete mercury?

11 A No, it doesn't for a number of reasons.
12 Number one, the data doesn't make any sense. The data
13 clearly had a problem that has not been addressed in
14 the study: Why the autistics have normal hair levels
15 and the controls have so very elevated hair levels.

16 Number two, this study studies hair. Hair
17 is not a significant excretory organ for mercury. We
18 don't get rid of our mercury through our hair. There
19 is some mercury that goes out in the hair, but that's
20 an insignificant mode of excretion.

21 Q And what is hair a measure of? If you were
22 to measure the mercury in hair, what is it a measure
23 of?

24 A It's a reflection of blood levels. So this
25 suggests if this data were true, which obviously

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1 there's an unaddressed problem with this data, that
2 the autistics have lower blood levels than the
3 controls, but then again the controls have such
4 numbers you really can't reach any conclusions about
5 that.

6 Q You stated earlier that this Holmes study
7 has never been replicated. Is that correct?

8 A Well, people have tried.

9 Q And we're now on Slide 33.

10 A There have been two subsequent studies that
11 have shown no difference in hair mercury levels
12 between autistics and controls. Actually there's been
13 three, but one of them has not been published yet.

14 Kern studied a number of cases of autism or
15 ASD with controls and found that there was no
16 significant difference in the hair levels between the
17 two.

18 Ip from Taiwan did a similar study with 82
19 cases and 55 controls and once again demonstrated that
20 there was no significant difference.

21 So it appears that the Holmes study,
22 probably because of the very unusual data that it had
23 in it, cannot be replicated.

24 Q Dr. Aposhian also relied in his testimony on
25 an MIT study, which I believe is the Hu study, H-U.

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1 A Yes.

2 Q We filed this as Respondent's Exhibit L, Tab
3 27, and we'll discuss it at Slide 34. Could you
4 describe the Hu study?

5 A Sure. I was sitting here as this was
6 described as the study that verifies that the Holmes
7 study was right. Basically it was a study from MIT
8 from an analytical laboratory where they reported hair
9 mercury concentrations in three people that had
10 autistic spectrum disorder.

11 Now, two of those individuals were
12 undergoing what they called having been "under
13 treatment for heavy metal detoxification." That
14 usually means no seafood, probably a chelating agent.
15 Lo and behold, these two individuals had low mercury
16 levels.

17 There was a third individual, an autistic
18 individual, who was not undergoing detoxification, and
19 his hair mercury concentration was 0.4 parts per
20 million, exactly what you'd expect from the general
21 population.

22 Q So this study is not a reliable scientific
23 basis to conclude that autistics cannot excrete
24 mercury?

25 A No, of course not.

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1 Q In addition to the hair studies, Dr.
2 Aposhian relies on a chelation study published by Drs.
3 Bradstreet, Geier, et al., in the Journal of American
4 Physicians and Surgeons, and that's Petitioners'
5 Exhibit 55 at Tab E. Have you read this article?

6 A Yes, I have.

7 Q We're now on Slide 35. Could you describe
8 the Bradstreet/Geier study?

9 A Sure. What that study involved was taking a
10 number of individuals who were diagnosed with either
11 autism or pervasive developmental disorder and
12 comparing them with controls, and they gave them a
13 mercury chelator succimer, also known as DMSA, and
14 they measured their urine mercury output.

15 Now, the control in this study were
16 individuals who were brought to Dr. Bradstreet's
17 clinic because of concern about mercury toxicity, and
18 what you can see here is that following the
19 administration of the succimer when they measured the
20 urine mercury levels there was higher mercury
21 concentrations in the urine in the autism and PDD
22 group than in the control group.

23 Q On page 77 of that Bradstreet article
24 there's a chart that I want to pull up for you to look
25 at. It's on the left-hand side.

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1 A Right. This chart basically gives the whole
2 population they studied. They did it in two parts.
3 They studied the whole population, and then they
4 studied a group where the autistics were matched by
5 age and sex to the controls.

6 This is the whole population study, and, as
7 you can see, looking at this whole population you had
8 the higher mercury excretion in the cases than in the
9 controls, but if you look one of the things that is
10 striking about this result is that their ranges are so
11 huge from zero to 60 micrograms of creatinine in the
12 urine, zero to six in the control, with standard
13 deviations, which is a measure of the variance of the
14 result, how different the results are from individual
15 to individual.

16 There are standard deviations here that
17 exceed the actual values that they were looking at.
18 This is a huge amount of variance in the study.

19 Q What are some of the other reliability
20 problems with the Bradstreet study? We'll go to Slide
21 36.

22 A Oh, there's a number of them. There is the
23 fact that the study clearly had some confounding by
24 diet. The authors themselves acknowledge it, but
25 didn't do anything about it.

BRENT - DIRECT

1 Remember, the individuals who made up the
2 control group were people that were brought to this
3 clinic because of a concern about mercury toxicity. I
4 can tell you, this is a population that avoids seafood
5 like crazy and so it's very likely that the control
6 population had relatively low urine mercury because
7 they were avoiding seafood. They did not control for
8 that fact. They could have controlled for it, but
9 they didn't.

10 As we saw, the ranges and the standard
11 deviations were huge. There was a large amount of
12 overlap between the values in the autistics and the
13 control population.

14 Another thing. I looked at those numbers,
15 and I said, you know, with those standard deviations
16 I'm surprised the result was statistically
17 significant. I spent a lot of time with their
18 statistical methodology, as did other people in my
19 office, and based on the statistical methodology that
20 they describe in their paper I could not come up with
21 a statistically significant result which they said
22 that they had.

23 Further, there was no assessment of
24 compliance with the chelation treatments. We don't
25 know if the control were taking the chelation

BRENT - DIRECT

1 treatment as much as the autistics were. It's
2 possible that they weren't because they might have
3 been less motivated to take it.

4 Q We'll go on to Slide 38.

5 A If you look at the urine excretion of the
6 autistics of the PDD population, it's really not
7 terribly different than what you would expect to see
8 in the general population under conditions of
9 chelation.

10 It's also important to realize, remember,
11 what they did is they gave the chelating agent, and
12 they measured the urine after that. They came to the
13 conclusion that yes, the chelating agent mobilized all
14 this amount of mercury.

15 Well, they don't know that. I think Dr.
16 Aposhian was very clear about this in his testimony.
17 He's done a lot of chelation research. What you have
18 to do in any chelation study is you measure the
19 unchelated urine, you give the chelator, and then you
20 measure the chelated urine to know if the chelator is
21 mobilizing any mercury.

22 For some reason, and I don't know what that
23 is, they didn't get a nonchelated urine. All they did
24 is they gave the chelator and they measured the urine.
25 That is a major flaw in this study. They also did not

BRENT - DIRECT

1 exclude people who had prior chelation, and there was
2 a high likelihood that some of these people had prior
3 chelation.

4 The other thing is the question is what does
5 it tell you anyway? It's important to remember that
6 chelation challenges don't really tell you anything
7 about body burden of mercury. Most mercury is stored
8 in the kidney, and when you give a chelating agent
9 basically what it does is it mostly removes the
10 mercury that's in the kidney, so it's a good
11 reflection of kidney mercury, but it doesn't really
12 tell you about body mercury.

13 This study was published in the Journal of
14 American Physicians and Surgeons, which is very much
15 of a fringe journal with lots of alternative agendas,
16 and it's not even indexed by the National Library of
17 Medicine.

18 I should point out that this study was
19 attempted to be replicated by a better study that was
20 published in a legitimate journal, and that study
21 could not replicate the results of the Bradstreet
22 study.

23 Q And that's the Soden, et al. clinical study?

24 A That's the Soden study where they gave DMSA
25 to children with autism and to normal controls that

BRENT - DIRECT

1 were also coming to their clinic, and they found no
2 difference in the excretion of metals, including
3 mercury, following DMSA.

4 The conclusion of their paper, and they were
5 talking about that there was this hypothesis about a
6 novel mode of heavy metal toxicity in autistics based
7 on the Bradstreet paper, and they were saying in the
8 absence of a proven novel model of heavy metal
9 toxicity the proportion of autistic participants in
10 this study with DMSA provoked excretion results
11 demonstrate an excess chelatable body burden of
12 arsenic, cadmium, lead or mercury is zero. The
13 proportion is zero that had an excess chelatable body
14 burden.

15 SPECIAL MASTER HASTINGS: And that was on
16 Slide 39. Go ahead.

17 BY MS. RENZI:

18 Q Is mercury efflux a recognized diagnosis in
19 the medical community?

20 A No.

21 Q We're on Slide 40.

22 A Yes. I have yet to find any standard
23 medical textbook that describes this condition.

24 You know, for all research that we do in
25 toxicology and research, that we do in medicine and

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BRENT - DIRECT

1 billing and virtually everything we do in medicine, we
2 communicate, is done on the basis of what we call ICD
3 codes, International Classification of Diseases.

4 Everything we do, every diagnosis we give,
5 has to be given in the form of an ICD code. This is
6 done internationally. If you look, there is no ICD
7 code for a mercury efflux disorder. It doesn't exist.
8 It's not recognized. There is fundamentally no
9 scientific support for the hypothesis that the
10 kinetics of ethyl mercury are any different in
11 patients with ASD than anybody else suggesting an
12 efflux disorder.

13 I heard testimony when I was here where Dr.
14 Aposhian said well, yes, the problem with the
15 Pichichero study is that they didn't study autistic
16 children, and had they studied autistic children they
17 would have gotten very different results.

18 Well, in fact there's not one shred of
19 scientific evidence that suggests that autistic
20 children have any different kinetics of ethyl mercury
21 than anybody else.

22 Q Dr. Aposhian presented the hypothesis
23 regarding mercury efflux to the IOM in 2004. Are you
24 aware of that?

25 A Yes, I am.

BRENT - DIRECT

1 Q And that's Respondent's Exhibit L at Tab 4.
2 What did the IOM conclude?

3 A The IOM basically rejected the efflux
4 hypothesis by concluding that they were rejecting the
5 entire concept of an association between thimerosal
6 and the development of autism or ASD.

7 In fact, when you look at the body
8 contradicting the Holmes and Bradstreet studies, which
9 are highly questionable studies, I think it makes the
10 efflux disorder hypothesis completely implausible.

11 Q I want to turn now to Dr. Aposhian's
12 hypothesis that there is a genetically susceptible
13 subpopulation to mercury in autistic spectrum
14 disorder. To your knowledge, is there any evidence
15 that supports this hypothesis?

16 A I have found none.

17 Q We're on Slide 42 now.

18 A I know the ASD population. I follow it on
19 the internet. It's a subject of interest to me. It's
20 intensively scrutinized. There has never been a
21 susceptible subpopulation to thimerosal in the ASD
22 population identified.

23 Now, what's interesting about this is that
24 in instances where there is a genetic component to
25 cause a susceptible population to a chemical -- for

BRENT - DIRECT

1 example, Wilson's disease where people are very
2 sensitive to copper -- with relatively little looking
3 the gene was easily identified. There are many
4 examples in toxicology where specific genes are
5 identified with specific kinds of susceptibility.

6 The ASD population has been studied more
7 intensively than almost any other population I can
8 think of with regard to genetic susceptibility to a
9 chemical substance, and not a single one has been
10 identified.

11 It's also important to realize if this
12 hypothetical genetic susceptibility hypothesis were
13 true there certainly has been no evidence presented
14 that Michelle Cedillo has whatever genetic
15 susceptibility.

16 Q I want to go to the next slide, which is a
17 bell curve representing dose amount necessary to cause
18 a toxic response. Could you explain this curve?

19 A Yes. It's important to understand what the
20 normal bell curve is when you want to talk about a
21 genetic susceptibility or a susceptible population.

22 If we take any toxicologic response -- let's
23 say the amount of alcohol that's required to render
24 somebody unconscious -- it's not going to be exactly
25 the same for everybody. There's going to be a good

BRENT - DIRECT

1 deal of variation.

2 If you look over the scope of the entire
3 population you find that it generally falls into sort
4 of a bell-shaped curve. Most people are going to be
5 kind of in this range, some people significantly less,
6 some people significantly more. You normally expect
7 to see that kind of variation within the general
8 population.

9 On the other hand, if you have a
10 hypersusceptible population to a substance and you
11 look at what happens then what you see is that you get
12 the bell-shaped curve for most of the population, but
13 then you can identify another population here where
14 you have this susceptible population.

15 This kind of demonstration has never been
16 done with regard to thimerosal or ethyl mercury and
17 autism.

18 Q Dr. Aposhian used the example of acrodynia,
19 Pink's disease, to demonstrate that there is a genetic
20 susceptibility to mercury toxicity, but he did so
21 without knowing the dose or mercury blood levels. Is
22 his reasoning valid?

23 A No, clearly not.

24 Q I want to turn to the next slide. If you
25 could just describe what Pink's disease is?

2366A

BRENT - DIRECT

1 A Sure. Here on Slide 45 we have some of the
2 clinical characteristics of so-called Pink's disease
3 or acrodynia, which has a lot of clinical features.
4 There's bright reddening of the skin, and feet
5 photophobia, intense discomfort, multiple other
6 manifestations. I didn't want to list all the
7 manifestations.

8 The manifestations, by the way, of acrodynia
9 are extremely similar -- almost identical -- to the
10 manifestations that you see from an acute high dose
11 exposure to inorganic mercury.

12 By the way, it is not autism or ASD. It has
13 nothing to do with it. It was linked to the fact that
14 when there was an outbreak of this children were using
15 calomel, which is mercurous chloride, as a teething
16 powder and hence were getting overexposed to mercury.

17 Q And what do we know about the blood levels
18 in acrodynia cases?

19 A Well, it's important to remember that in the
20 acrodynia cases they were almost all due to inorganic
21 mercury.

22 I could only find one case in the English
23 language literature and peer reviewed studies that has
24 suggested a possibility of acrodynia from thimerosal
25 in one individual who got massive amounts of

2366B

BRENT - DIRECT

1 thimerosal, so it's really all mercurous chloride.

BRENT - DIRECT

1 Mercurous chloride can be assays as what
2 comes out in the urine to measure urine levels and so
3 one of the things we know, and actually there is a
4 very interesting paper which I guess has recently come
5 up in this litigation. I hadn't seen this paper in a
6 while, but when it came up in this litigation I went
7 back and re-read it. It's truly a fascinating paper.

8 It demonstrates unambiguously that urine
9 mercury concentrations tend to be very high,
10 exceedingly high, in acrodynia, suggesting that
11 acrodynia is due to very high exposures to mercury, to
12 mercurous chloride.

13 Q And we'll bring up that article that you're
14 referring to.

15 A Right. This is basically reviewed.

16 Q Is this article the Court's exhibit that
17 we're referring to? It was given to me by the Court.

18 SPECIAL MASTER HASTINGS: It was given us by
19 what?

20 MS. RENZI: It was the article that was
21 given to Respondent by the Court.

22 SPECIAL MASTER HASTINGS: Go ahead.

23 THE WITNESS: This article was pointing out
24 that conventional wisdom had been some children get
25 acrodynia, and many do not, when using this teething

BRENT - DIRECT

1 powder.

2 You know, the conventional wisdom, which has
3 really been carried on in a lot of the literature, is
4 that therefore it must represent some sort of an
5 idiosyncratic reaction. Some get it. Some don't.
6 But, as a matter of fact, it's probably due to the
7 fact that the ones who got it had very high exposures.

8 In this article, this Warkany article,
9 they're reviewing studies, and they point out when
10 they're talking about this study of Holzel and James
11 of 94 children with active acrodynia, in 61, or 65
12 percent, there are increased amounts of mercury
13 ranging from 200 to 2,500 micrograms per liter found.
14 Now, they're talking about urine here. Normal urine
15 mercury is maybe one or two micrograms per liter, so
16 this is a very, very high mercury level.

17 These authors state that no abnormal mercury
18 secretion was detected in 33, or 35 percent, of the
19 patients, but it is not clear how many excreted
20 significant amounts under 200 micrograms per liter,
21 and that's because the techniques that were in play at
22 the time when this was done could not get below about
23 200 micrograms per liter, so there could be
24 individuals in there with 100, 150, 180, huge mercury
25 levels, that make up the rest of that group.

BRENT - DIRECT

1 BY MS. RENZI:

2 Q And finally, Doctor, has any agency or
3 scientific body ever concluded that there is a
4 relationship between the ethyl mercury contained in
5 thimerosal-containing vaccines and autism spectrum
6 disorder?

7 A No. You know, there are a number of
8 governmental agencies and mainstream nongovernmental
9 agencies who have taken the position that there is no
10 relationship.

11 That includes obviously the National Academy
12 of Sciences, the Institute of Medicine Panel, which
13 has rejected -- taken the unusual step of rejecting --
14 the possibility of a relationship. The American
15 College of Medical Toxicology has taken the position
16 there's no relationship. The American Academy of
17 Pediatrics has said there's no demonstrable
18 relationship.

19 The World Health Organization has said
20 there's no demonstrable relationship. The U.S. CDC
21 has said there's no demonstrable relationship. The
22 European Medicines Agency, which oversees
23 pharmaceuticals in the European Union, has said
24 there's no relationship.

25 To answer your question, not a single such

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BRENT - DIRECT

1 organization has taken the position that there is a
2 relationship.

3 MS. RENZI: Thank you. I have no further
4 questions.

5 THE WITNESS: Thank you.

6 SPECIAL MASTER HASTINGS: And that was
7 looking at Slide 47.

8 MS. RENZI: Slide 47.

9 MR. MATANOSKI: Before we take a break, I'd
10 just like to clarify for the record.

11 The Warkany article, the 1953 article, I
12 believe that that was provided by one of the Court's
13 clerks to both parties approximately two or three days
14 ago.

15 SPECIAL MASTER HASTINGS: All right. Thank
16 you for clarifying that.

17 MR. MATANOSKI: Certainly.

18 SPECIAL MASTER HASTINGS: Let's take our 15
19 minute break at this point.

20 (Whereupon, a short recess was taken.)

21 SPECIAL MASTER HASTINGS: All right. We're
22 back from our morning break.

23 We have Dr. Brent back in the witness chair.

24 Ms. Chin-Caplan will have some questions for him.

25 Before we do that I just want to note

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BRENT - DIRECT

1 something very briefly for the record to clarify.
2 There was a reference during Dr. Brent's testimony to
3 an article called "Acrodynia and Mercury" by Dr.
4 Warkany and Dr. Hubbard. Ms. Renzi called this a
5 Court exhibit.

6 I just wanted to clarify for the record the
7 history on that. This article is about the
8 relationship between Pink's disease and mercury, a
9 topic that was raised in a number of the expert
10 reports filed in this case, particularly Dr. Aposhian
11 and Dr. Brent.

12 After Dr. Aposhian's testimony, he in his
13 testimony cited to a figure that one in 500 people was
14 considered to be susceptible to Pink's disease. We
15 had a question of where that came from.

16 We noticed in the Clarkson 2002 article,
17 which was filed both by the Petitioner as Exhibit 55,
18 Tab G, and by the Respondent as Exhibit L, Tab 13, in
19 that Clarkson article it made reference to this
20 Warkany article as the source of that number, so we
21 had our law clerk give copies of this article to both
22 sides and simply stated that there was interest in
23 this article and there might be a question about it
24 later in the proceeding.

25 We hadn't made it a Court exhibit, but we

BRENT - CROSS

1 will. We are going to at this time and file it into
2 the record so this article becomes a part of the
3 record in the case.

4 With that clarification, Ms. Chin-Caplan,
5 please go ahead.

6 MS. CHIN-CAPLAN: Thank you, Special Master.

7 CROSS-EXAMINATION

8 BY MS. CHIN-CAPLAN:

9 Q Dr. Brent, you indicated that you are
10 currently a clinical professor at Colorado Sciences
11 Health Center. Is that it?

12 A University of Colorado. Is this on? Can
13 everybody hear me? University of Colorado Health
14 Sciences Center, yes.

15 Q And you indicated that as a clinical
16 professor your duties and responsibilities are divided
17 into three areas. One was patient care, the second
18 was teaching, and I didn't catch the third one.

19 A Academic activities.

20 Q Academic activities. And when you say
21 academic activities, does that mean sitting on
22 committees and things like that for the hospital and
23 medical school?

24 A No. It means more scholarly activities --
25 publications, research, a role in professional

BRENT - CROSS

1 organizations.

2 Q Okay. Now, approximately how much of that
3 time is spent in patient care?

4 A Are you talking about in my entire practice,
5 my private practice and the university?

6 Q Well, you said that you were a clinical
7 professor at University of Colorado.

8 A Yes.

9 Q I'm asking you how much of your time as a
10 clinical professor is spent in patient care?

11 A At the university?

12 Q Yes.

13 A Well, in my clinical professor role we see
14 patients at university and at Children's Hospital,
15 which are both part of the University of Colorado
16 system.

17 It depends on the year. It varies over
18 time. Right now I cover that service about two days a
19 month at the University of Colorado Health Sciences
20 Center, and I have about six days a month where I
21 cover the service at the Children's Hospital.

22 Q That's approximately eight days in the month
23 that you work as a clinical professor for the
24 University of Colorado?

25 A That I have responsibilities regarding

BRENT - CROSS

1 patient care consistent with my faculty appointment,
2 yes.

3 Q And would your teaching responsibilities be
4 included within that eight-day period?

5 A No. Well, I shouldn't say that. My bedside
6 teaching responsibilities are, yes, where we have
7 patients on the service that we round on and see as a
8 group and I supervise the care. But, no, I have other
9 teaching responsibilities beyond that.

10 Q And what are those other teaching
11 responsibilities?

12 A Well, you know, they vary quite a bit from
13 time to time. They are anything from months when it
14 can be one or two hours, or I've had months where I
15 have no hours of formal teaching responsibility other
16 than bedside teaching responsibilities, to I have had
17 months not long ago when I had six hours of formal
18 teaching responsibility. That includes, for example,
19 giving lectures to the medical school class.

20 There's been a little bit of a revolution in
21 the way medical education is carried out in the United
22 States right now. Traditionally it's been large
23 lecture hall classes.

24 It's making a transition now, which every
25 faculty member sets up, to a lot of small group

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BRENT - CROSS

1 teaching and so, you know, we do spend a lot more time
2 now doing small group teaching. We'll have on some
3 subjects six or eight individuals that we'd be
4 teaching on a topic for a while.

5 Q So your teaching responsibilities can range
6 anywhere from zero to six hours a month?

7 A Yes. I can't remember a month where it's
8 been more than six hours. You know, once again
9 excluding bedside teaching.

10 Q And would that be primarily to medical
11 school students?

12 A Medical students, interns, residents and
13 fellows in training.

14 Q Okay. The clinical people -- the interns,
15 the residents and the fellows -- would those be the
16 people at the bedside?

17 A They would be both the people at the bedside
18 and in my formal lectures.

19 Q Okay. You indicated that your academic
20 activities take up part of your responsibilities. How
21 much time do you spend in academic activities at the
22 medical school?

23 A Well, my primary office is at my private
24 practice, so in terms of the actual academic
25 activities that I participate in -- for example,

BRENT - CROSS

1 teaching. Excuse me. For example, writing, editing
2 is done either in my medical office or in my home
3 study.

4 Q Private practice?

5 A Either in my medical private practice
6 office, or I do a great deal of my academic work, just
7 because of space considerations, in my home study. I
8 mean, I do a lot of my writing there, for example.

9 Q Okay. So where is your research done?

10 A It varies, depending upon the particular
11 project that I'm doing.

12 For example, right now my research involves
13 pesticide residues that are transmitted to individuals
14 through tobacco smoke, pesticides that are used to
15 grow the tobacco plant. We're doing that in
16 conjunction with people at the Colorado School of
17 Mines who have a very good assay system for these
18 pesticides.

19 Q The Colorado?

20 A School of Mines.

21 Q School of Mines. Is that an academic
22 institution?

23 A Oh, yes. It's a primarily Ph.D. granting
24 institution.

25 Q Okay. So your research is done at other

BRENT - CROSS

1 areas outside of the university?

2 A It depends on the project. It depends on
3 the project. I mean, I've done many projects within
4 the university. I've done many projects within my
5 private practice.

6 The work on these pesticide residues in
7 tobacco smoke is done in the lab that has the greatest
8 expertise to do these kinds of assays.

9 Q So you have no research laboratory at the
10 University of Colorado?

11 A I don't have my own research laboratory, no.

12 Q Okay. And you're working right now on
13 studying pesticide residues at the Colorado Safety &
14 Mines program?

15 A The School of Mines. The Colorado School of
16 Mines. It's a very, very internationally known
17 institution in scientific research. It is done in
18 conjunction with several hospitals and coroner's
19 offices.

20 Q So would it be fair to say that you're a
21 consultant with them?

22 A No. I'm an investigator.

23 Q You're an investigator?

24 A Yes.

25 Q Now, you also discussed your private

BRENT - CROSS

1 practice, and I believe it's called Toxicology
2 Associates?

3 A That's exactly right.

4 Q Doctor, how do you get patients referred to
5 you?

6 A Well, we do it in a number of ways. It's a
7 very interesting thing. Our practice is pretty well
8 known, and there aren't many toxicology practices
9 around so I think anybody from the Rocky Mountain area
10 who needs to refer somebody to a medical toxicologist
11 most likely will refer them to our practice.

12 We get patients coming down from Wyoming,
13 from Montana, from Utah, from New Mexico, from
14 Arizona, from Canada, from Nebraska. What happens is
15 we probably get half a dozen calls a day into our
16 office, and probably more, from people who call us and
17 they say I think I've been poisoned. We want to see a
18 toxicologist.

19 We have found that most of those kinds of
20 patients tend not really to benefit from seeing us
21 because they tend not to end up actually being
22 poisoned and there are other issues, so we have taken
23 the position, as in most specialty practices these
24 days, that for a patient to come to us they have to be
25 referred in from another physician so that some

BRENT - CROSS

1 initial screening is done to be sure it's appropriate
2 to send to a medical toxicologist. So our patients
3 basically come -- or a lot of our patients anyway come
4 -- through referrals from other physicians.

5 In addition, we have some various workers
6 that we follow in our worker surveillance program, and
7 of course our patients in the hospital, many of them
8 come to us directly through the emergency department
9 or get transferred in from other hospitals or
10 sometimes are in the hospital for another reason on
11 somebody else's service and ends up either it becoming
12 clear to them that they had an unrecognized
13 toxicologic problem and therefore were admitted
14 directly to us and then it became clear it was and we
15 get involved or that they've had a very bad adverse
16 drug reaction that requires consultation.

17 Q So with reference to your patient care,
18 would it be fair to state that it overlaps with your
19 hospital responsibilities?

20 A Oh, yes. The hospital responsibilities are
21 a very big part of patient care.

22 Q Okay. So that's in your private practice?

23 A Private practice and at the university.

24 Q And you get approximately half a dozen phone
25 calls, but most of your practice entails referrals

BRENT - CROSS

1 from other physicians?

2 A Yes. Yes. Right. We don't tend to see
3 patients on the basis of cold calls.

4 Q So in your private practice how much time is
5 spent on patient care?

6 A Oh, it varies. I would say, you know,
7 between the hospital work and the outpatient work I'd
8 say it's 30 or 40 percent of my time.

9 Q Now, you also indicated that you did
10 teaching in your private practice.

11 A Most of my teaching is associated with my
12 university work, although sometimes physically I'll be
13 giving lectures in my conference room to students and
14 so on.

15 Q So the students from the medical school
16 would come to your private practice office for
17 lectures?

18 A That's correct. It was on the toxicology
19 service, the specific toxicology service of which I'm
20 one of the attending physicians overseeing the
21 service. We give them a lot of lectures, the
22 individuals on that service. They rotate.

23 Sometimes we'll give them lectures at the
24 university hospital, the medical center. Sometimes
25 they'll come over to my office for lectures.

BRENT - CROSS

1 Sometimes they see patients with me in my office.

2 Q Since your teaching responsibilities at the
3 university are approximately zero to six hours per
4 month, does your private practice teaching encompass
5 that? Is it encompassed within that zero to six
6 hours?

7 A It is.

8 Q You indicated that you do research on
9 medical toxicology. You don't have a private
10 laboratory you indicated. Where do you get the topics
11 to research on?

12 A Well, a lot of it depends. You know, it
13 varies over the years. I spent many years doing
14 laboratory research. I published many papers on
15 laboratory research.

16 My interest is more clinical. I'm more of a
17 clinician. I like being around patients. I like
18 taking care of patients and so my research evolved
19 into a clinical trial research. That was that FDA-
20 sponsored research that I discussed before.

21 For a number of years recently we worked on
22 a number of major clinical trials. Ultimately we
23 published them in the New England Journal of Medicine.
24 They ended up getting some new antidotes approved
25 through the FDA, and now I am doing this tobacco work.

BRENT - CROSS

1 Q I'm sorry? I missed that.

2 A And now I'm doing the tobacco work.

3 Q You indicated you're running a clinical
4 trial with FDA currently?

5 A No. I did.

6 Q You did?

7 A We're done with that now. We published it.
8 The drug is approved. We're done.

9 Q What was the drug?

10 A It's called Fomepizole.

11 Q And what is that for?

12 A Fomepizole is a drug. It's very
13 interesting. It's very interesting that you asked
14 that because as you'll recall, this morning we were
15 talking about methanol and how bad methanol was,
16 methyl alcohol.

17 Well, what's interesting about methanol is
18 that many people actually drink it, and we get a lot
19 of people come to the hospital that drink it. They
20 also drink a related substance called ethylene glycol,
21 which is an antifreeze.

22 These are potentially lethal things to
23 drink, and we developed a new antidote for the
24 treatment of methanol poisoning and for ethylene
25 glycol poisoning. The drug's name is Fomepizole.

BRENT - CROSS

1 It's marketed under the name Antizol. That's the
2 trade name.

3 We did clinical trials in both methanol
4 poisoning and in ethylene glycol poisoning that
5 resulted in the FDA approving the drug for both
6 indications.

7 Q Doctor, was that published in the Internet
8 Journal of Medical Toxicology?

9 A No. Both of those clinical trials were
10 published in the New England Journal of Medicine.

11 Q And was it also published in the Internet
12 Journal of Medical Toxicology?

13 A The clinical trials? No.

14 Q There's an article called, "Antidotes and
15 Alcohol: Has Fomepizole Made Ethanol an Obsolete
16 Therapy?" Is that the same topic that you speak of
17 for your clinical trial?

18 A That article relates to the clinical trials.
19 It's not the publication of the clinical trials. You
20 won't find the clinical trial data in that article.

21 Q And, Doctor, in that publication you
22 indicated that you received research support from is
23 it Orphan Medical?

24 A That's correct.

25 Q What is Orphan Medical?

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BRENT - CROSS

1 A Orphan Medical was my partner in the FDA
2 grant. It actually doesn't exist anymore, but it is a
3 company that specializes in the development of what is
4 called orphan drugs.

5 An orphan drug is a drug that is intended
6 for only a very limited use audience, and therefore
7 because of the small volume of people that intend to
8 use the drug major pharmaceutical companies generally
9 are not interested in developing these orphan drugs.

10 Orphan Medical's mission was to develop
11 these small, limited niche type of drugs that other
12 companies would not develop. Certainly this antidote
13 is an example of a drug, of a limited niche type of
14 drug, so they were very interested in developing that.

15 Q And what was their relationship to the
16 Fomepizole?

17 A Orphan and I had the FDA grant to develop
18 the drug, which is called an orphan drug grant. The
19 FDA has this program because once again it's important
20 to develop these orphan drugs, and since major
21 pharmaceutical companies don't have a big interest in
22 developing them the funds have to come from someplace.

23 The FDA developed this granting process and
24 so they were the company that was interested in
25 developing and subsequently marketing the drug.

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1 Q So did they provide the financial support
2 for this research?

3 A The support came through the FDA grant, and
4 it ran through Orphan.

5 Q It ran through Orphan?

6 A Right.

7 Q FDA granted fundings to a drug manufacturer
8 to fund research?

9 A Absolutely. This was the Orphan Drug
10 Development Grant Program, and it was specifically
11 intended to encourage the development of these
12 important orphan drugs.

13 Q But Fomepizole wasn't an orphan drug, was
14 it?

15 A Yes, it was.

16 Q Well, the title says "Has Fomepizole Made
17 Ethanol an Obsolete Therapy?"

18 A Right.

19 Q So ethanol was an existing therapy, correct?

20 A Yes.

21 Q So Fomepizole is not an orphan drug, is it?

22 A Well, there's two things about that.
23 Ethanol was used. It was never FDA approved for that
24 purpose, so it was not an approved drug for the
25 treatment of ethylene glycol and methanol poisoning.

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1 Although it was used for that purpose, it did not have
2 FDA approval for it.

3 The second thing is there is nothing in the
4 orphan drug context that says if there is a therapy
5 for one of these sort of low niche diseases, low
6 population niche diseases, that you can't develop a
7 better therapy, and this is certainly a much better
8 therapy than ethanol therapy was.

9 Q But most of the orphan drugs don't have any
10 other therapies. Isn't that true?

11 A Well, I don't know about the other ones, but
12 I know that at least in this area where I was doing
13 research that although we did have a drug, ethanol,
14 Fomepizole was potentially and it turned out in fact
15 to be a very great improvement over ethanol, and the
16 FDA felt that they wanted to support the development
17 of Fomepizole through an orphan grant to us.

18 Q So that was your prior clinical trial.
19 Where were the clinical trials run?

20 A Where were the clinical trials? It was a
21 multicenter trial in a number of centers across the
22 country. I was the primary investigator that
23 coordinated the whole trial.

24 Q Okay. And how did they find you?

25 A Well, because I had an interest in the area

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1 and in these particular poisonings. I had an interest
2 in the area of the poisonings. I had a very busy
3 clinical service where we saw a number of these
4 poisonings.

5 There was an investigator in Norway by the
6 name of Dr. Jacobsson who had done a lot of the basic
7 work in the development of the drug Fomepizole, and I
8 often contacted him just as a consultant to get some
9 information about how to proceed with the idea of
10 developing this drug.

11 Dr. Jacobsson could not be the primary
12 investigator. He was in Norway. He suggested that
13 they come and talk to me because I was very
14 knowledgeable in the area and I had a lot of
15 experience with these poisonings and I was a clinical
16 investigator.

17 Orphan called me and asked if I would be
18 interested in developing a clinical trial in this area
19 or two clinical trials actually.

20 Q So the individual whose research this really
21 was is in Norway and wanted to operate clinical trials
22 in the United States, and they needed a principal
23 investigator from the United States to coordinate
24 matters. Is that it?

25 A Well, no. Dr. Jacobsson had done a lot of

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1 the basic preclinical research, had not done really
2 any studies on or had not done very much work on
3 individuals who were truly poisoned, but had done some
4 of what we call the preclinical research, done the
5 volunteers, showed it was safe, did some mechanistic
6 studies.

7 So the natural thing now would be to put the
8 drug actually in clinical trials. Clinical trials had
9 to be done in the United States because the FDA does
10 not like to accept drugs based on international data.
11 They really put strong pressure to do studies in the
12 United States.

13 Therefore, there was I think no question the
14 trial had to be done in the United States. I'm not
15 sure if it was even a requirement in our FDA grant
16 that it be done in the United States. It might have
17 been.

18 In talking to Dr. Jacobsson, they felt that
19 I was somebody for them to go to to discuss developing
20 this FDA grant and if we got it to develop the drug.

21 Q Do you know how it got from Dr. Jacobsson to
22 FDA?

23 A It didn't go from Dr. Jacobsson to FDA.

24 Q Then how did FDA become involved in this
25 grants process?

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1 A Orphan Medical was interested in the drug,
2 and they contacted Dr. Jacobsson in Norway to act as
3 kind of a consultant to help them make an assessment
4 about whether this would be a good drug to pursue,
5 whether this would be an improvement over existing
6 therapy.

7 Dr. Jacobsson I think encouraged them to go
8 through with the drug, felt very strongly that this
9 drug would be an improvement and ultimately
10 recommended that they contact me to do the clinical
11 trial.

12 Q But where does FDA fit into this?

13 A Orphan and I then went to the FDA and
14 solicited an orphan medical grant from the FDA to do
15 the trial.

16 Q So you went to FDA with the drug company to
17 solicit a grant from the drug company to do the
18 research?

19 A No. From the FDA to do the research.

20 Q But the FDA grant was funded by the drug
21 company?

22 A No. The FDA grant was funded by the FDA.

23 Q And Orphan had nothing to do with the grant
24 process? They didn't pay for any of this research?

25 A I think it all came from the FDA grant.

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1 Q Okay. Now, Doctor, we have your research,
2 this one piece of research that you discussed. What
3 else are you researching other than the research that
4 you're working with with the Colorado Mines?

5 A That's primarily it. I am very busy right
6 now. I'd like to be doing some additional research
7 projects, but in addition to the tobacco research that
8 we're doing I'm very busy right now with two other
9 issues.

10 One is my editorial responsibilities, and
11 the second is about three years ago we published a
12 major textbook in medical toxicology, and this was an
13 extremely time consuming, labor intensive activity.
14 It almost ruined my marriage. It ended up being a
15 very good book, and now we are getting prepared to go
16 into the second edition.

17 So I sort of have the next couple years of
18 my life scheduled in addition to various other
19 academic activities and professional society
20 activities and my research to doing the second edition
21 of the book, because it's about five years since the
22 first edition.

23 Q Do you have an active consulting practice?

24 A Consulting in what sense? We do lots of
25 different kinds of consulting.

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1 Q Do you consult to industry?

2 A We do from time to time, yes.

3 Q Do you consult to the drug companies?

4 A Occasionally.

5 Q Are you currently consulting with drug

6 companies?

7 A I'm not consulting with any drug companies
8 regarding any research areas or anything of that
9 nature. There are one or two medical/legal cases -- I
10 can think of one -- where I am looking at a case on
11 behalf of a drug company.

12 Q And what case is that?

13 A It's a case that involves an infant death
14 and any possible relationship to a diphenhydramine-
15 containing skin cream that was put on.

16 Q A what? I'm sorry.

17 A A skin cream that contained a medication
18 called diphenhydramine.

19 Q And you testified that you worked in the
20 Easter case, correct?

21 A I did work in the Easter case, yes.

22 Q And that was on behalf of the defendants.

23 Is that true?

24 A That's correct.

25 Q And the defendants were drug manufacturers?

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1 A GlaxoSmithKline. I think there were some
2 others as well.

3 Q I missed that.

4 A GlaxoSmithKline was the company I was
5 working with most closely. I believe there were some
6 other defendants as well.

7 Q That was one of the drug manufacturers?

8 A That's correct.

9 Q How much did you get paid on that, Doctor?

10 A On the Easter case?

11 Q Yes.

12 A Oh, boy. I don't know the exact figure. I
13 had to go through all the records. It was a
14 substantial amount. I had to go through all the
15 records, actually went to Texas to participate in the
16 evaluation of the child, and then I had to prepare a
17 report, and I had a deposition in the case.

18 That was the end of the case. As I
19 mentioned, the case was dismissed on what's called a
20 Daubert motion, I believe. I'd be guessing, but it
21 could have been \$40,000, \$50,000.

22 Q Are you currently consulting on any other
23 thimerosal cases?

24 A No. I should say I have been sent on
25 occasion from pharmaceutical companies, to give a

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1 complete answer, occasional thimerosal cases, but I
2 don't have any active ones going on, no.

3 Q Okay. And so in your medical/legal work
4 does it involve working solely for the defendants?

5 A No.

6 Q And in these cases that you've just
7 described to me have they involved working solely for
8 the defendants?

9 A The ones you've asked about where I've
10 worked as a consultant for the pharmaceutical
11 industry, yes, those have been for defendants.

12 Q Okay. Do you consult to Third World
13 countries at all?

14 A I have done some. It depends on what you
15 call a Third World country.

16 I don't have a lot of opportunity to do
17 that. I have done some things for emerging nations
18 through the U.S. State Department.

19 Q And what have you done for them?

20 A Well, one thing is really a fascinating
21 thing. It's a really fascinating thing. These really
22 weren't Third World countries, but they were sort of
23 emerging into mainstream countries, into mainstream
24 activities. One was China. One was Russia.

25 A number of years ago China invited a

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1 delegation of medical toxicologists to come to China
2 to meet with their medical toxicology community, and I
3 was invited to lead that delegation. I was the
4 delegation leader and went there.

5 Then a really fascinating, an extraordinary
6 story in Russia.

7 Q Did you say in Russia? I'm sorry.

8 A In Russia.

9 Q What did you do in China?

10 A The delegation traveled and met with many of
11 their toxicologists or individuals who were interested
12 in toxicology, and we exchanged ideas and so on and
13 saw some patients together.

14 Q Okay. And you were moving on to Russia?

15 A Yes. It's a fascinating story, a
16 fascinating story.

17 I work with the United States Centers for
18 Disease Control in the rather scary area of chemical
19 weapons.

20 Q I'm sorry. I missed that. In the area of
21 what?

22 A Of chemical weapons because there's great
23 concern about what if there is a chemical weapons
24 attack, a terrorist attack.

25 They have harvested together a group of

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1 about 12 medical toxicologists from around the country
2 to have a high level of expertise working on these,
3 being knowledgeable about them and to be able to
4 respond and take on leadership positions in case of an
5 actual event to get the knowledgeable people there on
6 the ground very quickly. I have a secret security
7 clearance with doing that.

8 Now, this is a very fascinating story. One
9 of the issues that came up was that the Soviet Union
10 used to have a very active chemical weapons program,
11 and with the dissolving of the Soviet Union there was
12 concern about what are all the chemical weapons
13 scientists doing.

14 The United States Government had a great
15 interest in, number one, finding out what they were
16 doing and, number two, figuring out ways to engage
17 them and so they send a number of medical
18 toxicologists to Russia to meet with the Soviet
19 weapons experts and to establish a dialogue and to
20 engage them and mostly to find out sort of what they
21 were doing in general.

22 We didn't interrogate them with what are you
23 doing, but just what they were doing in general and
24 what they wanted to be doing, the idea being that if
25 we could figure out what they wanted to do we might be

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1 able to arrange funding for them to do it and to
2 prevent them from doing things that we didn't want
3 them to be doing.

4 That was a fascinating -- we did this two or
5 three years ago -- experience with the State
6 Department.

7 Q So this wasn't then at the invitation of
8 Russia?

9 A You know, I don't know exactly who
10 instigated it. I know what the agenda was from the
11 United States point of view, but I don't know who
12 instigated it.

13 Q Any other consulting to emerging countries?

14 A That's about all I can think of for now.

15 Q So there's nothing to Third World countries?

16 A No. No.

17 Q Any medical research in mercury?

18 A I published a number of papers on mercury
19 and have done academic assessments of the area. I
20 haven't done any primary research on mercury. I've
21 published a case or two on some treatment issues on
22 mercury.

23 Q Okay. So primarily on treatment issues?

24 A Yes.

25 Q So no primary research, but you have

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1 published a few articles on how to treat mercury
2 toxicity. Is that it?

3 A Articles, book chapters. I've lectured
4 nationally and internationally on mercury toxicity and
5 a couple of publications regarding treatment.

6 Q Now, you indicated that you've actually
7 treated three mercury cases, correct?

8 A No. I've treated many, many more than three
9 mercury cases. I gave three examples.

10 Q Okay. One of the examples that you gave
11 were two workers who were overexposed to mercury on
12 the jobsite. Am I wrong?

13 A Today?

14 Q Yes.

15 A I remember giving the example of the
16 dentist.

17 Q The dentist.

18 A I remember giving the example of the woman
19 whose --

20 Q Munchausen.

21 A -- husband was trying to kill her.

22 Q Right.

23 A Let me think. And the individual who
24 intravenously injected the mercury.

25 Q Who was the second one that you just

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1 mentioned, the woman?

2 A Yes, who she thought her husband was trying
3 to kill her from the mercury.

4 Q Oh.

5 A I just chose off the board three colorful
6 examples, not the more mundane mercury cases.

7 Q So there was no situation where you were
8 consulted where two workers who were exposed to
9 mercury on the worksite?

10 A Oh, yes. I've seen a number of cases of
11 workers exposed to mercury on the worksite. I didn't
12 mention those examples today. They're not nearly as
13 colorful as the ones I mentioned.

14 I can't catalog every case of mercury
15 exposure that I've seen. I don't even think I
16 remember all the cases of mercury exposure that I've
17 seen.

18 Q So what are the industries that are still
19 using mercury on the worksite?

20 A That is a good question. You know, I don't
21 necessarily even know what the job processes are
22 because that's not necessarily part of my -- I
23 strictly do medical assessments of exposure and
24 medical condition.

25 But, I do know that in some industrial

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1 thermometers they're still using a good deal of
2 mercury. Fluorescent bulb manufacturers are using
3 mercury. I'm sure there are others.

4 Q And have your cases come from those two
5 industries?

6 A I don't recall. Do you mean worker
7 exposure?

8 Q Yes.

9 A I don't recall specifically.

10 Q Now, I think you also mentioned that part of
11 your clinical responsibility is surveillance of
12 workers. Could you just describe what that involves?

13 A Oh, sure. I'd be glad to. OSHA has a
14 requirement that if workers are working in the area of
15 hazardous materials that they have to be in a medical
16 surveillance program, and that typically involves a
17 baseline evaluation before they start working and an
18 evaluation -- it can vary a little bit -- typically
19 once a year to assess them to assure that they are not
20 having any adverse effects from being exposed to
21 whatever the particular substances are.

22 Very often that often involves an assessment
23 of their ability to use an appropriate respirator as
24 personal protective equipment to prevent them from
25 inhaling material.

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1 There are a lot of workers that need to be
2 in these programs. We see a good number of them and
3 do their baseline evaluations. You know, if a worker
4 is going to go in working on a lead project they come
5 in and get their baseline evaluation just so we can
6 compare that with after they're finished working on it
7 or any other material. We see them annually.

8 We see them if they feel they've been
9 exposed, if something happened on the jobsite and they
10 feel they've been exposed. Sometimes if they really
11 are exposed we take care of them in the hospital, and
12 then often we'll see them at the termination of their
13 employment.

14 Q And how many programs are you currently
15 surveying?

16 A I don't know the number.

17 Q You don't remember?

18 A I have no idea.

19 Q Is it more than one?

20 A Oh, yes.

21 Q Is it more than 20?

22 A Probably, but I don't know. I can't tell
23 you for sure.

24 Q Do any of them involve mercury?

25 A I'm sorry?

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1 Q Any of them involve mercury?

2 A You know, it's possible because I know that
3 on some of the workers we've seen we've gotten mercury
4 levels, and usually what happens is our office -- not
5 me personally, but somebody in our office --
6 determines in advance, because we have to let the
7 employers know how much it's going to cost, what tests
8 we're going to get and so the first thing that we ask
9 is what are the exposures, and then they can get the
10 appropriate tests.

11 I know I've seen a number of workers come
12 through where we have gotten mercury levels, so they
13 probably at least had the potential for being exposed
14 to mercury.

15 Q So when you order a screening do you order a
16 screening such as a heavy metal screening? Is that
17 it?

18 A No. Usually what we do is we order a very
19 specific test, not just a general heavy metal
20 screening, and it can vary depending upon the
21 circumstances.

22 For example, for mercury we can get either a
23 blood mercury level or a urine mercury level,
24 depending upon the circumstances.

25 Q So you would have to know ahead of time that

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1 the person had already been exposed?

2 A Yes.

3 Q Now, Doctor, we discussed very briefly the
4 Federal Register, which you very kindly provided to
5 us. It's currently marked as Respondent's Trial
6 Exhibit 18. Doctor, this was proposed on January 5,
7 1982, is that correct?

8 A That is correct.

9 Q And the title of it is, "Mercury Containing
10 Drug Products for Topical Antimicrobial Over-the-
11 Counter Human Use: Establishment of a Monograph,"
12 correct?

13 A That is correct.

14 Q And it was a proposed rule?

15 A That is correct.

16 Q The summary says, "The Food and Drug
17 Administration, FDA, is issuing an advance notice of
18 a proposed rulemaking that would classify over-the-
19 counter or OTC mercury-containing drug products for
20 topical antimicrobial use as not generally recognized
21 as safe and effective and as being misbranded."

22 Have I read that correctly?

23 A You have.

24 Q So, Doctor, as you indicated, thimerosal had
25 never been evaluated by FDA for safety and

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1 efficaciousness, correct?

2 A That's right. It had been used for such a
3 long time with a good safety record that it just
4 continued to be being used without, to my knowledge,
5 an actual application for use, as was very common for
6 medications that had been around for a long time.

7 Q And it was grandfathered in, as you stated,
8 right?

9 A I believe that's the right term, yes.

10 Q Right. And there was a period of notice and
11 comment? Is that true?

12 A That's correct.

13 Q How long did it take for this law to become
14 effective?

15 A The rulemaking?

16 Q Yes. When did this law become effective?

17 A I don't know when it became effective. I
18 think it was a number of years later.

19 Q So the proposed rulemaking was first issued
20 on January 5, 1982, and the period of notice and
21 comment lasted until April 11, 2007, according to what
22 you handed out to us, correct, on Respondent's Trial
23 Exhibit No. 7?

24 A Let me take a look. What page? Written
25 comments by April 5, 1982. Reply by May 5, 1982.

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1 Where are you talking about 2007?

2 Q Well, the effective date. It says April 11,
3 2007, doesn't it?

4 A What page are you looking on?

5 Q Respondent's Trial Exhibit No. 7, page 1.

6 MR. MATANOSKI: Just to clarify, I think
7 you're actually now looking at 21 C.F.R. § 310.545.

8 SPECIAL MASTER HASTINGS: That's
9 Respondent's Trial Exhibit 19.

10 MS. CHIN-CAPLAN: Is it 19? Okay. Exhibit
11 19. Sorry.

12 MR. MATANOSKI: And the notice of proposed
13 rulemaking is 47 Federal Register 436.

14 BY MS. CHIN-CAPLAN:

15 Q So, Doctor, the effective date was April 11,
16 2007? Am I correct?

17 A I think you may have changed years. I just
18 want to be sure I follow what's going on.

19 You had originally asked me about the
20 proposed rulemaking, and now we're not talking about
21 that anymore, but we're talking about --

22 Q The rule. We're talking about the actual
23 rule.

24 A No, no, no. This rule did not derive from
25 this proposed rulemaking. These are two totally

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1 separate areas.

2 Q They are?

3 A Yes.

4 Q And what is your knowledge about that?

5 A Well, the proposed rulemaking dealt with the
6 propriety of using mercury-containing over-the-counter
7 compounds in an unregulated way as an antiseptic for
8 skin, and that's what these comments were about,
9 strictly mercury-containing over-the-counter compounds
10 in an antiseptic for skin.

11 The 21 C.F.R. 310.545 was a list of about
12 700 compounds, substances -- not just mercury
13 compounds, but everything; everything from wheat germ
14 to vitamins -- that had been used by the FDA through
15 sort of this grandfather policy and had never gone
16 through the approval process that they were pointing
17 out. Thimerosal was one of those substances.

18 That's a totally different issue than this
19 proposed rulemaking on mercury-containing compounds on
20 skin.

21 Q So your belief is that 47 Federal Register
22 436 dealt solely with a topical --

23 A Yes.

24 Q And, Doctor, 21 C.F.R. 310.545, which became
25 effective on April 11, 2007, involved thimerosal,

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1 correct?

2 A Yes.

3 Q So FDA actually broadened the category of
4 mercury-containing products, didn't they?

5 A No. Actually I think you're mistaken. If
6 you look at this proposed rulemaking for topical,
7 there is a long list of mercury-containing products.

8 If you look at 21 C.F.R. 310.545, that has a
9 couple of mercury-containing products in it -- in
10 fact, I think much fewer than the proposed rulemaking
11 -- but is about 700 different pharmaceuticals
12 completely unrelated to mercury. Honey and wheat germ
13 and vitamins don't have anything to do with mercury.

14 Q You're absolutely right, Doctor, but the
15 proposed rulemaking that you have testified about you
16 indicate involved merthiolate, correct?

17 A Yes.

18 Q Which is a topical antiseptic applied to the
19 skin, correct?

20 A That is correct.

21 Q And the final rulemaking contained at 21
22 C.F.R. 310.545 involves all over-the-counter
23 thimerosal-containing products, doesn't it?

24 A It contains thimerosal, yes. Yes. It
25 includes thimerosal, over-the-counter or not over-the-

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1 counter.

2 Q Correct. So hasn't FDA broadened their
3 category of mercury-containing products and there was
4 more than merthiolate that was being regulated in 21
5 C.F.R. 310.545?

6 A If you look at the proposed rulemaking,
7 there's a large list of mercury-containing products
8 here, more than merthiolate, in the original proposed
9 rulemaking.

10 Some of those products were carried on to
11 this other document, but most of the things on this
12 other document had nothing to do with mercury.

13 Q That's correct, Doctor. However,
14 merthiolate was just one kind of over-the-counter
15 product that contained mercury, wasn't it?

16 A That's correct.

17 Q And the final rule banned all thimerosal-
18 containing products over-the-counter, didn't it?

19 A Well, thimerosal is a merthiolate.

20 Q Yes.

21 A Yes.

22 Q But all of them. Anything that contained
23 thimerosal over-the-counter was banned, not just
24 merthiolate, wasn't it?

25 A Well, thimerosal was. This rule I don't

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1 think is a banning rule. I mean, they didn't ban
2 aspirin. They didn't ban vitamins. They didn't ban
3 wheat germ. It just listed those products that hadn't
4 gone through the approval process.

5 Q So let's look at this law then, Doctor.
6 Under (a) it says, "A number of active ingredients..."

7 SPECIAL MASTER HASTINGS: Now you're looking
8 at page 1 of Trial Exhibit 19?

9 MS. CHIN-CAPLAN: Page 1.

10 SPECIAL MASTER HASTINGS: Okay.

11 BY MS. CHIN-CAPLAN:

12 Q Under (a) it says, "A number of active
13 ingredients have been present in OTC drug products for
14 various uses as described below. However, based on
15 evidence currently available there are inadequate data
16 to establish general recognition of the safety and
17 effectiveness of these ingredients for the specified
18 uses."

19 Thimerosal is listed as one of those
20 ingredients. Isn't that true?

21 A I think it's on this list. I can find it.
22 Let's see.

23 SPECIAL MASTER HASTINGS: Ms. Chin-Caplan,
24 it's a long list.

25 MS. CHIN-CAPLAN: Yes. I'm trying to find

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1 the page for him.

2 SPECIAL MASTER VOWELL: It's on page 39, I
3 believe.

4 MS. CHIN-CAPLAN: Page 39?

5 SPECIAL MASTER VOWELL: Page 39.

6 MS. CHIN-CAPLAN: Thank you, Special Master.

7 SPECIAL MASTER VOWELL: At the bottom of the
8 page. Towards the bottom.

9 BY MS. CHIN-CAPLAN:

10 Q Page 39, Doctor.

11 A Okay. Now, on 39 are we still in (a)(1)?

12 Q Yes, we are.

13 A Okay. Actually, we're not. Page 17 becomes
14 (b). They go into bulk laxatives.

15 Q (a)(1).

16 A And then on page 18 they go into stimulant
17 laxatives, and then on page 19 they go into oral
18 health care products. We could go on and on, so I
19 think we're past that initial section by the time we
20 get to page 39.

21 Q Okay. Perhaps what we could do is get the
22 proper citation for the Court, so let's go through
23 this list here, Doctor, okay?

24 SPECIAL MASTER VOWELL: Ms. Chin-Caplan, in
25 the interest of time I believe rather than (a) it is

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1 (i), but that may be indented so it means something
2 else. We're talking about first aid, antiseptic drug
3 products.

4 MS. CHIN-CAPLAN: Yes.

5 SPECIAL MASTER VOWELL: That is where
6 thimerosal is located.

7 MS. CHIN-CAPLAN: Thank you. Thank you,
8 Special Master.

9 BY MS. CHIN-CAPLAN:

10 Q So, Doctor, if you look immediately above it
11 on that page it looks like it is 27(i), and it starts
12 listing a number of mercury-containing products.

13 A Okay. So now we're going to page 39. Is
14 that correct?

15 Q Page 39.

16 A Okay. So here they are listing first aid
17 antiseptic drug products?

18 Q Right.

19 A Okay.

20 Q And they list a number of mercury-containing
21 products, correct?

22 A That is correct.

23 Q And underneath it there is mercury, correct?

24 A Correct.

25 Q And there is thimerosal?

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1 A That's correct.

2 Q And merthiolate would be included within
3 this group of mercury-containing products, correct?

4 A That is correct.

5 Q But there is more than one mercury-
6 containing product here listed, isn't there?

7 A That's correct.

8 Q So hasn't FDA broadened its application of
9 the federal rule that they initially proposed in 1982
10 to include these other mercury-containing products?

11 A No. I think you missed the point. If you
12 look at the federal rule, there's a long list.

13 This proposed rulemaking, there's a long
14 list of mercury-containing products in here, a bigger
15 list than this, so I wouldn't describe it as
16 broadening.

17 Q Okay. Doctor, if we go to page 40, and the
18 citation there I believe would be 21 C.F.R.
19 310.545(b). Do you see where I am on page 40?

20 A I've got that. I'm looking for the (b).
21 Oh, the (b) on the bottom?

22 Q Yes.

23 A Yes.

24 Q It says, "Any over-the-counter drug product
25 that is labeled, represented or promoted for the uses

BRENT - CROSS

1 specified and containing any active ingredients as
2 specified in paragraph (a) of this section is regarded
3 as a new drug within the meaning of § 210(p) of the
4 Federal Food, Drug and Cosmetic Act for which an
5 approved new drug application under § 505 of the Act
6 and Part 314 of this chapter is required for
7 marketing. In the absence of an approved new drug
8 application, such product is also misbranded under §
9 502 of the Act."

10 I've read that correctly, haven't I?

11 A You have.

12 Q And, Doctor, while this was not an outright
13 ban, wasn't the practical effect of it a ban?

14 A You know, I don't know. You're asking me a
15 legal question, and you've certainly exceeded my legal
16 ability. I can tell you thimerosal is still used in
17 FDA approved pharmaceuticals.

18 Q That's right, in vaccines.

19 A And other stuff.

20 Q So, Doctor, in your report, and if I'm wrong
21 please tell me, you acknowledge that methyl mercury
22 has caused problems and Minamata Bay would be one of
23 those instances. Wouldn't that be true?

24 A That is correct.

25 Q And do you acknowledge, also, that methyl

2413A

BRENT - CROSS

1 mercury has caused problems in the Iraqi grain
2 contamination cases?

3 A It has.

4 Q And there were a number of those, correct?

5 A Yes.

6 Q And the Faroe Islands, that also looked at
7 methyl mercury, correct?

8 A Faroe Islands looked at methyl mercury.
9 Faroe Islands' data is a little complicated because of
10 the coingestion of polychlorinated biphenyl in high
11 concentrations that happens. We don't see those
12 polychlorinated biphenyls in the Seychelles Islands
13 and they don't see the same effects really in the
14 Seychelles Islands, so we don't know what to make of
15 the Faroe versus Seychelles dilemma. It's still an
16 unresolved question.

17 Q So are you aware of any literature that has
18 actually looked at the PCBs that were involved in
19 Faroe Islands and made a determination that it did not
20 affect the outcome of the study?

21 A They have attempted to control the PCBs and
22 concluded that they could not find evidence that the
23 PCBs were the cause of the difference. That has not
24 ruled out the PCBs certainly, but they could not find
25 evidence that the PCBs were causing the problem.

BRENT - CROSS

1 Q You mentioned the Seychelles Islands. The
2 Seychelles Islands was also a seafood population
3 people, group?

4 A Seafood eating population, yes.

5 Q And to be perfectly clear the Faroe Islands
6 involved the ingestion of pilot whale, didn't it?

7 A That's correct, and that's where the PCBs
8 came from.

9 Q Right. And it was not a steady state of
10 ingestion, correct?

11 A That's correct.

12 Q And the Seychelles Islands involved a steady
13 state, correct?

14 A That's correct.

15 Q Now, you were present in the Court when Dr.
16 Aposhian testified, weren't you?

17 A I was here, yes.

18 Q Did you hear him say that when the White
19 House conference was convened of which he was a member
20 they were there to try and resolve this issue of the
21 Seychelles Islands with their steady state exposure
22 and the Faroe Islands with their bolus type of
23 exposures, correct?

24 A Yes.

25 Q Did you also hear what Dr. Aposhian

BRENT - CROSS

1 indicated occurred at that meeting?

2 A You'd have to tell me what specific aspect
3 of his testimony you're referring to.

4 Q Do you recall him saying that the
5 recommendation of this White House conference on
6 mercury was that the Seychelles Islands should utilize
7 the same tests as those utilized by the Faroe Islands?

8 A Well, yeah. There was definitely the issue,
9 and this has been well written about in the
10 literature, that there was not exactly the same
11 testing protocol between the Faroe Islands and the
12 Seychelles group. There was concern that may be why
13 they see effects in the Faroes and they don't see it
14 in the Seychelles. The suggestion had been made,
15 well, let's just do exactly the same test on both
16 groups.

17 The fact is that if you look at the testing
18 protocols they tested pretty much the same domains,
19 the same aspects of neuropsychological function and
20 neurocognitive function, they just used slightly
21 different tests to do it.

22 So there was certainly a question of well,
23 that may be the source of the discrepancy, but I think
24 there is considerable doubt in peoples' minds that
25 it's simply a result of the testing protocol given the

BRENT - CROSS

1 fact that the domains that they look at are so
2 overlapping between the two studies.

3 Q Do you recall Dr. Aposhian saying that when
4 they did utilize the same tests as the Faroe Islands
5 that they obtained the same results?

6 A I think you have to look very closely at
7 that. The adverse effects in the Seychelles that they
8 ultimately found were on a test called the grooved
9 pegboard, and that was one test on a large testing
10 battery.

11 It's unclear whether that one result on that
12 one test, and it was primarily seen with the
13 nondominant hand, which is strange, so it was
14 questionable whether that actually -- and the
15 literature reflects this.

16 It's not in my opinion, it's well-written in
17 the literature. The literature reflects that nobody
18 really knows what the significance is. I mean, you
19 know, it tested a little bit more abnormally on the
20 grooved pegboard test. They then did subsequent
21 analyses because -- and I don't want to get too
22 complicated about this, and stop me if I get too
23 complicated -- all these tests had been done using a
24 so-called linear model.

25 In other words, looking for a dose response

BRENT - CROSS

1 whereby, you know, you double the dose you expect to
2 see double the effect or some proportionate effect to
3 dose, and they couldn't find any effect on the grooved
4 pegboard on the dominant hand. They then went back
5 and they said well, let's try a different model, and
6 so they used what they call a nonlinear model.

7 We're saying well, let's assume it's not a
8 discognitive dose response group, let's assume it gets
9 flat, flat, flat, flat, flat and you reach a threshold
10 and it goes up. Using the nonlinear model they were
11 able to say, well, maybe there's an effect here on the
12 dominant hand. That's a lot of data dredging, and as
13 reflected in the publications nobody really knows what
14 the significance is.

15 Nobody knows whether you're supposed to use
16 a linear or a nonlinear model. So, yes, they found a
17 test, one test, where there was an abnormality in the
18 Seychelles that they saw in the Faroe Islands at an
19 older age group with lots of other confounding
20 factors. What that ultimately means in the long run,
21 I think the dust has to settle on that.

22 Q There was also a New Zealand study done as
23 well, wasn't there?

24 A Well, there was. There was a study by a guy
25 by the name of Karrollstan, with a K, in New Zealand,

BRENT - CROSS

1 and they did some analysis, too. That study has never
2 been published in the peer-reviewed literature, but
3 there was a study, which actually, as best as we can
4 tell given the study has never been published has
5 reported results similar to the Faroes.

6 Q Now, Doctor, the Iraqi grain cases contained
7 contamination with thimerosal as well, too, didn't
8 they?

9 A No.

10 Q Or ethyl mercury?

11 A Well, no.

12 Q There haven't been?

13 A There have been Iraqi grain cases where
14 there's miscontamination with ethyl mercury,
15 paratoluene sulfonates, if that's what you're
16 referring to.

17 Q Yes.

18 A EMPTS. EMPTS is not ethyl mercury, although
19 it's got a ethyl mercury in the name. It is a
20 significantly more complicated molecule than ethyl
21 mercury.

22 Q So it's your testimony that none of the
23 Iraqi grain contamination cases involved ethyl
24 mercury?

25 A I don't recall. I know there has been

BRENT - CROSS

1 methyl mercury, I know there's been EMPTS. I don't
2 recall if there was another one with ethyl mercury.

3 Q Okay. Now, Doctor, in addition to the grain
4 contamination cases there have been a number of ethyl
5 mercury poisonings, haven't there?

6 A Yes, there have.

7 Q And you actually listed quite a few of them
8 in your report, didn't you?

9 A Yes. In my report?

10 Q Yes.

11 A Yes, I mentioned some. Yes.

12 Q Before we move on to that area, Doctor, do
13 you recall Dr. Aposhian saying that at the end of this
14 White House conference of which he was a member that
15 the FDA agreed to lower their standard to meet that of
16 EPA?

17 A He might have said that. I don't recall.

18 Q Okay. Now, on page 15 of your report you
19 say there is reliable scientific evidence that
20 thimerosal is not toxic to humans including infants
21 and children at doses delivered either individually or
22 cumulative by thimerosal containing vaccine, and on
23 page 16 you list a number of cases. I'd like to go
24 through those cases with you. The first one that I
25 see was the Stajich article.

BRENT - CROSS

1 A Uh-huh.

2 Q Stajich is contained at Respondent's
3 Exhibit L, Tab 54. Do you have that, Doctor?

4 A I don't have that article. I might have it
5 here on my computer. You have a hard copy of it?

6 Okay.

7 Q Okay. This involved mercury exposure after
8 hepatitis B vaccination in preterm infants, correct?

9 A I believe it was term and preterm infants.

10 Q Okay. They compared pre and postvaccination
11 mercury levels. Is that true?

12 A Yes.

13 Q And they indicated in the abstract that it
14 showed a significant increase in both preterm and term
15 infants after vaccination, correct?

16 A Sure.

17 Q Then they said that additionally
18 postvaccination mercury levels were significantly
19 higher in preterm infants as compared to term infants,
20 yes?

21 A Sure.

22 Q Then it says because mercury is known to be
23 a potential neurotoxin to infants further study of its
24 pharmacodynamics is warranted. I've read that
25 correctly?

BRENT - CROSS

1 A Yes.

2 Q You don't disagree with that, though, do
3 you?

4 A Well, once again, you know, I spent a lot of
5 time this morning talking about dose. Yes, there's no
6 question in my mind that at a high enough dose that
7 mercury is a neurotoxin to infants and to adults. I
8 think what we're showing here is if you look at these
9 levels that these levels are certainly not anything
10 close to what you would expect to be associated with
11 any toxic effects.

12 Q Doctor, I'd like you to take a look at the
13 Haeney report, which is contained at Respondent's
14 Exhibit L, Tab 23. Could you just tell the Court what
15 this case involved?

16 A Sure. I just want to see if I have it on my
17 computer. I'll take a look at it here in a second for
18 you. Okay. This one I believe is the study where
19 they gave long-term administration of infants who had
20 a condition known as hypogammaglobulinoemia, they had
21 decreased immunoglobulin levels, and so they infused
22 them with immunoglobulins.

23 Q I'm sorry. Did you say infants?

24 A Patients. I'm sorry. Patients.

25 Q And what were their ages?

2422A

BRENT - CROSS

1 A Let's see what their ages were.

2 Q It's at the top of page 13.

3 A Let's see. Twenty-six patients, four to 67.

4 Q Yes.

5 A And so they infused them with immunoglobulin
6 containing thimerosal and fundamentally these people
7 obviously developed elevations in their blood mercury
8 level because of the thimerosal, but it was basically
9 well-tolerated. Mercury levels went much, much higher
10 than anything you would see with vaccinations.

11 Q Doctor, on page 14, the very last sentence,
12 doesn't it say hence, most patients with
13 hypogammaglobulinemia are theoretically at risk for
14 mercury exposure, and although no clinical evidence of
15 toxicity is yet apparent physicians responsible for
16 each patient must be alert to the need for continued
17 long-term detailed clinical examination to detect any
18 subtle disturbances that may occur? I've read that
19 correctly, right?

20 A You've read that correctly. Basically, what
21 they're saying here is look, we have given this
22 immunoglobulin to all these people, and we have driven
23 mercury levels up very high, very high, and yet we do
24 not see clinical toxicity. They haven't driven it up
25 high enough to get clinical toxicity, but they're huge

BRENT - CROSS

1 compared to what you'd get from a vaccine.

2 So, yeah, I think they're saying look, we
3 don't see any toxicity, but bear in mind these mercury
4 levels are pretty high, so it's probably a prudent
5 thing to keep an eye on these people and make sure
6 they're not getting mercury toxin.

7 Q And they should do that, Doctor, because the
8 medical profession knows that there's a long latency
9 period between mercury exposure and injury, correct?

10 A Well, I don't think that was the crux of
11 what they were saying. I think what they were saying
12 is look, these levels are pretty high, and so when you
13 expose somebody to high levels of something even
14 though you don't see any sign of toxicity it is good,
15 particularly when you expose them, to keep an eye on
16 them.

17 I didn't see anything in here about raising
18 particular concern about latency because these people
19 were treated over a period of time, so that would have
20 included, you know, any latency for effect to occur.

21 Q But prolonged latency is known to medical
22 professionals, and you know it, correct?

23 A There is a latency period, yes.

24 Q And it's quite long from time of exposure to
25 the time when injury can occur, correct?

BRENT - CROSS

1 A Well, it depends on the dose, it depends on
2 the circumstances of the exposure. Could be months.

3 Q Could be months.

4 A Yeah.

5 Q In fact, for the Iraqi grain contamination
6 cases it was months, wasn't it?

7 A Yeah, months.

8 Q Months at the very high dose, correct?

9 A Could be months, yes.

10 Q So, if we go to the next article that you
11 speak of, Axton, which is contained at L, Tab 7, now,
12 in Axton you spoke of one six week old infant, but
13 this report actually involved six cases of poisoning
14 after a parental organic mercurial compound, and they
15 called it merthiolate, correct?

16 A Right.

17 Q Doctor, would you just generally describe
18 these cases to the Court?

19 A Sure. As I recall without stopping too fast
20 to read the whole article --

21 Q Sure. Take your time.

22 A -- and I may have to stop to look up certain
23 points, but I recall that there were six cases here
24 with deaths. Five of them died. If you look at the
25 survivor, it's actually the youngest one of the whole

BRENT - CROSS

1 group that survived, and that individual received
2 about 13,000 micrograms of mercury and maybe as much
3 as 220,000 micrograms of mercury.

4 Do you have any other questions about this
5 article?

6 Q Yes. Let's just go over this. The first
7 one, these cases all involve chloramphenicol, an
8 antibiotic, correct?

9 A Yes.

10 Q And the antibiotic had been preserved with
11 thimerosal?

12 A Right, and I believe they had used too much
13 thimerosal in the reconstitution of the antibiotic.
14 It wasn't the standard amount. Yes.

15 Q Correct. Yes. Rather than grams they put
16 in kilograms.

17 A They used a lot of thimerosal.

18 Q They used a lot. Yes.

19 A Yes.

20 Q Doctor, in Case No. 1 a seven year old child
21 was administered the chloramphenicol IM, correct?

22 A Seven year old child, da, da, da, IM
23 chloramphenicol. Yes.

24 Q Yes. That means by injection, yes?

25 A Correct. Intramuscular injection.

BRENT - CROSS

1 Q Yes. Then four days after administration
2 his right buttock was noted to be swollen and very
3 tender.

4 A Right.

5 Q Ten days after admission the skin over his
6 right buttock appeared necrotic.

7 A Right.

8 Q What does necrotic mean?

9 A It means the cells were dying.

10 Q Right. A similar area appeared on the
11 anterior aspect of the left thigh, both areas were
12 intramuscular chloramphenicol had been given. Is that
13 true?

14 A Correct.

15 Q Yes. And he died on the 21st day after
16 admission?

17 A Right.

18 Q And when they did a biopsy, Doctor, what did
19 they find on biopsy?

20 A Are you talking about biopsy or autopsy?

21 Q I'm sorry, autopsy.

22 A Okay. You want me to go over all the
23 autopsy findings?

24 Q Well, just let's go to this one.

25 A Go back to all the autopsy findings in this

2427A

BRENT - CROSS

1 child?

2 Q Yes.

3 A Oh, okay. Fine. Well, it says here he had
4 an ulcer covered by a black eschar, which is basically
5 dead skin, over the right side there.

6 Q How large was the ulcer?

7 A Ten centimeters.

8 Q And in inches?

9 A Five.

10 Q Five inches. A five-inch ulcer from being
11 injected with thimerosal?

12 A Right. It says the edge was undermined and
13 indurated, and the underlying muscles were brown and
14 necrotic. There was no free pus, and the changes
15 extended almost to the pelvic bone. A five centimeter
16 abscess containing thin brown material was found in
17 the left thigh. Muscle necrosis in this area was also
18 extensive. Areas of consolidation were found in both
19 lungs. The spleen was moderately enlarged.

20 The kidney was enlarged and pale. When they
21 did a histological examination, in other words stained
22 sections under the microscope, there were thrombi or
23 blood clots in blood vessels, there was an area of the
24 lungs which had infarcted or died, there was tiny
25 what's called petechial hemorrhages in the brain.

BRENT - CROSS

1 Then it talks about necrosis at the injection site.

2 In the kidneys microscopically there was
3 degeneration and necrosis in the tubules and blooming
4 of the proximal tubular cells, flattening of the
5 tubular epithelium, pigment casts, some inflammatory
6 aggregates in the kidney with some blood cells in the
7 kidney, and then they give the amount of mercury in
8 all these various samples that they assayed, which was
9 very, very, very high.

10 Q So there was no doubt that the death was
11 related to mercury, was there?

12 A No. This was due to the incorrect
13 constitution of the medication with too much
14 thimerosal.

15 Q Right. And the second case also given by
16 injection also had black necrotic areas where the
17 injection was given. Isn't that true? That would be
18 the next page, Doctor, page report 2.

19 A Right. I'm just looking at it.

20 Q Yes. It's on page 418 at the very top.

21 A Had an induration and the next day these
22 areas became black and necrotic at the injection
23 sites. Yes.

24 Q Okay. It says extended over an area of
25 approximately 12 x 6 centimeters on each thigh.

BRENT - CROSS

1 A Right.

2 Q How big is 12 x 6 centimeters?

3 A 6 x 3 inches.

4 Q Three inches on each thigh.

5 A At the injection sites, yes.

6 Q Okay. Doctor, this child died, didn't he?

7 A Yes.

8 Q And the concentration that he received was
9 quite high?

10 A Huge.

11 Q Then the case report of the child who
12 survived. She was a six week old child, correct?

13 A Wait a second. Let me see. The survivor,
14 yes. She was Case No. 3, and that was six weeks old.

15 Q Yes. And she had the same problem, didn't
16 she, with the injection site becoming necrotic?

17 A Yes.

18 Q But she got sent home, didn't she?

19 A Initially, yes.

20 Q And they eventually brought her back in when
21 they discovered the extraordinary dose of thimerosal
22 in the chloramphenicol, correct?

23 A They found out that she had received this
24 very high dose, yes, and that's right, they brought
25 her back and readmitted her.

BRENT - CROSS

1 Q Now, she was the only one out of these six
2 patients to survive, correct?

3 A That's correct.

4 Q They indicate a reason for why they believe
5 she survived, didn't they? If you look on the next
6 column, page 419, the next to the last paragraph.

7 A Right, right. I'm looking at it, I'm just
8 reading it. It's a classical dose issue. They think
9 that although she received a number of injections of
10 chloramphenicol for the treatment of her pneumonia
11 they think they weren't all contaminated with the very
12 high doses of thimerosal, some of them had the
13 appropriate doses of thimerosal.

14 Q So she was the lucky one. She got the lower
15 doses.

16 A That's correct.

17 Q The others all got the higher doses?

18 A That's correct.

19 Q And they all died?

20 A That's just what I was saying this morning,
21 the dose makes the poison.

22 Q Yes. Now, Doctor, you also talked about
23 Fagan. Do you recall that?

24 A Yeah.

25 Q Now, Fagan is contained at Respondent's

BRENT - CROSS

1 Exhibit L, Tab 17.

2 A Just seeing if I might have my own copy
3 here.

4 Q Doctor, before you go to that can I just ask
5 you one last question on that child who survived?

6 A Yeah.

7 Q Any long-term follow-ups?

8 A Hang on. I'll take a look. As I recall it
9 was ambiguous about to what degree that she was
10 followed-up. They say that the cavity that had
11 resulted from the necrosis in the area of injection
12 healed up in two months, and at that point her
13 physical signs were normal on examination and she
14 showed no signs of mercury toxicity.

15 Q That was at what? The end of two months?

16 A Two months.

17 Q Two months?

18 A Yes.

19 Q So if we could move on to Exhibit 17, which
20 is the Fagan article?

21 A Sure.

22 Q Okay. Now, Doctor, in Fagan there are 13
23 cases of, they call it omphaloceles.

24 A Omphaloceles.

25 Q Omphaloceles. And could you tell the Court

BRENT - CROSS

1 what omphaloceles are?

2 A Sure. You know, normally at postpartum
3 there is an umbilical stump and when the umbilical
4 cord is cut that stump becomes naturally necrotic.
5 Now, sometimes instead of that happening and it
6 involuting and go away it becomes large and
7 potentially problematic.

8 At the time what they were doing is they
9 were treating these omphaloceles by putting large
10 amounts of thimerosal tincture on the omphaloceles to
11 get them to see if they would necrose and go away.

12 Q In many instances it was put on until the
13 children were old enough so that a primary closure
14 could take place. Wasn't that true?

15 A It's possible. I don't recall. I could
16 look that up in the paper if you'd like.

17 Q Okay. If you'd like.

18 A I'll take your word for it.

19 Q Okay. Doctor, out of these 13 cases 10 of
20 them died, didn't they?

21 A Right.

22 Q They did an autopsy on these patients and
23 they had very high mercury levels, didn't they?

24 A Huge. They got highly overexposed to
25 mercury.

2433A

BRENT - CROSS

1 Q But there was one child that they were able
2 to find who survived, correct? Out of the three
3 survivors they found one.

4 A Okay.

5 Q If you go to page 963 on the bottom it talks
6 about that one survivor, doesn't it? Last paragraph.

7 A Under discussions?

8 Q Yes. Last paragraph on the right-hand side.

9 A On the right-hand side. We traced one of
10 the survivors. They did a neurological exam 10 years
11 of age, and they looked for evidence of mercury
12 toxicity looking for visual field narrowing, which is
13 what you'd expect to see, or paresthesia, which you
14 would expect to see. They didn't assess intellectual
15 development, but they said the school reports that he
16 was restless, easily distracted and not interested in
17 schoolwork.

18 Q So the one survivor, Doctor, they couldn't
19 comment on his intellectual development, and his
20 school says he's restless, easily distracted and not
21 interested in schoolwork, correct?

22 A Right. Not very unusual for a 10 year old.
23 No objective signs of mercury toxicity, though.

24 Q And, Doctor, you mentioned one other case
25 where there was a poisoning and that was the Zhang

2434A

BRENT - CROSS

1 case.

2 A Uh-huh.

3 MS. CHIN-CAPLAN: The Zhang case is
4 contained at Exhibit 60.

5 SPECIAL MASTER HASTINGS: Tab 60?

6 MS. CHIN-CAPLAN: Tab 60.

7 SPECIAL MASTER HASTINGS: Okay.

8 BY MS. CHIN-CAPLAN:

9 Q This was a grain contamination case in
10 China, wasn't it?

11 A Yeah. Let me just bring up my copy here.

12 Q With ethyl mercury? Yes?

13 A I think I have my own copy. Yes, that's
14 right. This was a paper from 1984 from the Peoples
15 Republic in China in Zhang of grain contamination with
16 ethyl mercury.

17 Q Yes. Doctor, you stated in your opinion on
18 page 17 that 40 of the 41 patients who were exposed,
19 they improved or completely recovered despite the fact
20 that they received estimated doses between 35,000 and
21 280,000 micrograms of ethyl mercury.

22 A Uh-huh.

23 Q Now, Doctor, 40 out of 41 did not recover,
24 did they?

25 A I believe -- they went through the math --

BRENT - CROSS

1 that was the case. If I could take a look at my
2 report there about this? What page are you on?

3 Q It's on page 256.

4 A Okay. What page of my report?

5 SPECIAL MASTER HASTINGS: Page 18 of your
6 report.

7 THE WITNESS: Okay. Yes. Thank you. Let's
8 see.

9 SPECIAL MASTER HASTINGS: Well, it's from 17
10 to 18.

11 THE WITNESS: Yes. I see. Thank you very
12 much, Special Master. They improved or recovered.

13 BY MS. CHIN-CAPLAN:

14 Q If you look on page 256, the first full
15 paragraph, it says in addition to the 27 cases treated
16 with chelation there were 13 cases that were not
17 treated. Two months later the untreated patients
18 showed little improvement in symptoms and signs. One
19 case deteriorated with the appearance of pathological
20 reflexes. These results indicate that chelation
21 therapy was valuable, albeit with a prolonged clinical
22 course.

23 So long as mercury persists in tissues
24 continued chelation therapy is recommended. So,
25 Doctor, when you said 40 out of 41 improved that's not

BRENT - CROSS

1 true, is it?

2 A Let me take a look here. I have to go
3 through the paper and see exactly what I was referring
4 to here. It said one patient died, the other 40
5 patients still showed a variety of clinical
6 manifestations after five months.

7 SPECIAL MASTER HASTINGS: Where are you
8 reading from that?

9 THE WITNESS: That is on the bottom of page
10 253.

11 SPECIAL MASTER HASTINGS: All right.

12 THE WITNESS: So they had clinical
13 manifestations at five months, but I think if you go
14 through the paper that you will find that they were
15 sicker when they came in.

16 BY MS. CHIN-CAPLAN:

17 Q Doctor, on page 256, didn't I just read to
18 you that there were 13 cases that were not treated
19 with chelation, two months later the untreated
20 patients showed little improvement in symptoms and
21 signs?

22 SPECIAL MASTER HASTINGS: That's at the top
23 of page 256?

24 MS. CHIN-CAPLAN: That's correct.

25 THE WITNESS: In addition to the 27 cases --

BRENT - CROSS

1 there were 13 cases that were not treated. Two months
2 later one case deteriorated. Right. That's at two
3 months. Let me just take a look here. But then if
4 you go to page 253 they talk about five months out,
5 and they say the other 40 patients still showed a
6 variety of clinical manifestations.

7 You look at these clinical manifestations,
8 and so, yes, they still have some clinical
9 manifestations. Some of them recovered, some of them
10 still have clinical manifestations. They clearly did
11 not appear to be as sick as when they came in.

12 MS. CHIN-CAPLAN: Okay. Special Master, I
13 think this is a good time to break. I'm going to
14 start another line of questioning.

15 SPECIAL MASTER HASTINGS: How long do you
16 anticipate being? I didn't know if we should go
17 through and finish with Dr. Brent.

18 MS. CHIN-CAPLAN: I may still have quite a
19 bit.

20 SPECIAL MASTER HASTINGS: All right. Let's
21 take our luncheon break at this point.

22 (Whereupon, at 1:10 p.m., the hearing in the
23 above-entitled matter was recessed, to reconvene this
24 same day, Friday, June 22, 2007, at 2:10 p.m.)

25 //

2439A

BRENT - CROSS (RESUMED)

1 In contrast, there's no suggestion
2 whatsoever that the doses of thimerosal that one
3 receives through a vaccination would have an adverse
4 effect on the immune system.

5 Q So you would admit that mercury does have an
6 effect on the immune system?

7 A Under the appropriate circumstances of dose,
8 yeah.

9 Q You mean there has to be a high dose to
10 effect the immune system?

11 A It has to be a high enough dose to effect
12 the immune system.

13 Q And do we know what that high enough dose
14 is?

15 A Well, I think there's no question that it is
16 considerably in excess of that which we get from
17 vaccines because there's no evidence whatsoever of any
18 activation of the immune system associated with
19 vaccines.

20 Q Okay. Have you read this article, which is
21 Petitioners' Exhibit 81, Effects of Mercury on the
22 Immune System?

23 A If I could take a look at the article I'll
24 tell you. Thank you very much. The Powell article?

25 Q The sections on up until I would say

2440A

BRENT - CROSS (RESUMED)

1 Section 3?

2 A Yes, I've seen this article.

3 Q Have you read it, Doctor?

4 A From page to page?

5 Q No, no.

6 A I've read it in the past, yes.

7 Q Okay. So, Doctor, this article, which is
8 entitled Effects of Mercury on the Immune System by
9 Michael Powell and Per Holzman, does it indicate that
10 low concentrations of mercuric mercury reduces cell
11 viability as a function of glutathione content?

12 A Can you show me where you're reading from,
13 please?

14 Q Sure. It's under two, Toxic Effects on
15 Lymphoid Components and Immune Responses.

16 A Uh-huh.

17 SPECIAL MASTER HASTINGS: What page?

18 MS. CHIN-CAPLAN: On page 422.

19 SPECIAL MASTER HASTINGS: Thank you.

20 MS. CHIN-CAPLAN: You're welcome.

21 BY MS. CHIN-CAPLAN:

22 Q It says that, correct?

23 A I was trying to find the section that you
24 just read.

25 Q Okay. Second sentence.

BRENT - CROSS (RESUMED)

1 A Shenker and colleagues?

2 Q Yes.

3 A Used peripheral blood, mononucleo cells to
4 argue that low concentrations of mercuric, that was
5 mercuric chloride, reduce cell viability as a function
6 of glutathione content with cells having low
7 intracellular glutathiones, which is monocytes, being
8 the most sensitive. You read that correctly.

9 Q Thank you. Doctor, in the next sentence
10 doesn't it indicate that different members of the
11 lymphoid cell population have different sensitivities
12 to mercury?

13 A Sure.

14 Q So the monocytes are apparently the most
15 sensitive, aren't they?

16 A Let's see. Well, once again, you're talking
17 about micromolar concentrations here, so you have to
18 bear in mind the concentrations that you're using. I
19 can't imagine that following a vaccination how any of
20 these cells could ever achieve an exposure to
21 micromolar concentrations. Also, bear in mind that
22 this is mercuric chloride. It's a totally unrelated
23 form of mercury.

24 Q The reason we use these doses is so we can
25 see a response. Isn't that correct?

BRENT - CROSS (RESUMED)

1 A That's right. You have to get to a high
2 enough dose so you can see a response because if you
3 go down to a low dose there is no effect.

4 Q Now, this is from Dr. Aposhian's slide, page
5 6, and it talks about the sources and forms and
6 mercury. We have mercury vapor, methyl mercury and
7 thimerosal, correct?

8 A Well, he has methyl mercury, mercury vapor
9 and thimerosal, right. Three of them. Right.

10 Q And thimerosal turns into ethyl mercury,
11 which turns into mercuric mercury, which is what we're
12 dealing with, correct?

13 A Well, yes and no. It's a small amount of
14 the thimerosal will turn into mercuric mercury, yes.

15 Q Right. But as it becomes inorganic it's
16 mercuric mercury?

17 A That small proportion that becomes inorganic
18 is mercuric mercury, yes.

19 Q Right. And mercury vapor becomes mercuric
20 mercury, correct?

21 A Some proportion of mercury vapor becomes
22 mercuric mercury.

23 Q Yes. And methyl mercury becomes mercuric
24 mercury?

25 A Much less so.

BRENT - CROSS (RESUMED)

1 Q Yes. These are the organic forms. Ethyl
2 mercury and methyl mercury are organic, and when they
3 become inorganic they become mercuric mercury.

4 A They become mercuric mercury, right.

5 Q So we're looking at mercuric mercury, the
6 inorganic form, correct, in this article?

7 A Right.

8 Q Right. Doesn't it indicate that the
9 monocytes are the most sensitive to mercuric mercury?

10 A Sure, but at concentrations way, way in
11 excess of anything that you'd ever get from a vaccine.

12 Q Okay. Then it indicates that the B cells
13 are next most sensitive, correct?

14 A Yes.

15 Q Yes. And the least sensitive are the T
16 cells?

17 A That's right.

18 Q So there's some hierarchy of sensitivity to
19 exposure to mercuric mercury?

20 A To mercuric mercury, yeah. Relatively high
21 concentrations of mercuric mercury.

22 Q Right. Doctor, if you'll go on to the next
23 page. Actually, let's continue on in that sentence.
24 It says electron microscopic examination of mercury
25 killed cells reveals condensation and fragmentation of

BRENT - CROSS (RESUMED)

1 nuclei and finally, loss of membrane integrity,
2 features that are consistent with an apoptotic-like
3 cell death. What does apoptotic life cell death mean?

4 A Well, cells can die in one out of two ways.
5 There is a necrotic cell death and there is an
6 apoptotic cell death. Necrosis is generally when
7 something goes wrong that caused a cell to die.
8 Apoptosis on the other hand is a natural process.
9 It's one that we need to live.

10 It is also sometimes referred to as
11 programmed cell death. All our cells are programmed
12 to die so that they make room for new, healthy cells.
13 A classical example is our skin cells. We're
14 replacing our skin all the time. Because the top
15 layers die by apoptosis we get nice, new fresh skin
16 cells. We don't have the same skin cells we were born
17 with.

18 It's why leaves fall off trees in winter.
19 It's apoptosis. You know, our liver cells. You're
20 constantly regenerating new, healthy cells from cells
21 that have been around for a while, and get abused, and
22 starting to function abnormally and then they undergo
23 apoptosis. So apoptosis is a natural response, it's
24 part of normal physiology, we'd be in big trouble
25 without it and it is a preprogrammed cell death.

BRENT - CROSS (RESUMED)

1 Q Okay. Does mercury lead to a cell death
2 that resembles a natural cell death? Is that it?

3 A No. It depends on the concentration, it
4 depends on the dose. If, for example, mercury is
5 given in low doses you don't see an effect. If you
6 get up to these kinds of doses on the other hand,
7 these kinds of exposures, then what they're talking
8 about here is that it induces apoptosis in these
9 cells.

10 Q Okay. If you go to the very next paragraph
11 it says that the lack of a toxic effect may not
12 preclude significant functional impairment of a cell
13 population. So even though it doesn't kill it it
14 could effect the way it functions, correct?

15 A Well, they may, and I think this is
16 indicating that it may or may not depending upon what
17 the evidence is. It doesn't say it does. Once again,
18 you know, it's all a question of dose because what
19 they are talking about here, and once again, remember
20 we're talking about mercuric chloride not thimerosal
21 or ethyl mercury, and they're talking about doses that
22 these cells would never be exposed to in the body.

23 Q Doctor, if you move on to page 425 of this
24 article, the very first sentence, it says reductions
25 in both humoral and cell-mediated immune responses.

BRENT - CROSS (RESUMED)

1 That's both arms of the immune system, correct?

2 A That's correct.

3 Q In a number of species were reported
4 following exposure to organic and inorganic
5 mercurials. So whether it's organic or inorganic
6 doesn't seem to matter, it affects both arms of the
7 immune system?

8 A Well, that's true. You can get effects.
9 They won't necessarily be the same, but you can
10 definitely get effects with the various organic
11 mercurials or the inorganic mercurials at the
12 appropriate dose.

13 Q Okay. The mechanism by which mercury
14 elicits immunosuppression, particularly its responses
15 toward infectious agents, remains unclear and warrants
16 further study. More recent studies, particularly in
17 rodents, have suggested that the genetic background
18 may be a key player in understanding how mercury can
19 tilt immunoregulation towards immunosuppression or
20 immunostimulation. I've read that correctly?

21 A Yes. You did it very well.

22 Q Thank you. You wouldn't disagree with that,
23 would you?

24 A No. There's a lot of data on genetically
25 altered rodent models that show unusual responses to

BRENT - CROSS (RESUMED)

1 mercury, so no.

2 Q So your genetics can determine whether
3 you're going to be resistant to mercury, or whether
4 you're going to be immunosuppressed, or perhaps even
5 whether you're going to tilt toward autoimmunity,
6 correct?

7 A If you're a rodent.

8 Q Right. If you're a rodent.

9 A Yeah.

10 Q Okay. Now, there have been other articles
11 written on mercury and its effect on the immune
12 system, haven't there?

13 A There's a huge literature on mercury in the
14 immune system.

15 Q Yes, there is, and you attached a few to
16 your opinion letter, didn't you?

17 A I think so.

18 Q Yes, you did. On Attachment 51 there's an
19 article by B.J. Shenker entitled Immunotoxic Effects
20 of Mercuric Compounds on Human Lymphocytes and
21 Monocytes. I. Suppression of T-Cell Activation.

22 SPECIAL MASTER HASTINGS: Which tab was
23 that?

24 MS. CHIN-CAPLAN: Fifty-one.

25 SPECIAL MASTER HASTINGS: Thank you.

BRENT - CROSS (RESUMED)

1 MS. CHIN-CAPLAN: You're welcome.

2 Are you there, Doctor?

3 THE WITNESS: Yes. I'm just looking to see
4 if I have it on my -- yes.

5 BY MS. CHIN-CAPLAN:

6 Q Now, this article looked at methyl mercury
7 and mercuric mercury, correct?

8 A Right.

9 Q And what it says in the middle of that
10 paragraph is that both forms of mercury caused a dose
11 dependent reduction in T-cell proliferation, however,
12 the effect was dependent upon the presence of
13 monocytes. In the absence of monocytes mercuric
14 mercury enhances PMA induced T-cell proliferation.

15 So it sounds like here, Doctor, and please
16 correct me if I'm wrong, if you don't have any
17 monocytes your immune system is in more trouble than
18 if it did have monocytes?

19 A Are you reading from the first page in the
20 abstract?

21 Q Yes.

22 A Both forms of mercury? Hang on. Let me
23 take a look. Here it is. Once again, remember this
24 doesn't deal with ethyl mercury or thimerosal, and of
25 course there's no dose discussion here, but, yeah, you

BRENT - CROSS (RESUMED)

1 can get a diversity of effects. Certainly.

2 Q Okay. In this article it also indicates
3 that methyl mercury is five to 10 times more potent
4 than mercuric mercury, correct?

5 A You're still on the first page?

6 Q Still first page.

7 A In this particular scenario that they've
8 described in the prior sentence, yes.

9 Q Right. Five to 10 times more potent.

10 A Right.

11 Q So the organic methyl is five to 10 times
12 more potent than the inorganic mercuric mercury?

13 A Right.

14 Q Okay. Doctor, if you go on to the next page
15 it says at the very top there the results of this
16 investigation clearly show that mercury-containing
17 compounds are immunomodulatory; moreover, the decrease
18 in T-cell function following exposure to mercury
19 indicates that this metal is immunotoxic at very low
20 exposure levels. I read that correctly?

21 A You've read that correctly.

22 Q Do you agree with that?

23 A Well, once again, they didn't define what
24 they mean by very low exposure levels. I point out
25 again this has never been shown, that the exposure

BRENT - CROSS (RESUMED)

1 levels you get from ethyl mercury in the vaccine, but
2 it depends on how they're defining low exposure
3 levels. I don't think they had the vaccines in mind
4 when they wrote this.

5 Q I agree with you. All right. So let us
6 continue, and actually, it's an article that dates
7 back to 1992, correct?

8 A It is.

9 Q At that time it was unknown that vaccines
10 contained mercury. Isn't that true?

11 A It was unknown that the vaccines contained
12 mercury?

13 Q Right.

14 A No.

15 Q In 1992?

16 A In 1992, of course it was known.

17 Q It was known?

18 A Yes.

19 Q Okay. So, Doctor, if you continue on in the
20 introduction, the third sentence. Epidemiological
21 surveys and laboratory studies have shown that when
22 individuals are exposed to low concentrations of heavy
23 metals the clinical symptoms appear to be "silent" or
24 asymptomatic. However, when the health status of
25 asymptomatic subjects is followed for long time

BRENT - CROSS (RESUMED)

1 periods, there is clear evidence of tissue or organ
2 dysfunction.

3 A Well, I have no idea what heavy metal
4 they're talking about here. I can't think of a single
5 paper with mercury that would suggest this, and
6 certainly there's no reference here for what they're
7 talking about.

8 Q Well, Doctor, this article is on mercuric
9 compounds, isn't it?

10 A Yeah, and they talk about heavy metals.
11 They don't talk about mercury here.

12 Q Isn't mercury a heavy metal?

13 A Yes, but not all heavy metals are mercury.

14 Q True, but don't most heavy metals have an
15 effect on the immune system?

16 A At appropriate doses most heavy metals have
17 effects on the immune system, yes.

18 Q Okay. Then, Doctor, further down in the
19 third paragraph there's a very long list of what
20 studies of mercury immunotoxicity have indicated could
21 occur, right?

22 A Right.

23 Q It says Nakatsuru demonstrated that murine
24 lymphocytes when cultured with mercurials mitogen
25 induced DNA synthesis was inhibited, correct?

2452A

BRENT - CROSS (RESUMED)

1 A Right.

2 Q And methyl mercury was 10 times more potent
3 than mercuric mercury?

4 A Uh-huh.

5 Q So the organic was 10 times more potent than
6 the inorganic, but the inorganic still had an effect?

7 A The methyl.

8 Q Yes. Then Nordlind demonstrated that both
9 murine thymocyte and splenocyte DNA synthesis were
10 inhibited by mercuric mercury. When they say
11 thymocyte and splenocyte are they referring to the
12 organs the thymus and the spleen?

13 A They are referring to the cells of the
14 thymus and the cells of the spleen.

15 Q And those are immune forming cells, aren't
16 they?

17 A More the spleen cells than the thymus cells.

18 Q They are? They're part of the immune
19 system?

20 A Yeah.

21 Q So the cells producing are affected
22 according to this individual?

23 A Well, you know, once again, I think we can
24 go through many, many, many papers on mercuric
25 chloride, and methyl mercury and the effects on the

BRENT - CROSS (RESUMED)

1 immune system. There's a huge literature out there.
2 That literature all says yeah, there's a lot of
3 effects of methyl mercury, there's a lot of effects of
4 mercuric chloride on the immune system.

5 But that is not ethyl mercury, it's not even
6 thimerosal, and none of this really indicates doses of
7 exposure that you'd expect to see with a vaccine. So
8 we could spend a lot of time going through all these
9 articles, and I will endorse all these statements, but
10 they're completely irrelevant to what we're discussing
11 today.

12 Q Okay. So your opinion is that all the past
13 literature that's been done on organic mercury and
14 inorganic mercury have no relevance to the ethyl
15 mercury that is contained within the vaccines that
16 eventually turn into inorganic mercury? Is that what
17 you're saying?

18 A I'm saying that if you want to enlighten
19 this discussion in the true scientific fashion about
20 what happened with ethyl mercury at doses associated
21 with vaccines then we should discuss literature on
22 ethyl mercury at exposures we see with the vaccine.
23 Now, I don't think we're going to have that discussion
24 and the reason being there are no papers that show any
25 adverse effects.

2454A

BRENT - CROSS (RESUMED)

1 So we can go through the exercise of talking
2 about mercuric chloride, talking about ethyl mercury
3 and talking about high doses if you'd like, and I will
4 agree with all these statements to make it easier for
5 you.

6 Q Okay. Good. Then we can agree, also, that
7 T lymphocyte functions are affected in their responses
8 to mitogens and that mixed leucocyte responses were
9 depressed in mice and rats given mercuric chloride in
10 their drinking water or by subcutaneous injection,
11 correct? We can agree on that then?

12 A That's probably true.

13 Q Yes. And we can also agree then that when
14 they state all our results indicate that low doses of
15 mercury have a profound inhibitory effect on human T
16 lymphocyte activation. We can agree on that?

17 A Where are you reading from?

18 Q That's on page 541.

19 A You jumped ahead of me there. Right. So
20 the mercuric chloride and methyl mercury under
21 circumstances and doses not associated with vaccines,
22 but yeah, so I think that's probably true what they
23 say.

24 Q Okay. So low doses of any other mercury can
25 affect the immune system?

BRENT - CROSS (RESUMED)

1 A No. We're talking micromolar doses here. I
2 don't think these are exposures that you're going to
3 get even if this was ethyl mercury.

4 Q Okay. But it says low doses, correct?

5 A Yes.

6 Q Of mercury?

7 A Correct, but not as low as vaccines.

8 Q So any other mercury other than ethyl
9 mercury can have a profound inhibitory effect on human
10 T lymphocyte activation?

11 A You can see effects with ethyl mercury, too,
12 but also at doses far in excess of what you get from a
13 vaccine.

14 Q Okay. Doctor, if we go on to the next
15 article, which is again an article by Shenker, and
16 we'll just do this very briefly.

17 A That's okay.

18 SPECIAL MASTER HASTINGS: When you say the
19 next article?

20 MS. CHIN-CAPLAN: Attachment 52.

21 SPECIAL MASTER HASTINGS: All right. Thank
22 you.

23 THE WITNESS: That's okay. Take your time.

24 BY MS. CHIN-CAPLAN:

25 Q Now, this study is a little bit of an

2456A

BRENT - CROSS (RESUMED)

1 expansion from the last one, isn't it?

2 A I'll tell you in a second. They're both the
3 1992 Shenker article. Okay.

4 Q Okay. It's a little bit of an expansion?

5 A Well, it looks like the same experiment.
6 They're talking about two different aspects of the
7 same experiment, the first dealing with
8 immunosuppression and the second dealing with
9 alterations in cell viability.

10 Q Right. The last one didn't indicate how
11 long it took for these cells to be affected, did it?

12 A As I recall in the last one if you took the
13 methyl mercury and you applied it to mitogen, because
14 remember this is mitogen stimulated cells, so you put
15 the mitogen on, stimulate the cells. Put the mitogen
16 on and methyl mercury on at high doses, then you get
17 suppression of cell stimulation.

18 However, once you go out a couple of hours
19 that suppression is lost. In fact, if you look at
20 this first Shenker article once you go out about 24
21 hours that suppression is totally 100 percent gone.
22 So this is a very, very transient effect that has no
23 persistence in terms of time.

24 Q Well, this Shenker article doesn't say that,
25 though, does it?

BRENT - CROSS (RESUMED)

1 A I think it does. In one of the Shenker
2 articles it does, and I believe it was this one.
3 Yeah.

4 Q This is the Immunotoxic Effects of Mercuric
5 Compounds on Human Lymphocytes and Monocytes.
6 Alterations in Cell Variety.

7 A No, and I said if you look at the first
8 article, the one on suppression, you can see that.
9 That's in Figure 3 of the article.

10 Q Okay. But in this article, Doctor, in the
11 abstract it says following treatment with mercuric
12 mercury or methyl mercury there was minimal reduction
13 in lymphocyte viability at one to four hours.
14 However, after exposure to mercury for 24 hours cell
15 death was apparent. In comparison, monocytes
16 exhibited significant loss of viability during the
17 early exposure period.

18 Again, it says methyl mercury is five to 10
19 times more potent than inorganic mercury, correct?

20 A I think at these concentrations it's
21 probably true.

22 Q So, Doctor, you would agree then that
23 mercury does have an effect on the immune system?

24 A I think I've been saying that all along, at
25 the appropriate dose, conditions --

BRENT - CROSS (RESUMED)

1 Q Now, your contention is that this does not
2 involve ethyl mercury?

3 A Well, I have two concerns about a dialogue
4 about this data as it applies to the questions that
5 are relevant to these proceedings. One is that we're
6 not talking about ethyl mercury, and the second is
7 that we're not talking about exposures that are
8 related to exposures that you get from the vaccine in
9 terms of dose and concentration.

10 Q So, Doctor, if you had designed the
11 experiment what would you design it as?

12 A Well, I would do a number of things. The
13 first thing I would do is I would begin the way you
14 begin in science with cheap and dirty to see if
15 there's anything there, and so I would do an in vitro
16 experiment just to see if there's anything there to
17 test in the animal like the Agrawal study.

18 Now, in doing that the Agrawal study clearly
19 demonstrated -- except I would have done it with ethyl
20 mercury, but they used thimerosal -- that at exposures
21 you get from thimerosal the doses don't have an immune
22 effect, so at that point I would stop. I would say we
23 don't even see it in this in vitro study, we're
24 certainly not going to see it in the animal.

25 Although, the one thing I would have done

BRENT - CROSS (RESUMED)

1 different is I wouldn't use ethyl mercury, I would
2 have used a more relevant exposure. So I think the
3 best data we've had is that it doesn't happen, but if
4 you want to do the perfect experiment that's the way I
5 would do it.

6 It's also perfectly possible to assess
7 immune parameters in thimerosal exposed people. That
8 can be done. It's very easy to do. We're still
9 exposing people to thimerosal. I had a patient about
10 two weeks ago who had a rattlesnake bite, and the
11 rattlesnake antivenom that we use has thimerosal in
12 it, and we gave it to the patient.

13 There's patients out there. A lot of people
14 all over the world are being vaccinated with
15 thimerosal containing vaccines. So it's very easy
16 even in humans to study various parameters of the
17 immune system and to assess whether you see an adverse
18 effect associated with thimerosal administration, but
19 there's not one documentation that there is.

20 Q Now, Doctor, you indicated that the Agrawal
21 study involved thimerosal?

22 A Thimerosal.

23 Q Yes. Were you present when Dr. Aposhian
24 indicated that thimerosal turns almost instantly into
25 ethyl mercury and these other components?

BRENT - CROSS (RESUMED)

1 A Well, we know that happens in the body. In
2 fact, some of it happens in the bile as I testified to
3 before. Whether that happens under the conditions of
4 the Agrawal experiment is not clear, and they did not
5 assay that.

6 Q Okay. When you talk about doing a study of
7 thimerosal ethyl mercury in the individual how would
8 you account for the fact that some people might be
9 more susceptible than other people?

10 A Well, I think if you're saying if we wanted
11 to determine if there's a susceptible population, I
12 mean, nobody's ever suggested or given data that there
13 was a susceptible population, but if we wanted to go
14 and investigate this further we'd just take a bunch of
15 people being immunized maybe in parts of the world
16 where they're still using thimerosal and assess their
17 immunological parameters.

18 Q Now didn't the earlier Shenker article
19 indicate that people who are affected by mercury might
20 be more susceptible than others or cells rather?

21 A Different types of cell types have different
22 susceptibilities.

23 Q Uh-huh. But didn't it also indicate that
24 individuals might also be more susceptible as in
25 hypersusceptibility?

BRENT - CROSS (RESUMED)

1 A As far as we know, there is no
2 hypersusceptible individual population. That is
3 strictly speculation.

4 Q So you wouldn't say that there's a genetic
5 makeup that might make people more susceptible than
6 others to the effects of mercury?

7 A I know of no genetic finding that supports
8 that with the single exception of some very
9 preliminary findings on the CPOX 4 gene which really
10 have to do with porphyrin synthesis, and it's still a
11 gene that's present in a very large proportion of the
12 population compared to a typical hypersusceptibility
13 seen that's present in 12 to 15 percent of the
14 population.

15 Q So roughly 15 percent of the population
16 might be more susceptible to the effects of mercury?
17 Is that what you just said?

18 A No. Roughly 12 to 15 percent of the
19 population will have a pattern of porphyrin synthesis
20 when exposed to mercury different from the other 85
21 percent.

22 Q What does that mean?

23 A As far as we know, nothing.

24 Q As far as we know, nothing?

25 A (Nonverbal response.)

BRENT - CROSS (RESUMED)

1 SPECIAL MASTER HASTINGS: I'm sorry. You
2 need to say yes.

3 THE WITNESS: Yes, that's correct. As far
4 as we know, nothing.

5 BY MS. CHIN-CAPLAN:

6 Q Now, Doctor, you had talked about the Holmes
7 study in your presentation today.

8 SPECIAL MASTER HASTINGS: The which study?

9 MS. CHIN-CAPLAN: Holmes study.

10 SPECIAL MASTER HASTINGS: Holmes.

11 MS. CHIN-CAPLAN: Holmes, yes. I'll find
12 the citation for you. It would be Tab 27.

13 SPECIAL MASTER HASTINGS: Of his?

14 MS. CHIN-CAPLAN: Of his.

15 SPECIAL MASTER HASTINGS: Thank you.

16 MS. CHIN-CAPLAN: You're welcome.

17 BY MS. CHIN-CAPLAN:

18 Q Now, Doctor, we've already talked about this
19 or you've talked about it already in your presentation
20 today, correct?

21 A That is correct.

22 Q You indicated they hadn't been reproduced at
23 all. Is that true?

24 A That's right. That there was no public
25 study that supports it. Dr. Aposhian mentioned the Hu

BRENT - CROSS (RESUMED)

1 study, but we had talked about the Hu study and it
2 clearly does not support the Holmes study.

3 Q Okay. Nobody's reproduced the study is what
4 you said, right?

5 A Well, people have tried. They haven't
6 gotten the same results.

7 Q You're probably referring to Ip, correct?

8 A And Kerns.

9 Q And Kerns. Okay. Now, in the Holmes study
10 she looked at first baby haircuts. Isn't that true?

11 A That's correct.

12 Q Before she looked at first baby haircuts
13 didn't she just look at the haircuts of the children
14 at the time that she saw them?

15 A I don't recall. Is that in the paper?

16 Q Yes, it is.

17 A Where is that?

18 Q On page 278. If you go down to the first
19 column, the next to the last paragraph, it begins with
20 in a clinical practice one of the study authors
21 submitted hair samples from autistic patients for
22 commercial laboratory testing for toxic metal
23 exposure. Most of these mercury hair levels were
24 found to be low contrary to a first order hypothesis
25 of heavy metal toxicity in autism.

BRENT - CROSS (RESUMED)

1 She then asked patients to submit first baby
2 haircut samples for analysis thereby testing a sample
3 that would more accurately reflect early exposure,
4 correct?

5 A Uh-huh.

6 Q Now, hair grows at approximately, what is
7 it, half inch a month?

8 A A centimeter a month, yeah.

9 Q So if you had a seven year old child the
10 hair that you need to be testing would be how long?

11 A No. Are you talking about the fact that it
12 would be to get the baby hair?

13 Q Yes.

14 A It's clearly not baby hair.

15 Q Yes. It's clearly not baby hair?

16 A Right.

17 Q So when she tested hair that was not baby
18 hair she got virtually nothing?

19 A Well, no. She says right here that when she
20 tested hair samples in general the results were very
21 low, and then she reports in which on her first baby
22 hair test the results are very low. So she's saying
23 here that general hair does the same thing as the baby
24 hair tested.

25 Q Okay. When you look at Ip, does Ip look at

BRENT - CROSS (RESUMED)

1 first baby hair?

2 A No.

3 Q Ip looks at hair that's of seven year old
4 children, don't they?

5 A I can take a look at the paper. Let's see
6 if I have a copy on my computer.

7 Q It's the next one. It would be Tab 32.

8 A Okay. 7.2 years for the autistic spectrum
9 disorder group and 7.8 years for the control group.

10 Q Were they, what, seven years old?

11 A Approximately.

12 Q So at seven years old the hair that they
13 would need would have to be very long, wouldn't it?

14 A It's not baby hair.

15 Q Right. It's not baby hair.

16 Q So it would be hard to say that this really
17 contradicts the Holmes study, wouldn't it?

18 A I think it definitely contradicts the Holmes
19 study because even Holmes as you have pointed out
20 showed that when you don't look at baby hair she
21 thinks that the results are very low, and here we see,
22 no, you just track these cases seven years and the
23 results aren't very low.

24 Q Now, would you go to Kerns? I'm sorry.

25 Kerns is 34. Is Kerns a hair test? It's a hair

BRENT - CROSS (RESUMED)

1 study?

2 A Yes.

3 Q It is a hair study?

4 A Yes.

5 Q Yes. But it looked at heavy metals in
6 general, didn't it?

7 A Heavy metals including mercury.

8 Q Right. If you look at the abstract doesn't
9 it indicate that the evidence from our study supports
10 the notion that children with autism may have trouble
11 excreting these metals resulting in a higher body
12 burden that might contribute to symptoms of autism?

13 A Hang on a second.

14 Q It does say that in the abstract, right?

15 A Hang on a second. I'm just bringing up my
16 copy of the paper here. Okay. I'm sorry. You were
17 looking at the abstract?

18 Q Yes.

19 A Right, but not mercury. He was talking
20 about arsenic, cadmium and lead were significantly
21 lower in the hair of children with autism than in
22 matched controls. With mercury there was no
23 difference.

24 Q So everything other than mercury?

25 A In this particular study. Now, another

BRENT - CROSS (RESUMED)

1 study has contradicted even I believe the arsenic,
2 cadmium and lead data.

3 Q Okay. So, Doctor, there's one study that
4 you didn't mention that Dr. Aposhian did mention, and
5 that was the Adams tooth study.

6 A Yes. Okay.

7 Q In the Adams tooth study wasn't there the
8 indication that the teeth of autistic children had two
9 times more mercury than controls?

10 A Well, that's what they reported. Let me
11 pull out the study because I'd like to make a couple
12 of observations about that study. I'm very familiar
13 with that study, and there's a couple of things about
14 it I want to point out.

15 SPECIAL MASTER HASTINGS: Does anyone have
16 the citation from our record? Thank you.
17 Petitioners' Exhibit 82 I believe.

18 (Pause.)

19 BY MS. CHIN-CAPLAN:

20 Q Doctor, my question to you was wasn't it
21 shown in this article that autistic children had two
22 times the amount of mercury in their teeth as opposed
23 to normal children?

24 A Well, that's what they reported.

25 Q Okay. And would that be an indication that

BRENT - CROSS (RESUMED)

1 autistic children have difficulty excreting mercury?

2 A No, for a number of reasons. Number one,
3 teeth, like hair, are not a normal excretory organ for
4 mercury. We don't lose a lot of mercury through our
5 hair. Teeth specifically, you know, a tooth is
6 basically bone. It's basically bone. We don't
7 incorporate mercury very much into bone, so I'm not
8 exactly sure what they're even looking at, but it's
9 just the opposite of what they see in hair.

10 I mean, the Holmes people have reported,
11 although it couldn't be replicated, that there's low
12 release of mercury through the hair. Even if that
13 were true how do you reconcile it with this study
14 which shows there's an increased release of mercury
15 through the teeth? It doesn't make any sense. Now,
16 the truth is with this study I'm not sure their
17 results are statistically significantly different
18 based on the statistical tests they did because they
19 do have an error in their statistical methodology.

20 I don't know if you want me to go into it.
21 I'll be glad to if you'd like.

22 Q Doctor, you're saying that teeth are an
23 excretory organ?

24 A No.

25 Q It's tissue, isn't it?

BRENT - CROSS (RESUMED)

1 A Teeth, like hair, are not excretory organs
2 for mercury. It is known that some organic mercury
3 gets incorporated in hair. Teeth is more analogous to
4 bone, and you don't usually get mercury in bone.

5 Q It's tissue, correct?

6 A Well, it's a tooth.

7 Q Yes. It's tissue, and it's tissue that
8 contains two times more mercury in autistic children
9 than in that of normal children?

10 A Well, I'm not sure it's even a statistically
11 significant difference. The group size is small. I
12 can go into that if you'd like, and it doesn't have
13 any meaning. If anybody wanted to know do autistic
14 children have more mercury than nonautistic children
15 all they have to do is get blood levels or get urine
16 levels on the autistic children.

17 I mean, I know so many autistic children
18 have had this done. Nevertheless, there's not one
19 single study in the peer-reviewed English language
20 literature that reports a difference in blood mercury
21 level in autistic children or in urine levels in
22 autistic children compared to controls, and so I don't
23 know what to make of it. Teeth. It doesn't make any
24 sense. I'm not even sure it's a statistically
25 significant difference.

BRENT - CROSS (RESUMED)

1 Q Now, Doctor, you're familiar with the
2 Burbacher study, aren't you?

3 A Burbacher study? Yes.

4 Q Burbacher study. Yes. That was a study
5 done on primate monkeys?

6 A Yes.

7 Q That was a situation where they tried to
8 recreate the vaccine schedule. Was that it?

9 A Yes.

10 MS. CHIN-CAPLAN: Let me find it for you.
11 Twelve.

12 SPECIAL MASTER HASTINGS: I'm sorry?

13 MS. CHIN-CAPLAN: Twelve.

14 SPECIAL MASTER HASTINGS: Tab 12.

15 MS. CHIN-CAPLAN: Yes.

16 SPECIAL MASTER HASTINGS: Of Dr. Brent?

17 MS. CHIN-CAPLAN: Dr. Brent.

18 SPECIAL MASTER HASTINGS: All right. Thank
19 you.

20 BY MS. CHIN-CAPLAN:

21 Q So, Doctor, tell the Court what this study
22 consists of.

23 A Sure. I would be glad to. Thank you. This
24 was a comparison of mercury levels in infant monkeys
25 who were given either dietary methyl mercury or

BRENT - CROSS (RESUMED)

1 intramuscular thimerosal as in a vaccine. They did
2 the intramuscular injections once a week and gave over
3 a period of about three weeks roughly the amount of
4 thimerosal that an infant would receive in about six
5 months of vaccinations on a per kilogram basis.

6 Then they assessed the kinetics of what
7 happened following the exposure. In other words,
8 where the mercury went, what the rate of excretion
9 was, what was left behind, half-life, that kind of
10 thing.

11 Q They found out what the half-life was in the
12 primates at least for ethyl mercury, didn't they?

13 A Right.

14 Q And it was comparable to what has been noted
15 in humans, correct?

16 A Very, very close. It was about eight days.

17 Q Yes. Did they measure the amount of mercury
18 that was in the brain?

19 A Yes, they did.

20 Q When they measured the amount of mercury
21 that was in the brain what was the comparison between
22 the inorganic mercury from methyl mercury exposure and
23 that of ethyl mercury exposure?

24 A Well, it depends on the timeframe. Ethyl
25 mercury entered the brain and then effluxed from the

BRENT - CROSS (RESUMED)

1 brain.

2 Q It what?

3 A Effluxed. Left the brain. The other
4 process that goes on for both methyl mercury and ethyl
5 mercury is that there is some deorganification of the
6 mercury. In other words, it becomes inorganic
7 mercury. It happens a little bit more with ethyl
8 mercury than with methyl mercury. So as time goes on
9 there is faster loss in the brain with ethyl mercury
10 than with methyl mercury, but there's also faster
11 conversion of ethyl mercury to inorganic mercury in
12 the brain.

13 Q And the conversion of organic to inorganic
14 in the brain occurred with roughly three times the
15 amount for ethyl as opposed to methyl, wasn't it?

16 A I can give you the exact amount. Let me
17 just take a look here. It was more like twice the
18 amount, but you might be right. I'm just trying to
19 see where I can find it here in the paper. Well, I
20 can't find it right now. Instead of taking time
21 looking for it I thought it was twice as much, three
22 times as much, that ballpark.

23 Q Around three times more?

24 A Two or three times. Yes.

25 Q Right. So, Doctor, once it turns into

BRENT - CROSS (RESUMED)

1 mercuric mercury or inorganic mercury in the brain can
2 it leave?

3 A There is an efflux. It's very, very, very
4 slow.

5 Q Dr. Aposhian had given this example about a
6 family who ate a pig that drank mercury, and when the
7 woman died 29 years later the mercury was still 100
8 times the normal amount that was seen.

9 A Yeah. This is a very highly exposed
10 population. They had a huge exposure to mercury, and
11 a number of the family members died and there's one
12 survivor who when she ultimately died still had a
13 significant amount of mercury in her brain. That's
14 correct.

15 Q So inorganic mercury can be pretty toxic to
16 the brain, correct?

17 A Well, not necessarily. You wouldn't
18 necessarily expect that because the bad news, Ms.
19 Chin-Caplan, is that you, and I and everybody else in
20 this courtroom have nontoxicologically consequential
21 but significant amounts of inorganic mercury in our
22 brain. As a matter of fact, every time we eat a
23 seafood meal we're getting a bolus, some of which
24 becomes inorganic mercury in the brain.

25 We know that if people ate through both

BRENT - CROSS (RESUMED)

1 their diet, maybe to some degree from their dental
2 amalgams if they have it and from just the air around
3 us, which has mercury in it, we naturally accumulate
4 mercury in the brain, which becomes inorganic mercury
5 and stays there for a very long time, and that has no
6 pathological significance at all.

7 It doesn't cause an adverse effect unless
8 you get to very high levels, and there have been
9 multiple studies demonstrating that. So, yes, you get
10 inorganic mercury in your brain. You get inorganic
11 mercury in the brain from many, many, many different
12 sources. Not only people, every animal on the Earth
13 has a significant amount of inorganic mercury in the
14 brain because mercury is a naturally occurring
15 substance. It's in the air.

16 We've all developed very sophisticated
17 mechanisms to inactivate the mercury in the brain, and
18 you only actually can get an adverse effect from the
19 inorganic mercury in the brain if you have so much in
20 your brain that you overwhelm the very well-developed
21 defense mechanisms that we have.

22 Q Now, Doctor, you're a pediatrician, correct?

23 A I'm a toxicologist.

24 Q Did I also hear you say that you were a
25 pediatrician?

BRENT - CROSS (RESUMED)

1 A I'm a professor of pediatrics, but I'm a
2 medical toxicologist.

3 Q Okay. You do know that the nervous system
4 and the immune system of infants are continuing to
5 develop for the first two years of their lives,
6 correct?

7 A To some degree.

8 Q Yes. And during those first two years is
9 the same time that the thimerosal containing vaccines
10 are being administered, correct?

11 A They were.

12 Q Yes. So these vaccines are being
13 administered at one of the most vulnerable periods in
14 their lives?

15 A Yes, that's right, but very unlikely with
16 any ill effect.

17 Q How do you know that?

18 A Well, number one, there has never been,
19 other than the very, very rare allergy -- we're not
20 talking about allergy, you can get allergy with any
21 medication, I assume you don't want to talk about that
22 -- a demonstration that thimerosal in doses in
23 vaccines given to infants causes an adverse effect.

24 As you know this has been extremely well-
25 studied, this has been extremely well-scrutinized and

BRENT - CROSS (RESUMED)

1 as a matter of fact it wouldn't even be plausible, and
2 I'll tell you why. It's a very interesting analysis
3 that was just published from Brazil where their
4 immunization schedule using thimerosal was pretty much
5 similar to the United States.

6 Q Did you say McGill?

7 A Brazil.

8 Q Brazil?

9 A Yes. The country Brazil. They looked at
10 the mercury exposure from breast feeding, and they
11 breast feed about the same amount in Brazil as they do
12 here, and from the thimerosal in the vaccines. It
13 turns out there's twice as much mercury exposure from
14 breast feeding as there is from ethyl mercury in the
15 vaccines.

16 So it's hard to imagine how the amount of
17 mercury that we get from breast feeding is going to
18 have an adverse effect or that the amount of mercury
19 that we get from vaccines is going to have an adverse
20 effect.

21 Q Well, Doctor, you are aware that there's at
22 least one breast feeding study that was done from the
23 Iraqi grain contamination cases, aren't you?

24 A Well, yeah, but those were very, very highly
25 exposed individuals.

BRENT - CROSS (RESUMED)

1 Q You must know that those babies did not
2 demonstrate ill effects for quite some time after they
3 were exposed?

4 A That's true, but this was following a very
5 large exposure. We've had a number of epidemiological
6 studies now, which I think will be discussed on
7 Monday, where children have been followed for long
8 periods of time following their thimerosal containing
9 vaccines and at least with regard to the question of
10 autism or ASD there's clearly no relationship based
11 on --

12 Q Well, when you say there's no relationship
13 you're relying solely on the epidemiological studies?
14 Is that it?

15 A I'm relying on the epidemiological studies
16 and the fact that there's nothing to the contrary that
17 suggests there is a relationship.

18 Q However, the molecular study seems to
19 indicate that there is an effect, doesn't it?

20 A What molecular study?

21 Q Well, the studies that we looked at on the
22 immune system.

23 A At high doses of mercury chloride or methyl
24 mercury?

25 Q Yes, those studies.

BRENT - CROSS (RESUMED)

1 A Well, no. You can't translate that to say
2 that low doses of ethyl mercury are going to have an
3 effect.

4 Q So you disagree with the statement earlier
5 that people could be asymptomatic from low doses, but
6 that further on in their lives that it would result in
7 symptomatic disease?

8 A Which statement was that? Was that the
9 reference statement about heavy metals? Is that what
10 you're referring to?

11 (Pause.)

12 Q Maybe it's Shenker. Yes, it's in Shenker.

13 A Was that the reference statement about heavy
14 metals?

15 Q Yes. It was on Tab 51 on page 540, and
16 you've already indicated with me that you agree with
17 these statements.

18 A Let me just take a look here.

19 Q It says epidemiological surveys and
20 laboratory studies have shown that when individuals
21 are exposed to low concentrations of heavy metals the
22 clinical symptoms appear to be silent or asymptomatic.
23 However, when the health status of asymptomatic
24 subjects is followed for long time periods there is
25 clear evidence of tissue or organ dysfunction.

BRENT - CROSS (RESUMED)

1 A That's a heavy metals statement, it's not a
2 mercury statement and it's completely unreferenced. I
3 have no idea what they're talking about.

4 Q Of course, the title of this article is
5 Immunotoxic Effects of Mercuric Compounds, correct?

6 A That's true. If they were talking about
7 mercury here in a specific study they would have said
8 mercury, and they would have cited the study.

9 Q So the fact that the title was on mercuric
10 compounds and they mentioned heavy metals makes you
11 think it's not mercuric compounds that they're talking
12 about?

13 A I think what they were trying to do is try
14 to generalize some other heavy metal and relate it to
15 mercuric compound.

16 Q Is there any reason to believe that mercury
17 does not act in the same manner as these other heavy
18 metals?

19 A Absolutely there are. There are no two
20 heavy metals that I can think of that have a similar
21 effect on the immune system. All of them at
22 appropriate doses will potentially have adverse
23 effects on the immune system, but they're different,
24 just like even different forms of mercury have
25 different effects on the immune system.

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BRENT - CROSS (RESUMED)

1 MS. CHIN-CAPLAN: Okay. Thank you, Doctor.

2 THE WITNESS: Thank you.

3 SPECIAL MASTER VOWELL: Dr. Brent, I have a
4 number of questions for you. This is Special Master
5 Vowell speaking.

6 THE WITNESS: Please.

7 SPECIAL MASTER VOWELL: You've used two
8 terms, as did I believe Dr. Aposhian, efflux and
9 hypersusceptibility. Would you define those terms for
10 me, and are you both using them in the same way?

11 THE WITNESS: Thank you very much for asking
12 that question. That's a great question. Efflux. I'm
13 not sure how Dr. Aposhian viewed efflux, but from the
14 context in which he was talking it was clear by the
15 fact that he was stating that he was discussing the
16 hair studies of Amy Holmes and the chelation study of
17 Bradstreet, and in fact he pretty much came out and
18 said this, and it's certainly what he said before the
19 IOM, that autistic children do not excrete mercury
20 well.

21 When we talk about in biological processes
22 molecules moving from one place to another they either
23 move in or they move out between compartments, and
24 efflux is basically moving out meaning out of the body
25 in this case. So his efflux disorder hypothesis is

BRENT - CROSS (RESUMED)

1 that the hair studies of Holmes and the chelation
2 study of Bradstreet are pointing to the fact that
3 these kids don't excrete mercury, don't efflux it out
4 of their bodies.

5 SPECIAL MASTER VOWELL: So they retain it,
6 and therefore more would be available to work its ill
7 effects on whatever system we're talking about?

8 THE WITNESS: That's exactly the hypothesis.
9 Precisely. Now, hypersusceptible, Dr. Aposhian did
10 not really define what he meant by hypersusceptible
11 other than, and this is what I infer from his
12 testimony, some hypothesized group of children that
13 react to mercury to get toxic at doses that nobody
14 else in the world would ever get toxic to, so they're
15 hypersusceptible.

16 Because of that ambiguity in that testimony
17 is one of the reasons I drew up that bell-shaped curve
18 with the second curve showing the hypersusceptible
19 population.

20 SPECIAL MASTER VOWELL: Yes.

21 THE WITNESS: There is a formal
22 toxicological concept of hypersusceptibility, and
23 that's what I tried to illustrate by those curves and
24 to say that when there is a hypersusceptible
25 population we have a way of looking for it, we know

BRENT - CROSS (RESUMED)

1 exactly what it is, although they've never been found
2 in the autistic group with regard to mercury.

3 SPECIAL MASTER VOWELL: That was the example
4 I think you used of Wilson?

5 THE WITNESS: Yes. That's exactly right.
6 That where there is hypersusceptibility to toxins very
7 often with not too much research we've actually
8 identified the hypersusceptibility. Wilson's disease,
9 hypersusceptibility to copper. We know the gene.
10 It's very clear. You can do a genetic test. They
11 either have it or they don't.

12 SPECIAL MASTER VOWELL: Bear with me for a
13 minute here.

14 THE WITNESS: Take your time.

15 SPECIAL MASTER VOWELL: In Dr. Aposhian's
16 testimony he talked about one in 500 children exposed
17 to the teething powder that caused acrodynia or Pink
18 disease developing the disease. Do you know how that
19 figure was derived, the one in 500?

20 THE WITNESS: Yes. Yes, I do. That I
21 believe derives back from one of the Dr. Warkany
22 articles.

23 SPECIAL MASTER VOWELL: Doctor? I'm sorry?

24 THE WITNESS: Warkany, W-A-R-K-A-N-Y.

25 SPECIAL MASTER VOWELL: Okay. The third

BRENT - CROSS (RESUMED)

1 exhibit?

2 THE WITNESS: Yes. Well, he wrote a couple
3 of articles. I'm not sure if it's that exact one, but
4 it's from that body of research. That number has been
5 carried forward and requoted in the literature.
6 Basically, what that number is is that if you look at
7 kids who were exposed to mercurous chloride from the
8 teething powder not all of them get mercury toxic in
9 the form of acrodynia, only some of them do.

10 There are two potential explanations for
11 that. One is that it's a hypersusceptible population
12 that does, and the other, which would be the more
13 common reason in toxicology, is it's simply a matter
14 of dose. Some got more, some got less, and it's only
15 the ones that got quite a lot that came down with the
16 disease, so they got the high dose.

17 In fact, looking at that Warkany study that
18 the Court now has come up with that clearly
19 demonstrates that the children who get acrodynia have
20 very, very high mercury levels, so it appears to be
21 just simply a dose-related phenomenon. The reason
22 that not everybody got it is you had to get a
23 significant dose.

24 SPECIAL MASTER VOWELL: So you're not aware
25 of any study that looks at a dose response level to

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BRENT - CROSS (RESUMED)

1 teething powders?

2 THE WITNESS: No. There's never been a dose
3 response level. We only have the study that shows
4 that children that have it have a very high titer in
5 terms of urine mercury, but it's never actually been
6 looked at in terms of a formal dose response analogy.

7 SPECIAL MASTER VOWELL: Right. And this was
8 not a study then that said of 2,000 children in this
9 town, assuming all of them were teething and got
10 teething powders, one in 500 developed this disease?

11 THE WITNESS: No.

12 SPECIAL MASTER VOWELL: Okay. All right.
13 Let me move on to a couple of other questions then.
14 One is the term used in much of the medical literature
15 you and Dr. Aposhian cited to refer to toxic I guess
16 levels of mercury is mercury intoxication. Does that
17 term have -- at some point you can say someone is
18 mercury intoxicated? Can you explain that term for
19 me?

20 THE WITNESS: Absolutely. Intoxication
21 simply means having enough of the substance on board
22 that it is causing some kind of an adverse of a toxic
23 effect. Classic example is alcohol. We use the word
24 intoxication all the time. You just have enough on
25 board, you get alcohol intoxicated, then you start to

BRENT - CROSS (RESUMED)

1 stagger and so on.

2 So toxicologically when you use the word
3 intoxication it simply means you've had a sufficient
4 exposure, you've had a sufficient dose, such that you
5 are now getting adverse effects from that substance.

6 SPECIAL MASTER VOWELL: Well, let me follow-
7 up on that compared to my previous question then.

8 THE WITNESS: Sure.

9 SPECIAL MASTER VOWELL: One of us could have
10 four drinks and the other have two drinks, each drink
11 containing the same amount of alcohol, and we would
12 have different reactions. One of us with four drinks
13 might be able to walk a straight line. If I had two
14 I'm sure I couldn't. Can you analogize the effects of
15 alcohol intoxication to mercury intoxication?

16 That if someone who is, for example, more
17 used to drinking, can walk that straight line at a
18 higher level of alcohol?

19 THE WITNESS: Yes. This is the bell-shaped
20 curve that we were talking about that if you look at
21 the dose of a substance, in this case alcohol,
22 necessary to cause a specific response, say walk a
23 straight line, that it's not going to be exactly the
24 same for everybody in the population, and that if you
25 look at enough people in the population it forms sort

BRENT - CROSS (RESUMED)

1 of this bell-shaped curve where most people are going
2 to sort of be in the middle, two to three drinks
3 probably do it for most people, but for some people it
4 could be seven and for some people it could be one.
5 So that's how this curve --

6 SPECIAL MASTER VOWELL: Okay. I'm not
7 articulating this well because I understand that.
8 What I'm getting at is if I'm used to drinking a great
9 deal and then I have two drinks the alcohol might have
10 a less apparent effect on me.

11 THE WITNESS: That's true.

12 SPECIAL MASTER VOWELL: So if someone is
13 exposed to low levels of mercury over a period of time
14 would they show intoxication, that is ataxia at the
15 same blood or urine mercury levels as someone else who
16 is getting a bolus dose?

17 THE WITNESS: I'm sorry. I misunderstood
18 your question. With alcohol there is a very well-
19 known phenomena, which I think everybody has had a
20 chance to see in people who drink a lot, it's known as
21 tolerance, where some people one or two drinks and as
22 we were saying you have an excess, but if people drink
23 quite a bit that curve shifts for them and they
24 develop a tolerance.

25 They could have six or seven drinks and, you

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BRENT - CROSS (RESUMED)

1 know, we'd never know they were drinking. That's
2 tolerance. It happens with alcohol, well, for several
3 reasons, metabolic adaptations and so on. There is no
4 similar tolerance with mercury. There are some minor
5 adaptations, but for the most part there is no similar
6 tolerance for mercury.

7 We already have our body's protection in
8 place and they can up regulate and down regulate a
9 little bit, but they don't change in a marked fashion.

10 SPECIAL MASTER HASTINGS: So while people
11 might fall at a different place in the bell curve the
12 fact that you were working at a thermometer
13 manufacturing plant would not have any effect on where
14 you would fall on that bell curve?

15 THE WITNESS: That's exactly right.

16 SPECIAL MASTER VOWELL: Okay. You've
17 indicated the different species of mercury have
18 different effects. At the level of intoxication how
19 are the effects of methyl mercury distinguished from
20 ethyl mercury in terms of clinical signs and symptoms?

21 THE WITNESS: Yeah. That's a very good
22 question. This might be in the record. There was a
23 major review on this subject by Tom Clarkson where he
24 had listed all the different kinds of mercury and the
25 clinical effects of the different kinds of mercury to

BRENT - CROSS (RESUMED)

1 show how different they are. My reading of that
2 review is that it is a very good reflection of what I
3 believe to be in the literature.

4 So, for example, with methyl mercury almost
5 all of the effects are in the central nervous system,
6 in the brain, as with methyl mercury. With ethyl
7 mercury because of the rapid separation of the mercury
8 off the ethyl group then it generates this inorganic
9 mercury as we were talking about before. Inorganic
10 mercury tends to effect primarily the kidney.

11 That doesn't happen much with methyl
12 mercury. So with methyl mercury we would see at high
13 doses effecting the brain, low doses don't worry about
14 having your seafood dinner tonight, it's good for you.
15 Ethyl mercury on the other hand, similarly at high
16 doses you could see the effects in the brain if you
17 have a sufficient dose, but you will also see effects
18 of the kidney.

19 SPECIAL MASTER VOWELL: All right. Let's
20 leave aside the things that we're not going to observe
21 with our eyes. Let's just talk about the clinical
22 picture of the Iraqi farmer who ate the methyl mercury
23 contaminated wheat walks into a medical clinic along
24 with the Chinese farmer who ate the ethyl mercury
25 contaminated rice. How are their symptoms going to

BRENT - CROSS (RESUMED)

1 differ at the level of intoxication?

2 THE WITNESS: Their central nervous system
3 symptoms would probably be the same, the tunnel vision
4 would probably be the same, the tremor would probably
5 be the same, the paresthesias would probably be the
6 same, but you would also see some renal effects,
7 abnormal renal function, in the ethyl mercury exposed
8 version.

9 SPECIAL MASTER VOWELL: Okay. Are the
10 amounts of ethyl mercury that would produce those
11 physically apparent toxic effects the same amounts as
12 ethyl mercury?

13 THE WITNESS: As methyl mercury?

14 SPECIAL MASTER VOWELL: Yes, as methyl
15 mercury.

16 THE WITNESS: Right.

17 SPECIAL MASTER VOWELL: I mean, if we're
18 comparing grain, rice, wheat, whichever we're eating,
19 does the amount of the ethyl mercury in the rice
20 differ from the amount of methyl mercury in the
21 wheat --

22 THE WITNESS: Yeah. That was well-covered
23 in the Burbacher paper that we were just discussing
24 because one of the things that they considered was
25 this whole business about the difference between the

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BRENT - CROSS (RESUMED)

1 reference dose for methyl mercury in application to
2 ethyl mercury, and he pointed out that if you use the
3 reference dose for methyl mercury and apply it to
4 ethyl mercury you will over estimate its toxicity
5 compared to what it really is because you would expect
6 the ethyl mercury to be less toxic.

7 SPECIAL MASTER VOWELL: Okay. So if I
8 understand what you're saying it would take more ethyl
9 mercury to produce the same effect that you would see
10 with a smaller amount of methyl mercury?

11 THE WITNESS: Right. And in fact, that's
12 only experimentally shown. Laslo Magos published a
13 paper in 1985 where he gave animals equivalent doses
14 of methyl mercury and ethyl mercury and then higher
15 doses, and he showed that you need more ethyl mercury
16 to get a degree of damage to the brain than you need
17 methyl mercury.

18 SPECIAL MASTER VOWELL: If I ingest a
19 certain amount of ethyl mercury versus having it
20 injected, how does that impact the toxicity of the
21 substance?

22 THE WITNESS: Well, the toxicity will depend
23 on the blood level, and so you would probably get a
24 little higher blood level from an ingestion than you
25 would from an injection.

BRENT - REDIRECT

1 SPECIAL MASTER VOWELL: I'm talking about
2 intramuscular injection.

3 THE WITNESS: That's exactly right. The
4 reason is because it's an intramuscular injection and
5 it's slowly absorbed you don't get very high blood
6 levels.

7 SPECIAL MASTER VOWELL: So intravenous
8 injection versus ingestion you would get a higher
9 level depending on how you were administering it?

10 THE WITNESS: Absolutely.

11 SPECIAL MASTER VOWELL: All right. I think
12 those are all my questions. Thank you very much, Dr.
13 Brent.

14 THE WITNESS: Thank you.

15 SPECIAL MASTER HASTINGS: Any redirect for
16 this witness?

17 MS. RENZI: I just have one question.

18 SPECIAL MASTER HASTINGS: Please go ahead.

19 REDIRECT EXAMINATION

20 BY MS. RENZI:

21 Q Dr. Brent, Ms. Chin-Caplan spent a great
22 deal of time this afternoon going through the
23 literature on mercury and its effect on the immune
24 system. At one point you said that you would agree
25 with any of the statements that she read from that

BRENT - REDIRECT

1 literature to the effect of mercury on the immune
2 system. I know you've said this, but I want to make
3 it abundantly clear.

4 What significant caveats do you place on the
5 statement with respect to the form of mercury, and
6 also, the dose?

7 A Well, those are the two most important
8 considerations. I hope I haven't been redundant
9 today, but I really wanted to make these points.
10 They're fundamental points.

11 When we're talking about mercuric chloride,
12 when we're talking about methyl mercury, we're not
13 talking about ethyl mercury, we're not talking about
14 the exposures in vaccines, so you cannot assume that
15 all the statements, which I agreed with -- yeah,
16 methyl mercury at this concentration will cause that,
17 and mercuric chloride at that concentration will cause
18 something else -- have anything do with the exposures
19 to ethyl mercury.

20 The other issue of course is that ethyl
21 mercury we can make to have adverse effects on the
22 immune system. They won't be exactly the same as
23 methyl mercury or mercuric chloride, but it can be
24 shown to have some adverse effects on the immune
25 system, but you have to go once again to very, very

BRENT - REDIRECT

1 high doses compared to anything that anybody could
2 possibly expect to experience from a vaccine.

3 So both of those concepts have to be taken
4 into consideration. You want to know about ethyl
5 mercury you have to ask what the data is on ethyl
6 mercury. If you want to know what happens in a
7 vaccine you have to ask what happens if the dose is
8 associated with a vaccine?

9 MS. RENZI: Thank you. I have no further
10 questions.

11 THE WITNESS: Thank you.

12 SPECIAL MASTER HASTINGS: Anything further
13 for this witness?

14 MS. CHIN-CAPLAN: No, Special Master.

15 SPECIAL MASTER HASTINGS: All right. Dr.
16 Brent, we kept you up there all day. We thank you
17 very much. You're excused at this point.

18 THE WITNESS: Well, thank you, Special
19 Master.

20 (Witness excused.)

21 SPECIAL MASTER HASTINGS: Before we break
22 for the day I understand that's all the testimony we
23 have for today.

24 Mr. Matanoski?

25 MR. MATANOSKI: That's correct, sir.

1 SPECIAL MASTER HASTINGS: The schedule for
2 Monday is Dr. Griffin and Dr. Fombonne?

3 MR. MATANOSKI: That's correct.

4 SPECIAL MASTER HASTINGS: In what order?

5 MR. MATANOSKI: I believe it will be Dr.
6 Fombonne first, sir.

7 SPECIAL MASTER HASTINGS: Okay. All right.
8 So that's the witnesses we have for Monday, and that
9 will conclude the government's case I assume?

10 MR. MATANOSKI: That's the government's case
11 in chief, yes, sir.

12 SPECIAL MASTER HASTINGS: Case in chief.
13 Correct. Then we'll be adjourned for today. We'll
14 see you folks Monday morning at 9:00 a.m. Thank you,
15 all.

16 (Whereupon, at 3:32 p.m., the hearing in the
17 above-entitled matter was adjourned, to reconvene on
18 Monday, June 25, 2007, at 9:00 a.m.)

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REPORTER'S CERTIFICATE

DOCKET NO.: 98-916V
CASE TITLE: Theresa Cedillo v. HHS
HEARING DATE: June 22, 2007
LOCATION: Washington, D.C.

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 Office of Special Masters.

Date: June 22, 2007

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