

1 IN THE GENERAL COURT OF JUSTICE
SUPERIOR COURT DIVISION
2 STATE OF NORTH CAROLINA, COUNTY OF FORSYTH
3 Civil Action No. 07-CVS-3770

4
TELEPHONE DEPOSITION OF: DAVID W. PYATT, Ph.D.
5 August 11, 2009

6 ANDREW WOLFE and DENISE WOLFE,

7 Plaintiffs,

8 v.

9 E.I. DUPONT DE NEMOURS AND COMPANY, et al.,

10 Defendants.

11
12 PURSUANT TO NOTICE the telephone
13 deposition of DAVID W. PYATT, Ph.D., was taken on
behalf of the Plaintiffs at the St. Julien Hotel, 900
14 Walnut Street, Boulder, Colorado 80302, on August 11,
2009, at 10:07 a.m., before Teresa Coogle, Registered
15 Professional Reporter and Notary Public within
Colorado.

A P P E A R A N C E S

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(Appearing Telephonically)

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Also present: Ellie Detherage

I N D E X

EXAMINATION OF DAVID W. PYATT, Ph.D.: PAGE
August 11, 2009

By Mr. Kiwala 4

INITIAL
REFERENCE

DEPOSITION EXHIBITS:

1 Curriculum Vitae of David W. Pyatt	7
2 Testimony Given by Dr. David Pyatt	9
3 Declaration	15
4 Letter to Salveson from Pyatt, 7/9/09, Subject: Andrew Wolfe and Denise Wolfe v. E.I. DuPont De Nemours and Co., et al., In the General Court of Justice, Superior Court Division, No. 07-CVS-3770	15
5 Article entitled, "The Environment and Disease: Association or Causation?"	21
6 Article entitled, "Translocation t(7;11(P15;P15) In A Patient With Therapy-Related Acute Myeloid Leukemia Following Bimolane and ICRF-154 Treatment For Psoriasis"	70
7 Article entitled, "Benzene metabolites antagonize etoposide-stabilized cleavable complexes of DNA topoisomerase IIalpha	104

1 WHEREUPON, the following proceedings were
2 taken pursuant to the North Carolina Rules of Civil
3 Procedure.

4 * * * * *

5 DAVID W. PYATT, Ph.D.,
6 having been first duly sworn to state the whole truth,
7 testified as follows:

8 EXAMINATION

9 BY MR. KIWALA:

10 Q. Dr. Pyatt, this is -- I'm sorry, have I
11 pronounced that correctly?

12 A. Yes, thank you, you did.

13 Q. Okay. This is Ryan Kiwala of Simmons
14 Browder Gianaris Angelides & Barnerd, LLC. Could you
15 state your full name for the record, please.

16 A. David William Pyatt.

17 Q. And, Dr. Pyatt, what is your current
18 business address?

19 A. 1944 Cedaridge Circle, Superior,
20 Colorado, 80027.

21 Q. Okay. And, Dr. Pyatt, by which party or
22 parties in this case have you been asked to provide
23 expert services?

24 A. I was -- my understanding is all of them.
25 I was asked to provide service for PPG, Sherwin

1 Williams, Valspar, Safety-Kleen, DuPont, and 3M.

2 Q. Are you prepared to render your opinions
3 in this case today?

4 A. Yes, sir.

5 Q. Have you brought any materials with you
6 today for the -- for the deposition?

7 A. Yes, I have.

8 Q. Okay. Could you tell me what you brought
9 with you?

10 A. Sure. I brought a copy of
11 Dr. Garabrant's, Dr. Natelson's, and my report, both
12 the original as well as the supplemental report. I
13 brought a copy of the various exposure expert reports.
14 I think there were five or so. All right. So those.

15 I have a copy of Dr. Zukerberg's,
16 Zahalsky, and Dr. Milman's reports that they produced
17 in this case. Then I have four binders with various
18 scientific studies that have all been produced to you,
19 at least that's my understanding. I -- I produced
20 them. But I have a hard copy in case you want to talk
21 about specific studies. And they are studies
22 regarding cytogenetics and benzene exposure, studies
23 regarding the disease APL, acute promyelocytic
24 leukemia, studies on formaldehyde, epidemiology, and
25 painters. The epidemiology on the painter literature.

1 So that's -- I have a hard copy of those studies.

2 Q. Okay. Those studies that you mentioned,
3 are those the studies that you have cited in the two
4 declarations that you made?

5 A. Yes.

6 Q. Are there any studies or other literature
7 in that collection of four binders that are not cited
8 in your declaration?

9 A. I'm sure there are.

10 Q. Would you be able to say which ones are
11 in there that are not cited?

12 A. Sure, I could do that. I mean, it would
13 be a fairly time-consuming process. We would just go
14 through my report and pick out the one. But I know,
15 like, the benzene cytogenetic binder, it's got every
16 single study in there where anyone has ever reported
17 or discussed cytogenetic abnormalities associated with
18 benzene exposure. And I -- there was no reason to
19 cite all of that in my report.

20 So, for sure, there's going to be a lot
21 of studies in that binder. The formaldehyde binder, I
22 think most of those I cited in my -- in my
23 supplemental report. There might be one or two that I
24 didn't. The APL binder, I suspect there are some
25 papers in there that are not in my report.

1 Q. Okay. Just for the sake of brevity, we
2 won't go through one by one and figure out which ones
3 are and which are not cited in the report. We'll just
4 move along.

5 Have you done all of the work required to
6 reach your opinion or opinions in this case?

7 A. I don't -- I don't think I understand
8 your question. Have I done all of the work?

9 Q. Well, is there any work that you had to
10 do that -- but you were unable to do before you signed
11 the declarations or before you came today for the
12 deposition?

13 A. Oh, I see. No. No, I'm prepared to
14 render my opinions. I mean, there -- yes, I'm
15 prepared to render my opinions.

16 Q. Okay.

17 MR. KIWALA: Teresa, I believe there were
18 some documents that were sent to you. Do you have
19 those with you there?

20 (Deposition Exhibit 1 was marked.)

21 Q. (BY MR. KIWALA) Dr. Pyatt, I'm going to
22 ask you to take a look at Exhibit 1. Is this your CV?

23 A. Yes.

24 Q. Is the CV up to date?

25 A. I'm checking. No.

1 Q. Okay. Can you tell me what's missing?

2 A. Well, yeah. This is actually probably
3 two years old. I mean, my last publication in this CV
4 that I'm looking at here was from 2006. And I've
5 published probably five or six, or maybe even more,
6 papers since then. The assistant clinical professor
7 on the first page, the Biometrics and Preventative
8 Medicine Department is no longer in existence. It's
9 now been folded into the new Colorado School of Public
10 Health, which I'm a -- you know, I have the same
11 appointment, but it's a different school. So -- I
12 mean, for the most part, it's going to be reasonably
13 accurate; but it is just not completely up to date.

14 Q. Okay. Do you have a more recent version
15 of your CV?

16 A. You know, I don't think I brought it. I
17 had in my mind that it would be here and that I didn't
18 need to. I can certainly send it to you.

19 Q. Okay. You don't have it with you, but a
20 more recent version does exist is what you're saying,
21 correct?

22 A. Yes. Oh, yes, absolutely.

23 Q. Okay. I would ask you to just give a
24 copy of that to counsel for defense, whoever you're
25 communicating with, and have them pass that along to

1 plaintiffs counsel.

2 A. You bet.

3 Q. And, Dr. Pyatt, what would you consider
4 to be your particular area or areas of expertise?

5 A. Well, by training, I am a toxicologist;
6 so I think that would be the broad category. I've
7 spent my whole career, including my training --
8 post-doctoral training working in the hematopoietic
9 system. So bone marrow toxicity, hematopoietic
10 toxicity, immunological toxicity. That, I think,
11 would be my specialty within the broader category of
12 toxicology. Most of my work and research has been on
13 benzene and benzene metabolites as they are -- relate
14 to those first two categories. I mean, I think I have
15 expertise in that area as well.

16 Q. Okay.

17 MR. KIWALA: And, Teresa, could you go
18 ahead and mark the document that's entitled Testimony
19 Given by Dr. David Pyatt.

20 (Deposition Exhibit 2 was marked.)

21 Q. (BY MR. KIWALA) Dr. Pyatt, could you
22 take a look at Exhibit 2. And can you tell me, does
23 that accurately reflect all of the testimony that you
24 have ever given either by deposition or at a trial or
25 hearing?

1 A. The trial or hearing part is accurate.

2 There has been one additional deposition.

3 Q. Okay.

4 A. So I guess that would bring the list up
5 to 18.

6 Q. Okay. In that one additional deposition
7 that's not listed, what did that case involve?

8 A. The case was called Mallory versus.
9 Goodyear. And it was an allegation that Mr. Mallory's
10 disease was related to his occupational exposures as a
11 rigger and repair person in the Goodyear facility in
12 Ohio.

13 Q. Was there any claim of exposure to a
14 particular chemical or substance?

15 A. Yes, sir, it was -- it was benzene just
16 from the manufacturing of tires, et cetera, within the
17 -- within the facility. He didn't actually use that,
18 but that was the allegation.

19 Q. Okay. And did you testify for the
20 plaintiff or for the defendant in that case?

21 A. It was for the defendant.

22 Q. I take it that was Goodyear; is that
23 correct?

24 A. Yes. It was Goodyear, correct.

25 Q. Of the testimony that's listed on

1 Exhibit 2, which of those cases involved a claim of --
2 or somebody alleging disease as a result of exposure
3 to benzene or benzene-containing products?

4 A. I -- they all have. That's really the
5 only area that I have ever given testimony in.

6 Q. And for -- for all of those, on which
7 side did you testify, plaintiffs or defendants?

8 A. I have -- I have never given testimony on
9 behalf of a plaintiff at this point in my career.

10 Q. Okay. I'm going to just get into some
11 questions about this case in particular. When were
12 you first contacted regarding this case?

13 A. I think it was -- I can't give you an
14 exact date, but it was sometime in the fall of 2008.

15 Q. Okay. And do you recall who contacted
16 you at that time?

17 A. I -- my recollection is that it was Chris
18 Stofko or Mike Sweeney from his office, or it might
19 have been Andrew Schirrmeister. But I -- I don't --
20 it was -- it all kind of happened about the same time.
21 And then I believe they formed kind of a collaborative
22 agreement, and so then it -- I kind of was working for
23 everyone and it stopped mattering, really, who was the
24 first. But I believe it was Chris Stofko's office.

25 Q. And when you were first contacted by

1 Mr. Stofko's office, what did they tell you about the
2 case?

3 A. I don't remember that conversation, but
4 generally how this process works is that they will ask
5 me if I have time, based on what the scheduling is,
6 and if I will take a look at the case. And then I
7 agree or not. If I agree, then they send me
8 information, and I take a look at it. And then at
9 some point after that, we have a discussion about
10 what, you know, my initial thoughts are. And I have
11 no reason to think that this worked any differently.

12 Q. Okay. I think you said that they had
13 initial discussion where they asked if you had time to
14 take on the case. I take it you said yes. And am I
15 correct they sent you some materials to review? Is
16 that correct?

17 A. Yes. They would have -- I'm trying to
18 think what would have come in that earlier -- probably
19 the first volume of Mr. Wolfe's deposition, maybe the
20 original complaint. I -- some MSDS sheets. I know
21 that was kind of early from various defendants. And
22 medical records.

23 Q. Did you -- when did you first form any
24 opinion, formal or informal, about this case?

25 A. I would say that's going to be in the

1 fall of '08 as well.

2 Q. Okay. At the time that you were first
3 contacted?

4 A. Well, it wouldn't have been a spur of the
5 moment decision like that, but -- but sometime within,
6 say, a month or two months of that initial
7 conversation.

8 Q. Okay. So after you reviewed the -- the
9 initial materials that you were sent -- and I think
10 you said it was the first volume of the deposition,
11 the complaint, and some MSDS. There may have been
12 others -- other documents, but the record will speak
13 for itself. At that point, what was your initial
14 opinion from your review of those materials?

15 A. Yeah, in the list that I gave you -- and
16 that's the best that I can recall; but like you said,
17 there should be a record of what was sent. So I don't
18 have to remember all of that.

19 My initial opinion, which I probably
20 provided to whoever I originally talked to, was that
21 based on my understanding and my appreciation of the
22 literature, APL, the type of AML that Mr. Wolfe had,
23 was not a benzene-related malignancy. So I think that
24 was the overriding and the most important opinion that
25 I have in this case. And -- because I've worked on

1 another APL case, and I've thought about this a lot
2 through the years, that was something that I could
3 provide, you know, reasonably quickly.

4 Q. At what point -- was there any
5 information that you had asked for to review to arrive
6 at an opinion -- anything that you requested from the
7 defendants at that time when you gave -- after you
8 gave your initial opinion?

9 A. Anything that I requested?

10 Q. Yeah, any materials that you thought
11 would be particularly relevant for you in developing
12 your opinions or creating a report.

13 A. At that time or in general, the whole
14 time.

15 Q. Let's just start at that time.

16 A. I don't think there was anything that I
17 felt like I needed at that -- at that point in time.
18 And then as the case progressed, they were sending me
19 new information as it became available. So early on,
20 there wasn't anything that I felt like I needed that I
21 had asked for that -- at that point.

22 Q. Okay. Was there ever a point where you
23 asked for something and you did not receive it from
24 counsel for the defense?

25 A. I can't think of anything, no. They have

1 been very responsive.

2 Q. And there are two declarations that you
3 -- that you signed.

4 MR. KIWALA: And, Teresa, could go ahead
5 and mark those as Exhibits 3 and 4.

6 (Deposition Exhibits 3 and 4 were
7 marked.)

8 Q. (BY MR. KIWALA) And, Dr. Pyatt, if you
9 take a look at what's been marked as Exhibit 4, it
10 appears to be a second declaration or supplemental
11 declaration for this case. It's addressed to an Erik
12 T. Salveson. Would it be -- is it correct that at
13 some later point, you were asked to give an opinion
14 about what the existing scientific and epidemiological
15 evidence was regarding formaldehyde exposure in
16 leukemia?

17 A. That's -- that's precisely what happened.

18 Q. Okay. Do you know when you were
19 initially contacted to -- regarding this supplemental
20 opinion and declaration?

21 A. I -- no, not specifically. I mean, if I
22 had the report, July 9, it was a fairly short
23 turn-around when Mr. Salveson called me and asked if
24 -- if I knew anything about this and whether I could
25 address it in a supplemental report. So I'm going to

1 say sometime mid-June, but I don't -- you know, I
2 didn't write it down. I don't know precisely when,
3 but somewhere two or three weeks prior to when this
4 report was submitted.

5 Q. And in preparing this supplemental
6 declaration or report, did defense counsel provide you
7 with any additional materials?

8 A. Not that I recall, no. Things were
9 coming all the time, so I --

10 Q. Okay.

11 A. But nothing -- you know, nothing
12 specifically -- I had all of the formaldehyde
13 literature. This is something that I've done some
14 other work on, so there wasn't really anything that I
15 needed.

16 Q. Over the course of this case, has there
17 been any scientific or medical literature that was
18 supplied to you by counsel for the defendants?

19 A. No, sir. I think the converse is true.

20 Q. And can you tell me, do your declarations
21 -- well, before I get to that, if you would take a
22 look at Exhibit 3. Do you recognize that as your
23 original declaration for this case?

24 A. It -- it looks -- I mean, it's got this
25 funny box around it, so it's not exactly my -- the

1 original one that I submitted, but I have no reason to
2 doubt that it's accurately reproduced. It looks like
3 it's been scanned or something, so it's not actually
4 what I -- what I produced, but it's -- I'm sure it's
5 right.

6 Q. Okay. At any rate, do you have any
7 reason to believe that Exhibit 3 did not set forth a
8 true and accurate reflection of your opinions in this
9 case?

10 A. No. No, sir, and I didn't mean to imply
11 that.

12 Q. Okay. Nothing inferred. And do -- your
13 declarations set forth in Exhibit 3 and 4, do they --
14 do those two declarations set forth all of the
15 opinions that you're prepared to give in this case?

16 A. I -- I think there could be additional
17 information regarding plaintiff experts that I might
18 be asked to discuss; but as far as my own professional
19 opinions about this case, these two reports accurately
20 reflect that.

21 Q. Would you agree that the opinions
22 that are stated in your declaration are generally --
23 generally deal with what's known as general causation?

24 MR. DETHERGE: Objection, lack of
25 foundation. And, Ryan, can we agree that an objection

1 by one defendant is good for all as we have in the
2 other depositions?

3 MR. KIWALA: Sure.

4 A. Well, I guess I'm not quite sure how to
5 answer that. While I addressed both with formaldehyde
6 and benzene in APL, what the scientific literature
7 says with regards to those exposures and the disease,
8 since Mr. Wolfe had APL, then those opinions are
9 relevant and directly germane to my opinions regarding
10 him as well when that would be more of a specific
11 causation. So I'm not quite sure how to answer your
12 question.

13 Q. (BY MR. KIWALA) Let me see if I
14 understand you correctly. Do you mean to say that you
15 have an opinion as to specific causation in this case
16 insofar as your opinion on general causation is that
17 benzene exposure and formaldehyde exposure cannot
18 cause APL specifically or leukemia or -- well, APL
19 specifically?

20 MR. DETHERGE: Same objection.

21 A. Yeah, I don't think I said it very
22 clearly, and so what you said wasn't very clear to me
23 either. Let's try again. I don't believe the
24 literature supports an association between APL and
25 benzene or APL and formaldehyde. So from that

1 standpoint, that is more of a -- I guess you would
2 classify that as a general causation argument. But
3 that analysis and that literature is directly germane
4 to Mr. Wolfe, because that's the kind of disease that
5 he had.

6 Q. (BY MR. KIWALA) And just to follow-up,
7 the point is that you can't have specific causation
8 without general causation established first, correct?

9 MR. DETHERGE: Same objection.

10 A. I think that's a reasonable
11 interpretation, yes.

12 Q. (BY MR. KIWALA) Dr. Pyatt, if you'll go
13 ahead and turn to Exhibit 3. You spent some time
14 discussing Bradford-Hill criteria. Can you tell me
15 what the Bradford-Hill criteria are?

16 A. Well, it was a presidential address that
17 Sir Bradford-Hill gave to a medical conference. And
18 it was -- set forth a criteria or a guideline, or
19 however you want to describe what his list was, that
20 would, to some degree, formalize the process that
21 would allow scientists to evaluate the difference
22 between causation and association. And that's the
23 title of his -- title of his address.

24 So it set forth a series of
25 considerations that one needs to have in order to be

1 able to say, yes, I -- I think this disease was, in
2 fact, caused by these exposures. That's the
3 Bradford-Hill so-called criteria or whatever you --
4 you know, whatever term you would like to put on them.

5 It's not the only ones that are out
6 there. As I referenced in my report, Evans had
7 something very similar. The Koch postulates are very
8 similar. You know, it's just a methodology for
9 establishing causation.

10 Q. Okay. And if you'll take a look
11 specifically at paragraph 7 in Exhibit 3.

12 A. Yes, I'm there.

13 Q. You set forth seven questions that you
14 say must be addressed to reach a tenable conclusion on
15 general causation, correct?

16 A. Well, these -- I mean, I didn't set these
17 forth. These were the ones that came directly from
18 Dr. Hill's address.

19 Q. Are there any in that list that are --
20 any questions in that list that are not set forth in
21 Dr. Hill's address?

22 A. I -- not that I am aware of, no.

23 Q. Okay. Are there any guidelines or
24 criteria that were set out in Dr. Hill's address that
25 don't appear on that list of seven questions?

1 A. I think I might have combined a couple.
2 Let's see. Because I know he has nine and I have
3 seven. But without comparing them directly, I
4 couldn't tell you which ones those are. I mean, these
5 are, I think, by everyone's interpretation, the most
6 important. But I may have -- I may have combined one,
7 because I know he has nine.

8 Q. Okay.

9 (Deposition Exhibit 5 was marked.)

10 Q. Dr. Pyatt, is this a copy of the address
11 that you mentioned earlier that was given by Austin
12 Bradford-Hill?

13 A. Yes.

14 Q. And can you tell me from looking at that
15 address what factors you believe you may have combined
16 into those seven questions and specifically how?

17 A. It's -- okay. Looks like I didn't
18 include No. 9, the analogy.

19 Q. Okay. Is that an important question to
20 consider when rendering an opinion as to causation?

21 A. Well, I don't think it's nearly as
22 important as the first two or three.

23 Q. Okay.

24 A. Coherence, I kind of think of that really
25 in terms of plausibility, what we know about the

1 disease, what we know about the chemical. So that one
2 -- that might be a combination.

3 It looks like most of the first ones are
4 -- are the same. Specificity, consistency, strength
5 of the association. Those are really the most
6 important.

7 Q. Okay. The seventh question you had in
8 paragraph 7 mentions -- well, it says, "Are there
9 alternative mechanisms or known risk factors that
10 potentially could have caused the disease or
11 confounded interpretation of the results?"

12 Where do those -- where does that
13 question fit in, in your opinion, to the Bradford-Hill
14 criteria? Or does it?

15 A. I'm looking. That's a good question.
16 Well, I don't -- I'm not seeing it specifically
17 addressed in this one, so perhaps that came from
18 reference 1, Evans, "Causation and disease: The
19 henkle-koch postulates revisited". It may have come
20 from that Yale publication. I don't -- I don't see it
21 in Bradford-Hill's paper.

22 Q. Okay. Let's move along to paragraph 8 in
23 Exhibit 3.

24 A. Okay.

25 Q. You mention -- you state in paragraph 8

1 -- and I'll go ahead and read it directly -- "The
2 minimum standard within the scientific and
3 epidemiological communities for determining
4 quantitatively if the risk of disease is truly higher
5 in the exposed population is a relative risk (or some
6 comparable measurement) greater than 1.0 with a
7 95 percent confidence interval that does not include
8 the value of 1.0."

9 Did I read that correctly?

10 A. Yes.

11 MR. DETHERGE: Actually, you left out the
12 word statistical, Ryan, which is probably an important
13 word in that sentence.

14 MR. KIWALA: Oh.

15 THE DEPONENT: I thought he did say
16 statistical.

17 MR. DETHERGE: I don't think so.

18 A. Okay. The minimal statistical standard.
19 We all agree with that.

20 Q. (BY MR. KIWALA) I would agree to that.
21 It does say that. Can you --

22 A. Thank you.

23 Q. Can you explain to me what you mean by
24 that, the phrase "minimal statistical standard"?

25 A. Well, what I mean by that is if you want

1 to -- I mean, if it's -- in order to decide whether or
2 not there's truly an increase in an exposed
3 population, which is something that you obviously want
4 to do if you think exposure caused the disease, you --
5 you -- the relative risk, however you define that,
6 whether it's standard mortality ratios or odds ratios,
7 or whatever, need to be greater than 1, whereas 1
8 would be there is no difference between the two
9 populations. But because there is variability and,
10 basically, noise in all of these experiments, then you
11 conduct a statistical analysis to rule out or at least
12 limit the possibility that chance played in the
13 numbers that you're looking at. And so that's where
14 the 95 percent confidence interval or a p-value of
15 less than .05 comes in, because it will allow you to
16 get your arms around the role that chance may have
17 played in your number.

18 Q. Okay. I guess what I'm asking is -- and
19 maybe I didn't phrase the -- the question very well.
20 Do you mean to say that a study showing a relative
21 risk greater than 1.0 with a 95 percent confidence
22 interval -- is that something that you have to have in
23 order to render an opinion that there's a positive
24 cause -- you know, causal association? Is that
25 relative risk higher than 1 something you absolutely

1 have to have?

2 MR. GOTTLIEB: Object to form.

3 A. Yeah, sorry. That was a fairly
4 convoluted question. Can we try that again?

5 Q. (BY MR. KIWALA) Sure. Are you saying
6 that a relative risk higher than 1 and a -- with a
7 confidence interval of 95 percent -- is that a -- is a
8 study showing that something necessarily you have to
9 have in order to render an opinion as to causation?

10 MR. GOTTLIEB: Object to form.

11 A. Okay. The way you worded your question,
12 you just said a 95 percent confidence interval.

13 Q. (BY MR. KIWALA) Um-hum.

14 A. I don't know what that means. I mean,
15 you need to calculate the 95 percent confidence
16 interval, but you didn't put any values with that. So
17 I don't know how to answer your question.

18 Let me -- let me try this: If you have a
19 relative risk that's greater than 1, then that means
20 by definition that you saw more of the disease in the
21 exposed population than you did in the control group.
22 All right. If it's less than 1, then you saw less.
23 It's just a simple ratio, it's not magic. But there's
24 a lot of variability and there's all kinds of
25 uncertainties in these studies. And so that's why you

1 need to do a statistical analysis or a statistical
2 comparison that you can, with any degree of scientific
3 confidence, say, yes, there really was an increase in
4 the exposed population compared to the control
5 population. And that needs to happen irrespective of
6 what the relative risk is.

7 The relative risk could be 1.2 or the
8 relative risk could be 12. And that doesn't negate
9 the requirement of having some statistical analysis
10 done to rule out the role that chance could play in
11 your findings.

12 The scientific standard that is used
13 today is that the 95 percent confidence interval
14 cannot include the value of 1. So then if the
15 95 percent confidence interval is greater than 1.0,
16 then you can be 95 percent sure that whatever the
17 right answer is, it is also greater than 1.0, which
18 would indicate that there is, in fact, an increase.

19 Q. Okay.

20 A. Even with that, you still have a
21 5 percent chance that -- well, a 5 percent chance that
22 chance is what happened and that you're really not
23 seeing a true association or a true -- anything that
24 has anything to do with the causal effect
25 relationship, but that at least limits it based on the

1 statistical comparison.

2 Q. Okay. And I guess my question is, What
3 you just described there, is that the bare minimum?
4 You have to have a study that shows a relative risk
5 higher than 1.0 and also has -- that value has a
6 95 percent confidence interval; that without a study
7 showing that, you cannot make a determination as to
8 whether a particular substance or agent, or whatever
9 you want to call it, has a causal association with a
10 given health effect?

11 MR. GOTTLIEB: Object to form.

12 MR. DETHERGE: Objection, lack of
13 foundation.

14 Q. (BY MR. KIWALA) Do you understand the
15 question?

16 A. Well, what I heard was you still did the
17 same thing with the 95 percent confidence interval,
18 and you didn't put any values for it. You just said
19 that it has a 95 percent confidence interval.

20 Q. Okay.

21 A. So if you -- if you -- yeah, just -- I
22 mean, if you're wanting to ask me that with regard to
23 that that is greater than 1, let's try it again, and
24 I'll try to answer your question.

25 Q. Okay.

1 A. I'm not trying to be difficult. I'm --

2 Q. I'm just trying to understand -- you're
3 the expert here. I'm just trying to get along. Let's
4 say you have -- I want to make sure I understand this.
5 I understand -- what I'm getting wrong -- what I'm
6 getting wrong is when I say 95 percent confidence
7 interval, correct?

8 A. Right. You're not providing values for
9 what that 95 percent confidence interval tells you.

10 Q. Okay. So, for instance, if the relative
11 risk was 2 and the confidence interval was yet a
12 p-value of .05, let's say, that -- at that point, that
13 study shows a causal association or indicates a causal
14 association, correct?

15 A. No.

16 MR. GOTTLIEB: Object to form.

17 Q. (BY MR. KIWALA) No?

18 A. No, that's -- I mean, your question was
19 understandable.

20 Q. Um-hum.

21 A. So my answer is no. My answer is the
22 answer to that question is no, not that I don't
23 understand your question.

24 Q. Okay. Let me -- I don't know if I'm
25 going to be able to phrase this correctly, but let me

1 move on to the -- further on in the paragraph. You
2 state, in general, the higher the risk ratio, the less
3 likely that a given finding is artifactual. Did I
4 read that correctly?

5 A. In general, the -- yes, you did.

6 MR. GOTTLIEB: Ryan, where are you
7 reading?

8 MR. SCHULTZ: Paragraph 8 still?

9 THE DEPONENT: Yeah, five lines down.

10 Q. (BY MR. KIWALA) Now, does a lower risk
11 ratio necessarily indicate the given finding is
12 artifactual?

13 A. It doesn't necessarily indicate that, no.
14 And that's where you rely on the statistical
15 comparison, which is indicated by the p-value and the
16 95 percent confidence interval.

17 Q. Okay. Let's go on to the next paragraph,
18 the second criterion that you described. And I
19 believe you state here in paragraph 9, "If one study
20 reports marginally positive findings (even if they are
21 statistically significant), but others are negative or
22 inconclusive, it is scientifically unsound and
23 speculative to rely solely on the one positive study
24 and opine unequivocally that a positive relationship
25 exists."

1 Did I read that correct?

2 A. Yes.

3 Q. Okay. If a study had not been repeated,
4 is it your opinion that it would be unsound or
5 speculative to rely on that study in arriving at a
6 conclusion about causation?

7 MR. DETHERGE: Objection, lack of
8 foundation.

9 A. Okay. So you're saying that you have a
10 positive study that is statistically significant?

11 Q. (BY MR. KIWALA) Yes.

12 A. And it is describing an association
13 between some disease and some chemical exposure and
14 there is no other data in the world that would allow
15 you to evaluate that finding. So it was just that one
16 stand-alone study, right?

17 Q. Yes. Let's just say one stand-alone
18 study.

19 A. Okay. And your question is based on that
20 scenario -- what's your question based on that
21 scenario?

22 Q. Well, based on that scenario, would it be
23 unsound or speculative to rely on that study and -- in
24 arriving at a conclusion about causation?

25 MR. DETHERGE: Same objection.

1 A. Well, it's a hypothetical that certainly
2 doesn't apply to this case; but, yes, I think even in
3 that situation, it would be fairly speculative. I
4 mean, I don't think anyone would do that. I think
5 people would say, All right, this suggests that there
6 is an association. We need to repeat this. Other
7 people need to look at this. Does it fit in with our
8 understanding of the chemical, the disease, et cetera?
9 I don't believe anyone would take a single finding and
10 run with it and say, yes, we have established
11 causation. I certainly wouldn't.

12 Q. (BY MR. KIWALA) Okay. What if repeating
13 that study would be impossible? Would it still be
14 your conclusion -- or, I'm sorry, would it still be
15 your opinion that it would be unsound or speculative
16 to rely on that study at arriving at a conclusion
17 about causation?

18 MR. DETHERGE: Same objection.

19 A. I don't -- I don't -- I mean, if you did
20 it -- if the study was done, how can it be impossible
21 to repeat it? Because the people are all gone or dead
22 or -- I mean, this is just pretty far out there.
23 You're -- I mean, I guess if there's -- if you had
24 this piece of data and there was no other data that
25 could ever be derived for whatever reason, I think you

1 would say, Okay, there is a suggestion that something
2 is going on here.

3 Q. (BY MR. KIWALA) What -- continuing with
4 this, what if you have -- if you have one study that
5 shows a positive relationship and it's statistically
6 significant and you don't have any other studies out
7 there, but you all have evidence or data that is
8 relevant to other Bradford-Hill criteria -- for
9 instance, there is evidence of a biologically
10 plausible mechanism -- at that point, is that level of
11 information or evidence sufficient to reach a sound
12 conclusion as to causation?

13 MR. GOTTLIEB: Objection.

14 MR. DETHERGE: Same objection.

15 A. I don't think you could ever reach a
16 conclusion on causation with a single -- with a single
17 epidemiological study. I just think that would be
18 really hard to do. I mean, the way you describe, you
19 know, changing the scenario, that certainly would give
20 someone confidence and it would strengthen their
21 opinion that maybe this is, in fact, real. But there
22 are just too many examples throughout, you know, our
23 scientific history where one study popped up and it
24 was elevated and it was statistically significant,
25 like coffee and pancreatic cancer, and people got

1 pretty worked up about it. And then it never came
2 again. People reviewed it over and over and over.
3 And the association was never repeated. So, you know,
4 you see that enough times, and epidemiologists and
5 scientists across the board start taking a more
6 cautious view of this kind of data.

7 Q. (BY MR. KIWALA) Okay. If one study
8 finds positive findings that are statistically
9 significant and you have a second study that reports
10 negative findings or inconclusive findings, would your
11 opinion be that the second study refuted the first
12 one?

13 MR. DETHERGE: Same objection.

14 A. Well, I don't think you could make that
15 determination without looking at the studies. I mean,
16 if they were exactly the same study, the same
17 population done the same way, the same numbers, the
18 same investigators, well, yeah, I mean, I don't see
19 how you could not come to that conclusion. But if
20 there were differences between the way the studies
21 were set up or designed, different statistical powers,
22 et cetera, I don't know that you would necessarily say
23 that it refuted it, but you would say that it's
24 inconsistent with an association being present, and
25 you would still be left with a question mark.

1 Q. (BY MR. KIWALA) Okay. So at that point,
2 it would be scientifically unsound and speculative to
3 draw a conclusion, correct?

4 A. I think it would be scientifically
5 speculative and unsound to draw a conclusion on
6 causation.

7 Q. Okay.

8 A. And say that that first study is all that
9 we need. I think anyone would look at that data set,
10 as you just described it, and say this is
11 inconsistent. This doesn't match.

12 Q. Okay. Let's look at paragraph No. 10.
13 You say, "The remaining criteria as outlined by
14 Bradford-Hill are also important in reaching a
15 conclusion on medical causation, but cannot serve as
16 adequate substitutions for fulfilling the first two."

17 Did I read that correctly?

18 A. Yes, sir.

19 Q. Can you tell me what you mean by that
20 statement?

21 A. Well, what I mean by that, in terms of
22 causation in -- medical causation with disease, having
23 statistically significant findings that have been
24 reproduced for multiple studies from independent
25 investigators in other countries -- you know,

1 reproducibility and consistency in the findings,
2 that's the most important criteria in any scientific
3 discipline. And epidemiology is no different.

4 Having -- you see a -- see a finding in
5 one laboratory, and that's the only place you ever see
6 it, you start wondering whether or not there's
7 something going on with that investigator or something
8 is going on in that particular lab.

9 When you see that same finding in four or
10 five different labs, then you start developing a
11 stronger confidence that it's real; that what you're
12 looking at is truly occurring. I don't think that's
13 any different -- perhaps it's even more important --
14 in epidemiology. So my point is, yeah, anyone that
15 understands the science and has been trained in this
16 area can probably come up with some biological
17 plausible pathways that may or may not have any data
18 supporting them.

19 You can say, Well, this chemical could do
20 X, Y, and Z, and that will allow it to cause this
21 disease. We can all do that. You can do that in your
22 sleep. That's really easy to do. So biologic
23 plausibility really doesn't get you very far in terms
24 of establishing causation.

25 So that's -- the point was that these

1 first two, consistency and reproducibility in the
2 epidemiological evidence and the strength and
3 statistical analysis associated with those findings
4 is, by far, the most important aspect of medical
5 causation.

6 Q. Okay. Just to go back -- we talked a
7 little bit about epidemiological studies. Let me ask
8 you about a case report. Would a case report
9 indicating a causal association between a given
10 substance and a given health effect -- would that be
11 enough to -- to render a scientifically sound and not
12 speculative opinion about causation, that causal
13 relationship?

14 MR. GOTTLIEB: Objection.

15 A. That's not possible. I mean, the context
16 of your question is impossible. You said a case
17 report that indicates a causal relationship. There's
18 no way. A case report does not indicate a causal
19 relationship. At the absolute best, and no matter how
20 speculative you want to be, a case report suggests
21 there might be an association. But without control
22 populations and all of the other things that you need
23 in quantitative epi, a case report, by no stretch of
24 the imagination, indicates a causal association or a
25 causal relationship.

1 Q. (BY MR. KIWALA) Okay. I just want to be
2 clear that what you're saying is that a case report is
3 absolutely insufficient to establish causation; is
4 that correct?

5 A. A case report is absolutely insufficient
6 to establish causation, you bet.

7 Q. Okay. Let's go back to paragraph 10 and
8 the "consistently positive results obtained from
9 quantitative epidemiology studies."

10 Is it your opinion that if you have
11 consistently positive results obtained from
12 quantitative epidemiology studies, but evidence or
13 data relevant to the other Bradford-Hill criteria do
14 not exist, would it be -- would it still be
15 scientifically sound to conclude that a causal
16 relationship exists?

17 For instance, to give you an example, you
18 have a series of studies that all find a -- a
19 statistically significant positive finding, but there
20 is no -- nothing that would indicate a biologically
21 plausible mechanism, none of the other guidelines or
22 criteria that are mentioned by Bradford-Hill in his
23 article are present for this particular association.
24 If the only two things you have -- well, if the only
25 two things you have are strength of the association

1 and reproducibility of it, is that -- are those two
2 elements alone enough to reach a conclusion about
3 causation?

4 MR. DETHERGE: Objection. It's compound
5 and lacks foundation.

6 A. Well, the only one that Bradford-Hill --
7 and I think everyone would agree, the only one that is
8 absolutely essential is the temporality. And the
9 exposure has to come logically before the disease, or
10 no one will think that the disease was caused by the
11 exposure, right? So that's a given. So the answer to
12 your question would be, of course not. If no other
13 Bradford-Hill criteria are satisfied, then the
14 temporality part would not be satisfied, and there
15 would be no way that you could think that the disease
16 was caused by the exposures.

17 Q. (BY MR. KIWALA) Okay.

18 A. So if you -- if that's positive, then we
19 can discuss the next part, I guess.

20 Q. Well, if -- let's say if you have
21 positive -- if you have strength in the association,
22 you have the temporal relationship, you have
23 consistency in the findings, but information as to the
24 remaining criteria or guidelines is simply not there,
25 given the information that you have at that point, is

1 that enough to reach a conclusion about causation
2 that's scientifically sound and not speculative?

3 MR. GOTTLIEB: Objection.

4 MR. DETHERGE: Ryan, can we have a
5 continuing objection to lack of foundation to these
6 incomplete hypotheticals so we don't have to keep
7 objecting?

8 MR. KIWALA: Yeah, okay.

9 A. I don't know that I can answer that. You
10 know, it would be on a case-by-case, kind of,
11 evaluation. I mean, it would depend on the -- what
12 these studies looked like and what that data really
13 tells you. You know, if you have a dose response
14 relationship in these studies, then that would
15 strengthen my confidence that there really was
16 something going on. If that was lacking, then I'm not
17 sure what I would think about them.

18 I mean, the biologic plausibility is
19 important, but if you had consistent -- truly
20 consistently positive epidemiological findings
21 indicating an association between exposure and
22 disease, but you didn't know how it worked, so there
23 was no biological plausible explanation for it, I
24 don't think that would prevent people from making a
25 conclusion that at least there appears to be something

1 here, and we just don't know enough about it. I've
2 never seen that situation.

3 I mean, I've seen where there is some
4 inconsistent epidemiological support. There's a lot
5 of inconsistent epidemiological support that goes
6 along with it, and it is not biologically plausible.
7 So, I mean, there's a whole bunch of permutations to
8 that; but I really can't answer the question in the
9 general sense.

10 Q. (BY MR. KIWALA) Okay. Let me -- let me
11 make sure I've got this correct. Your opinion is that
12 you need to have consistently positive results
13 obtained from quantitative epidemiological studies to
14 reach a scientifically sound conclusion on a causal
15 relationship, correct?

16 MR. SHEAKS: Objection, form.

17 A. I'm -- say that again, that I -- that you
18 need to have --

19 Q. (BY MR. KIWALA) You need to have
20 consistently positive results obtained from
21 quantitative epidemiological studies.

22 A. Well, consistently, what does that mean
23 to you?

24 Q. Well, let me -- let's just take it as you
25 -- as you meant it in paragraph 10 where you say the

1 -- these cannot substitute for consistently positive
2 results obtained from quantitative epidemiology
3 studies.

4 A. Well, what I mean by that is if you have
5 got inconsistent results, and you've got one study
6 that's positive, and you've got four studies that
7 aren't, and then you've got one study that maybe
8 doesn't really address the question very well, so
9 you've got this pile of data that doesn't really get
10 you there, it doesn't really help you, in my opinion,
11 you can't then go to and say, Well, it's biologically
12 plausible, and here's how, and make up a story that
13 the chemical can cause the disease through these
14 various mechanisms and then have that support the
15 epidemiological data. That's what I mean in this
16 paragraph, that these other --

17 Q. What your -- your opinion -- what you're
18 saying is that you can't take studies -- such studies
19 that have inconsistent findings, and then look to the
20 other Bradford-Hill criteria to help you reach a
21 conclusion about causation. At this point, you have
22 inconsistent findings in the epidemiological studies,
23 and that there's just necessarily a question mark; is
24 that correct?

25 MR. DETHERGE: Objection,

1 mischaracterizes.

2 A. Yeah, I don't think that's what I said.

3 Q. (BY MR. KIWALA) Okay. What if you have
4 four studies that have positive findings that are
5 statistically significant and one study that has
6 negative findings?

7 MR. GOTTLIEB: Objection.

8 Q. (BY MR. KIWALA) Based on those studies
9 alone, can you make a conclusion as to causation?

10 MR. GOTTLIEB: Objection.

11 A. Well, I don't -- I don't -- I don't know.
12 I mean, if the four studies that are positive are all
13 small questionnaire-based community case-controlled
14 studies, and then the one negative is a large cohort
15 with really good exposure data and, you know,
16 well-defined -- yeah, well-defined exposure data, and
17 that doesn't support it, I'm not sure that you could
18 take that and reach a conclusion of causation. I
19 mean, it would just depend on the relative strengths
20 and what those studies told you. It's really hard to
21 answer these questions in the abstract.

22 Q. (BY MR. KIWALA) Okay. I guess what I'm
23 trying to get at here, Doctor, is you say in your
24 report -- or your declaration in paragraph 6 that
25 "Only through the use of a standardized" -- I'm sorry.

1 Are you with -- are you with me there at paragraph 6?

2 A. Yeah, I got there.

3 Q. Okay. "Only through the use of a
4 standardized and accepted methodology, can the
5 evidence in support of a hypothetical relationship
6 between the chemical exposure and the development of
7 disease be rigorously tested and evaluated."

8 Did I read that correctly?

9 A. Yes.

10 Q. And what I'm trying to figure out is how
11 these -- these Bradford-Hill criteria or the seven
12 questions that you've set out in the subsequent
13 paragraph there, paragraph 7, if this is a methodology
14 that is supposed to be used to support a relationship
15 between chemical exposure and the development of
16 disease, I'm trying to figure out how this -- how
17 these work.

18 MR. DETHERGE: Is there a question?

19 MR. KIWALA: Well, I'm getting there.

20 Q. (BY MR. KIWALA) Are these -- are the
21 seven questions merely a -- are these something you
22 have to answer? Each of the seven questions that you
23 set out in paragraph 7, do you have to have an answer
24 to each of those before you can come to a conclusion
25 about -- about the causal relationship?

1 A. Well, I think we've discussed that, and
2 the answer would be, no, with the exception of,
3 perhaps, the fourth one. If you don't have a temporal
4 relationship, I don't think that anyone would think
5 there was a causal relationship or even association.
6 And then I discussed in paragraph 8, you know, the
7 consistency and reproducibility of the findings and
8 epidemiological studies is more important than some of
9 these other -- other criteria in terms of establishing
10 causation. So, I mean, I think we -- we have
11 discussed that.

12 Q. Okay.

13 A. I just can't apply these criteria to
14 these abstract scenarios that you're presenting me in
15 these questions and necessarily give you an answer
16 without looking at the actual data.

17 Q. So at the end of the day, it's really a
18 case-by-case analysis, correct?

19 MR. DETHERGE: Objection,
20 mischaracterizes.

21 Q. (BY MR. KIWALA) You need a set of
22 specific facts before you can come to a conclusion
23 about whether a causal relationship exists?

24 MR. DETHERGE: Compound.

25 A. I don't know what that means. I mean, I

1 think -- I think my answer speaks for itself.

2 Q. (BY MR. KIWALA) Okay. Let's go ahead
3 and move on then. If you look at paragraph 12 on
4 Exhibit 3 --

5 A. Yes, sir.

6 Q. -- you state that -- let me make sure I
7 get this right -- that "acute myelogenous leukemia,"
8 or AML, "itself is not a single disease, but a
9 collective grouping of seven or eight different
10 subtypes."

11 Did I read that correctly?

12 A. You read that correctly, yes.

13 Q. I guess my first question, why is it
14 seven or possibly eight? Is there a disagreement as
15 to how many subtypes there are?

16 A. I wouldn't think there's a disagreement.
17 This is based on the FAB, French American British,
18 classification system. And some classification
19 systems have what's called an M0, which is acute
20 myelogenous leukemia that is undifferentiated, and you
21 don't always see that in some characterization. So
22 you've got M1 through M7, and then you either have M0
23 or you don't, and that's where you get the 7 or,
24 possibly, 8, depending on how you consider the M0.
25 And, again, this is based on the FAB classification

1 system, which is kind of on its way out in terms of
2 nosology and what people are doing to classify these
3 diseases. So the World Health Organization has a more
4 sophisticated classification system for AML, and its
5 quite a bit larger in terms of the groupings.

6 Q. Okay. Further on in that paragraph, you
7 say, "APL is distinctly different from other subtypes
8 of AML, in terms of its diagnostic criteria,
9 treatment, prognosis, cell of origin, and of
10 particular relevance to this case, etiology."

11 Can you tell me how APL is different from
12 the other subtypes of AML in terms of diagnostic
13 criteria?

14 A. Certainly.

15 Q. Please do.

16 A. Well, I mean, there's lots of morphologic
17 characteristics that would allow one to classify or
18 diagnose a case of APL, but the easiest one is -- the
19 hallmark of APL is a cytogenetic abnormality involving
20 a balance translocation between chromosomes 15 and 17.
21 No other subtype of AML has that. Only APL has it.
22 You need to see it to classify a disease as APL. So
23 that's probably the easiest example of where that is a
24 unique criteria for APL and nothing else.

25 Q. Okay. How is APL different from the

1 other subtypes of AML in terms of treatment?

2 A. Because of the molecular base of the
3 disease, it is treated predominantly with a drug
4 called altransretinoic acid which induces terminal
5 differentiation of the promyelocyte. There is no
6 magical treatment like that for any other AML. It's
7 the only one that is treated with altransretinoic
8 acid. It's the only one that is treated with these
9 agents that induce differentiation. So it has an
10 absolutely unique treatment regiment than any other
11 form of AML.

12 Q. Okay. And how is APL different from
13 other subtypes of AML in terms of cell of origin?

14 A. The cell of origin -- and this is through
15 a very eloquent system of experimentation -- has been
16 pretty conclusively shown -- although you can
17 certainly find some disagreement in the literature,
18 but has been pretty conclusively shown to occur at a
19 granulocytic-committed progenitor cell, not at a
20 myeloid stem cell or early progenitor cell, which is
21 most of the other forms of AML are thought to have
22 arisen, the cell origin for those other forms of AML.
23 So it is a more mature committed differentiated cell
24 type that is thought to harbor the first (15;17)
25 cytogenetic lesion.

1 Q. What can you tell me about these -- all
2 of these subtypes? How are all of these subtypes
3 similar such at that they are able to be collectively
4 identified as AML?

5 A. Well, I think they are collectively
6 classified as AML because they are all acute. So
7 that's the A. They are not chronic diseases, and they
8 all are arising in cells of a myeloid lineage. So
9 there's your M. And they are all leukemia, so there's
10 your L. But other than that pretty broad brush
11 generalization, APL is really very different than
12 these other subtypes of AML.

13 Q. Okay. Would you agree with the statement
14 that all subtypes of AML are -- they all derive from a
15 genetically damaged pluripotent stem or progenitor
16 cell which can differentiate into all myeloid cell
17 types?

18 A. No, I would --

19 Q. That statement.

20 A. -- I would not. I think the evidence is
21 pretty clear -- I mean, that's a pretty important "or"
22 that you had in that sentence, that it's a primitive
23 or a stem cell or a progenitor cell. I think you
24 would describe the cell of origin as best understood
25 today that it isn't a myeloid committed progenitor

1 cell, but that progenitor cell does not retain
2 multiple lineage capacity, and it is committed to
3 going down the granulocytic pathway. So I would not
4 agree with that sentence the way you read it.

5 Q. Okay. I didn't think you would. Can you
6 tell me -- can you tell me if there's anything in the
7 medical or scientific literature that you can cite for
8 me today that you rely on for that disagreement with
9 the statement?

10 A. Certainly. There's a nice study by
11 Grimwade, G-r-i-m-w-a-d-e, that discusses in great
12 detail the cell of origin for APL. There's a study by
13 an author N-a-s-r that was published in 2008. There
14 are probably five or six other studies that -- where
15 they were basically, like I said, conducting some
16 fairly sophisticated analysis to try to determine
17 where the (15;17) is arising, at what point in the
18 hematopoietic differentiation you start to see that
19 lesion. And you don't ever see it in a lymphoid cell.
20 So if you never see it in a lymphoid cell in APL, then
21 it is not likely occurring at a stem cell that still
22 has the ability to go down those different lineages.

23 So there's a lot of data out there
24 discussing the cell of origin for APL and how it is
25 likely to be different. I mean, we don't know

1 differently where the cell of origin is for any of
2 these diseases. So it's not with 100 percent
3 certainty, but it certainly appears to be different.

4 You can find it Yandell's textbook from
5 1997 where he's got a really nice little diagram of
6 the hematopoietic flow chart. And he points to these
7 various cells and says this is where AML occurs and
8 this is where APL occurs. And it's pointing to a
9 different place. I mean, I think that is pretty
10 well-established.

11 Q. Okay.

12 MR. KIWALA: Dr. Pyatt, I've just seen
13 that we've been going a little bit for an hour now one
14 thing I didn't tell you before we got started if at
15 any point you want to take a break, you know, please
16 ask, and we can do that. Are you ready to keep going
17 or do you want to take a break at this point?

18 THE DEPONENT: No, let's -- let's take a
19 five minute break, if you're okay with that.

20 MR. KIWALA: I'm fine with that.

21 (Recess taken, 11:24 a.m. to 11:41 a.m.)

22 Q. (BY MR. KIWALA) Dr. Pyatt, what is the
23 threshold of benzene exposure for the development of
24 AML?

25 A. Well, can we agree for this deposition

1 that when we talk about AML, we are talking about it
2 collectively, but we're excluding APL from that
3 classification?

4 I mean, since, really, the whole bulk of
5 my opinion is that APL is not caused by benzene, then
6 it's going to be hard for me to answer that question
7 including APL as a subtype of AML. But if you want to
8 take APL out of it and we're just going to talk about
9 all of the other forms of AML, then that will be
10 easier.

11 Q. Okay. Let's -- let's go ahead. We'll
12 take APL out of the mix. But what is the threshold
13 level of benzene exposure for the development of AML
14 with that -- with that caveat?

15 A. Thank you. I would say that the
16 scientific literature supports that the threshold
17 appears to be somewhere around 40 to 50 part per
18 million years to meaningfully statistically increase
19 the risk of developing AML. And that exposure needs
20 to have occurred sometime within, say, 15 years, 20
21 years, at the outside, prior to diagnosis. So those
22 are really the two kind of important criteria.

23 Q. Okay. Let me get that correct. It was
24 40 to 50 ppm years?

25 A. Correct.

1 Q. Okay. And within that exposure that had
2 to occur within 15 to outside -- well, to within a
3 total of 20 years, at the very least, of the
4 development of AML?

5 A. At the very most.

6 Q. Okay.

7 A. Yeah, 15, I think, is a reasonable
8 estimate, but it goes somewhere between 10 and 15 --
9 10 and 20. So somewhere in that range, the exposures
10 need to have occurred within 20 years of diagnosis.

11 Q. Okay. What scientific or medical
12 literature do you rely on for that statement of a
13 threshold level, that range?

14 A. I rely on all of the quantitative
15 epidemiology that's been conducted for benzene and AML
16 specifically.

17 Q. Okay. Are there any studies or
18 literature that statistically point out the 40 to 50
19 ppm year in the 10- to 20-year time period, any --
20 anything in the scientific literature that basically
21 states that as the threshold level?

22 MR. GOTTLIEB: Objection.

23 A. Well, I think that -- yes, there are
24 definitely studies that are more important than others
25 in terms of what they have looked at and what they

1 have evaluated that support my opinion with regard to
2 the quantity -- quantity and the duration.

3 Probably the most important study -- and
4 particularly in the United States, because it forms
5 the basis of all of our regulatory positioning on
6 benzene, is the pliofilm cohort. And it's pretty
7 clear that you need exposures greater than 40 to 50
8 part per million years in order to significantly
9 increase the risk. And the range is based on the fact
10 that in the original study, Bob Rinsky's study from
11 '87 looked at 40 to 200. But then there have been --
12 and I think even in that study, it was something
13 greater than 200 before there was a statistically
14 significant increase.

15 But anyway, there have been at least two
16 and, perhaps, three other quantitative exposure
17 assessments of that cohort. And Mary Paxton did a
18 really nice summary of that data and put them into
19 slightly different exposure bins. And that is where
20 the 50 ppm came from.

21 Otto Wong and others argue -- and there's
22 certainly studies that support it -- that it has to be
23 as high as 200 ppm years before you have a meaning
24 fully increased risk of AML.

25 Then the pliofilm also supports the

1 latency argument, the 15-year latency argument. The
2 NCI China study supports that. The Health Watch study
3 supports that. It's supported by just about every
4 analysis of chemically-induced AML associated with
5 chemotherapeutic agents, radiation, smoking, et
6 cetera. So it's a very consistent cogent picture with
7 regard to the timing of exposure and the development
8 of AML.

9 Q. (BY MR. KIWALA) Okay. Now -- but you
10 say you've considered all the -- all of the relevant
11 scientific literature out there on this issue,
12 correct?

13 A. Yes, sir.

14 Q. Okay. And you find all of it valuable,
15 but you feel that the -- some -- some of the
16 literature is more important than others. In
17 particular, I believe you mentioned Paxton, Rinksy,
18 Wong in terms of arriving at the -- the range for the
19 ppm years, correct?

20 A. I think that is the clearest study,
21 because there were -- they had a nice dose response.
22 They were using pure benzene. There was reasonably
23 decent description of what these workers were doing.
24 There was not a lot of confounding chemical exposures,
25 so -- and that's the reason why OSHA bases their PEL,

1 the ACGIH basis their TLV. I mean, our regulatory
2 standards for benzene are based on that cohort. But
3 it is consistent with Constantini, it's consistent
4 with Rishtan and Snadder, it's consistent with Hays
5 '97, the NCI China study. I mean, all of those have
6 done quantitative analysis of benzene exposure. They
7 have all got pluses and minuses, strengths and
8 weaknesses, but it presents a consistent picture.

9 Q. Okay. If you go ahead and take a look at
10 paragraph 14 back on -- I believe it's still
11 Exhibit 3.

12 A. I'm with you.

13 Q. Okay. Let me read portions of this --
14 the last full sentence of the paragraph before it
15 carries on to the next page. It states, "Potential
16 biological mechanisms for benzene-induced AML include
17 toxic disruption of regulatory processes involving
18 cell growth and differentiation, dysregulation of
19 hematopoiesis" -- did I say that correctly?

20 A. I would know what you meant if you said
21 that.

22 Q. Okay. -- "via genetic or epigenetic
23 clastogenic (chromosomes) in hematopoietic progenitor
24 cells, direct damage to the bone marrow stroma and/or
25 microenvironment or some combination of these events."

1 And then it goes on to say that "All of
2 these potential molecular or cellular steps would
3 likely exhibit a threshold providing a strong
4 biological rationale for the existing epidemiological
5 evidence."

6 And let me make sure I'm setting these
7 out -- these -- potential biological mechanisms, if
8 I'm reading your -- your declaration correctly, you're
9 saying it's a -- there are three potential mechanisms
10 or is there -- the fourth option is a combination of
11 those mechanisms? Do I have that correct?

12 A. Well, I mean, I -- each of these
13 processes, there could be -- there are multiple papers
14 written on them discussing various aspects. I mean, I
15 think this is a fair summary. I wouldn't say that
16 this is the only possibility that people have raised
17 or hypothesized that benzene may be doing.

18 For example, the topoisomerase II
19 inhibition argument has been raised about benzene and
20 its various metabolites. So these are ones that have
21 solid scientific documentation that these are likely
22 occurring.

23 Whether or not they are an underpinning
24 for the ultimate pathogenesis or the ultimate
25 leukemogenesis of benzene's metabolites, we don't know

1 that. But we know that these things are occurring.

2 Q. Okay. And, really, it's just -- my
3 question was really just about the -- the comma usage.
4 I just want to make sure that -- I guess there are --
5 you say several potential mechanisms, but the -- the
6 mechanisms are grouped, so the mechanisms -- I think
7 you can summarize into three separate ones; is that
8 correct? Is that -- do that I have correct?

9 A. Let's see. So you've got growth and
10 differentiation, dysregulation of hematopoiesis,
11 various sources, that's second. Cytogenetic
12 abnormalities. Perhaps genotoxic effects, that would
13 be third.

14 Q. Okay.

15 A. Potential damage to the bone marrow. The
16 microenvironment that maybe plays a role. So in terms
17 of groupings, I think there are four --

18 Q. Four?

19 A. -- or some definition of the various
20 things that are in there with the caveat that we
21 really don't know today how benzene does what it's
22 doing.

23 Q. Okay. Let's go to the -- the toxic
24 disruption of regulatory processes involving cell
25 growth and differentiation. You say that that would

1 likely exhibit a threshold. What specific literature
2 are you relying on for that statement?

3 A. Well, you could look at some of my work
4 and Patrick Kerzic's work looking at TNF alpha
5 dysregulation, which could very well be important, and
6 it's clearly a threshold. You could look at Rich
7 Iron's work. He published in '92, published it again
8 in '96 regarding GM-C SF dysregulation. We looked at
9 AP-1 alterations. Dave Ross looked at reactive oxygen
10 in various transcriptional regulatory elements that
11 have to do with hematopoiesis and how these cells
12 behave. And in all of this in vitro experimentation,
13 there was clearly a threshold. There were doses below
14 which nothing was happening.

15 So if those are playing a role in
16 leukemia, then there's going to be doses of benzene
17 that are not going to be leukemogenic because they are
18 not capable of causing these types of dysregulatory
19 events.

20 Q. Okay. And I think -- what was the --
21 going back to that -- that sentence, the second
22 grouping, dysregulation of hematopoiesis -- I'm going
23 to mess that word up all day --

24 A. Hematopoiesis.

25 Q. Hematopoiesis. Thank you.

1 A. Yes.

2 Q. -- dysregulation of hematopoieses via
3 genetic or epigenetic -- I'm sorry, is that -- do I
4 have that right?

5 A. Yes, epigenetic, correct.

6 Q. All right. What specific literature are
7 you relying on for your statement that the
8 dysregulation of hematopoiesis via genetic or
9 epigenetic would likely exhibit a threshold?

10 MR. DETHERGE: I think you might correct
11 that, Ryan. The sentence goes on.

12 MR. KIWALA: Clastogenic damage?

13 MR. DETHERGE: Right.

14 Q. (BY MR. KIWALA) I'm sorry. Is that part
15 of the same -- that's why I'm getting confused on
16 these commas.

17 A. Well, I didn't, perhaps, write it that
18 clearly. I mean, the genetic would certainly be --
19 the most common one that people have written about are
20 clastogenicity or chromosomal damage. And there's
21 in vitro studies, there's animal studies, there's
22 occupationally exposed workers who were healthy.
23 There are studies looking at people who actually have
24 disease and what their diseases look like.

25 So there's a lot of data associated with

1 that. The epigenetic simply means that it's having
2 something to do perhaps with the DNA, like methylation
3 status, or other things, that's not directly
4 interacting with the specific DNA sequence. That is
5 not completely separate from the first grouping. I
6 think there's going to be some overlap there.

7 So George Kalf has done some of this
8 work, Rob Snyder has done some of this work, Steven --
9 well, his is a little different. Martin Smith has
10 done -- I mean, there's a lot -- there's a lot of
11 literature to support all of these.

12 Q. And the work that you describe there, you
13 say that is -- those works support your statement that
14 the -- that the process would likely exhibit a
15 threshold?

16 A. Right. That when you look at the data,
17 there are doses below which you don't see anything
18 occurring. So to the extent -- I mean, you can always
19 argue -- you know, this notion of a threshold can turn
20 into a theological argument pretty quickly because you
21 just get out of where there's any data to support it.
22 But -- I mean, so the argument is, well, yeah, but
23 your assays weren't sensitive enough to detect
24 changes. You know, I can't disprove that, but the
25 fact remains when you look at these studies and you

1 look at these mechanisms that there are doses below
2 which you don't see any kind of alterations. And Dick
3 Albertini and others, you know, really smart guy,
4 really well-respected, he thinks that even a genotoxic
5 mechanism, which Milman pointed out as one that is
6 clearly not going to have a threshold, that's
7 incorrect.

8 You look at the radiation data, you look
9 at some of the mechanisms about how chemicals actually
10 damage DNA, and when you look at the precise
11 mechanism, even then you're going to -- you're going
12 to see a threshold. You're going to see doses that it
13 takes a certain amount to cause these kinds of
14 changes.

15 Q. Okay. Now you've mentioned names. Are
16 there any specific studies that you can cite to in
17 support for that statement?

18 A. Well, I mean, I gave you authors in terms
19 of specific studies. No, I'm not -- I don't have them
20 all memorized, so I can't give you dates, but --

21 Q. Are any of them cited in your -- in your
22 declaration -- do you have any notes at the back? In
23 particular at the end of paragraph 14, you mention end
24 notes No. 36 and then 38 through 45.

25 A. Okay. 36 is a good one. And what are

1 the other ones? 38? Okay. That's an epidemiology
2 study, so was Aksoy, but I think it supports. 40 is
3 Irons '92 paper, which I talked about. 41, 42, those
4 are Mary Paxton's analysis. So this is kind of a
5 combination up to 45. So Rinsky, Rushton, Wong, those
6 are more of the epidemiology. So it looks like there
7 were only two cites in there that talk about these
8 potential mechanisms.

9 Q. Let's move on to the -- the next one in
10 the group on paragraph 14. Do I have this correct,
11 it's damage in the hematopoietic progenitor cells? Is
12 that the next one of the four?

13 A. Well, that's associated with the
14 clastogenetic damage, so that's the chromosomal thing.
15 And Rich Irons published in the '80s that hydroquinone
16 and/or para-Benzoquinone's ability to disrupt
17 microtubule formation, which is required for
18 chromosomal separation, is clearly a threshold. It is
19 a stoichiometric process. And you have to have a
20 certain amount of hydroquinone before you can start
21 seeing those changes.

22 So that is clearly -- you can argue that
23 that's not playing a role, but you cannot argue that
24 there will not be a threshold for those kinds of gross
25 chromosomal abnormalities that you can see in

1 benzene-exposed cells. Or -- you know, by benzene, I
2 mean the metabolites.

3 Q. Okay. And the next one there was direct
4 damage to the bone marrow stroma?

5 A. I think Dave Ross has published some
6 papers on that. George Kalf has published some papers
7 regarding cytokine disruption. Even the one that I
8 mentioned that Patrick Kerzic published with regard to
9 TNF alpha, that's going to be part of this
10 microenvironment.

11 It's associated with the fact that most
12 evidence suggests that leukemias and other hemopoietic
13 malignancies do not arise in isolation. They arise
14 within the bone marrow stroma or their
15 microenvironment. And that microenvironment likely
16 plays some role in the pathogenesis of the disease.
17 So it is conceivable that damage to the
18 microenvironment to the bone marrow stroma, or
19 whatever, is an integral part of the leukemogenic
20 process.

21 Q. Okay. Is there -- what specific studies
22 are out there that suggest that direct damage to the
23 bone marrow stroma and the microenvironment would
24 exhibit a threshold?

25 A. Well, just sitting here right now, I

1 would have to say George Kalf's work and, maybe, some
2 of David Ross's studies.

3 Q. Okay. But there's no specific references
4 to the literature you can give to me today?

5 A. No.

6 Q. Okay.

7 A. And it wasn't in the ones that I
8 referenced in that statement.

9 Q. Okay. If you do -- I would ask that if
10 you could go back and find the -- the specific studies
11 that you used to rely on the statement that all of
12 these cellular and molecular steps would likely
13 exhibit the threshold, if you could collect those and
14 maybe give those to counsel so that they can be sent
15 along to the plaintiff's counsel.

16 MR. DETHERGE: Ryan, that's certainly
17 something we can talk about as counsel. I suspect
18 there are things that went both ways. So as long as
19 we have some mutuality in that kind of work, we can
20 discuss it.

21 MR. KIWALA: Okay. I mean, we can
22 discuss that later.

23 Q. (BY MR. KIWALA) But, Dr. Pyatt, would
24 you be amenable to doing something like that?

25 A. Sure. I don't have a problem with that.

1 Sitting here talking to you about it, I probably
2 should have had some more references in this
3 paragraph. No one has ever argued with me about it
4 before. You're the first person who has, you know,
5 questioned me on this paragraph. And now, for future
6 reference, I will certainly have some more citations
7 there.

8 Q. It pleasures me to be the first. Let's
9 see. Let's move along. Before I move along,
10 actually, let's go back -- before we got into the
11 discussion of benzene and the threshold for the
12 capacity to cause AML, we talked about excluding APL
13 from -- from the definition of AML.

14 Do the -- do any of the studies that you
15 relied on for your statement that there is a threshold
16 for the development of AML from benzene exposure -- do
17 any of those studies separate out APL from the
18 analysis?

19 A. Well, most of the mechanistic work that
20 we discussed, this was done in bone marrow cells and
21 peripheral lymphocytes and cell lines and things that
22 people are using.

23 Q. I'm sorry. What I meant was the -- the
24 epidemiological studies that --

25 A. Okay.

1 Q. -- you discussed, you know, the works
2 particular by Paxton, Rinsky, Long, any of those, did
3 any of those separate out -- exclude APL from the
4 analysis?

5 A. The -- the Rinsky -- the pliofilm
6 analysis did not specifically address APL, even though
7 at that time it was a recognized clinical entity, but
8 it would -- did not appear on any birth certificates.
9 So you could either -- sorry -- death certificates.
10 So you could either argue that there were none or that
11 the pathologist or funeral director, or whoever filled
12 out the death certificates, didn't know or didn't
13 write it down.

14 So within that cohort, there -- there is
15 no evidence that it exists, but I can't definitively
16 say there wasn't one. The Long analysis seemed to be
17 in that list, and he -- he separate -- well, it would
18 be the same argument, because he looked at AML only.
19 And I think maybe one of those could potentially have
20 been APL just based on the limited information that
21 was present.

22 In the NCI China study, while the
23 analysis of the cumulative exposures and the risks
24 associated with those cumulative exposures, they used
25 ANLL of which APL would have been part of that overall

1 discussion and overall calculation, but they also did
2 separate out the various subtypes and made mention of
3 the M3 subtype that -- that was in that cohort.

4 So those investigators didn't make a
5 quantitative evaluation, but at least made a
6 qualitative separation of the various subtypes.

7 Q. So just to recap, the study that -- the
8 epidemiological study that you're relying on for your
9 statement for a threshold for the development of
10 benzene-induced AML, they all include -- none of them
11 exclude specifically APL, correct?

12 MR. GOTTLIEB: Objection.

13 A. None of them specifically exclude APL,
14 no.

15 Q. (BY MR. KIWALA) Okay. But in your
16 statement of your opinion as to what the threshold for
17 -- the threshold level for benzene-induced AML, in
18 this case, you are excluding APL from that definition,
19 correct?

20 A. Well, I just didn't want it to be
21 mistaken where you're asking me questions about AML,
22 and then somehow that gets turned around to say that I
23 support that all forms of AML are caused by benzene.

24 Since this is an APL case, and I've made
25 that pretty clear, that's important to my opinion. I

1 just wanted the record to be clear that when I'm
2 talking about AML in a general sense, I am not talking
3 about APL as part of that grouping.

4 Q. Okay. Just as a general question, is it
5 your opinion that before reaching a conclusion about
6 whether or not benzene exposure is capable of causing
7 APL, one must consider all of the available literature
8 on the topic of benzene exposure and it's relationship
9 to APL?

10 MR. GOTTLIEB: Objection.

11 A. Could you say the first part of that
12 again?

13 Q. (BY MR. KIWALA) Sure. Is it your
14 opinion that before reaching a conclusion about
15 whether or not benzene exposure is capable of causing
16 APL, one must consider all of the available literature
17 on the topic of benzene exposure and its relationship
18 to APL or its potential relationship to APL?

19 MR. GOTTLIEB: Objection.

20 A. Of course. I mean, I think you've got to
21 evaluate the data that's relevant to your opinions.

22 MR. DETHERGE: Hey, Ryan, can we
23 stipulate to that on both sides?

24 MR. KIWALA: I'm just going to move on.

25 Q. (BY MR. KIWALA) Have you considered all

1 of the available literature on the topic of benzene
2 exposure and its relationship to APL in reaching the
3 opinions to which you're testifying today?

4 A. As far as I know, I have looked at and
5 carefully considered every piece of data that is in
6 the published literature that addressed the potential
7 relationship between benzene and APL. I mean, I can't
8 rule out the possibility that there's some obscure
9 journal somewhere that's published something that I've
10 never seen; but every study that discusses this, to my
11 knowledge, I have evaluated and have with me.

12 Q. Okay. Let's take a look at paragraph 15.
13 And in paragraph 15, you mention the NCI China study.
14 And did that study report an increase in APL among
15 benzene-exposed workers?

16 A. No.

17 Q. Okay. And one of your criticisms of this
18 study is it failed to account for the potential use of
19 -- I believe it's called bimolane?

20 A. That's what it's called, yes.

21 Q. And you state "Bimolane was widely used
22 in China as a treatment for psoriasis and is an
23 established epidemiological risk factor for the
24 development of AML."

25 A. APL.

1 Q. I'm sorry, "APL."

2 A. Correct.

3 Q. Now, does that mean that bimolane is
4 established as being capable of causing APL?

5 A. Yes.

6 Q. Okay.

7 MR. KIWALA: Teresa, if you could go
8 ahead and mark the article. It's entitled
9 "Translocation" --

10 (Deposition Exhibit 6 was marked.)

11 MR. DETHERGE: Hang on, Ryan. Can we see
12 what you've marked?

13 THE DEPONENT: I have it, too. I have a
14 copy of it, if you want to look at that one. In fact,
15 I think that's my reference 49. It is. Yeah, it's
16 reference 49 in my declaration. Okay. I'm looking at
17 it.

18 Q. (BY MR. KIWALA) Okay. Going back to
19 paragraph 15 on Exhibit 3, you state, "Bimolane was
20 widely used in China as a treatment for psoriasis and
21 is an established etiologic risk factor in the
22 development of APL." And then you specifically cite
23 this article, No. 49, correct?

24 A. Yes.

25 Q. Okay. In this article, can you tell me

1 what was the reported relative risk for
2 bimolane-induced APL?

3 A. Not sitting here. Let me look through
4 it. I'm not seeing it. I thought they had 12 out of
5 24 cases. So their first report was 14 cases of
6 therapy-related AML caused by bimolane with 8 cases of
7 M3 and 4 of M2. So that was their earlier study.

8 Q. Well, let me -- let me ask you,
9 Dr. Pyatt, what kind of quantitative epidemiological
10 study is Exhibit 6?

11 A. It looks like this study is a case
12 report.

13 Q. Okay. So it's a case report and not a
14 cohort study or a case-controlled study, correct?

15 A. This particular one is, yes.

16 Q. Okay. And the -- the other -- earlier
17 study that you mentioned -- let's see, it's -- on
18 here, it's page 109 at the top right-hand corner
19 beginning at -- it mentions 14 cases of t-AML caused
20 by bimolane therapy for psoriasis in 1992, and it
21 references No. 5. Do you know if the -- that article
22 reference in No. 5, what kind of quantitative
23 epidemiological study is that?

24 A. I -- I don't know sitting here, but hold
25 on a second. I think I have it. I guess this would

1 be best classified as a case series.

2 Q. Okay. So it would be a collection of
3 case reports, basically, correct?

4 A. Well, it's not a collection of case
5 reports, but it's a series where they are just
6 reporting the 14 or 15 cases that they conducted or
7 that they did this evaluation on. So it's not a
8 collection of independent case reports.

9 Q. Okay. But at any rate, it's not a
10 quantitative epidemiological study, is it?

11 A. It doesn't appear to be, no.

12 Q. Okay. Are you aware of any quantitative
13 epidemiological studies that report a positive
14 association between -- positive association between
15 exposure to benzene and APL?

16 A. I don't know. I don't have it -- I don't
17 have it with me.

18 Q. Okay. I would ask that if you do conduct
19 a search and are able to find any that you would pass
20 those along to defense counsel so they can be, in
21 turn, passed on to plaintiffs' counsel.

22 A. Sure. That's fair.

23 MR. DETHERGE: Subject, obviously, to the
24 same discussion we had earlier, Ryan, about follow-ups
25 being mutual on both sides, right?

1 MR. KIWALA: Okay.

2 MR. DETHERGE: To be discussed between
3 the lawyers.

4 MR. KIWALA: We can -- we can discuss
5 that off the record.

6 Q. (BY MR. KIWALA) But let me -- let me get
7 back -- is it your -- it is your testimony today that
8 consistently positive results obtained from
9 quantitative epidemiological studies are necessary to
10 reach a scientifically sound conclusion about
11 causation, correct?

12 A. That's certainly a very important
13 feature, yes.

14 Q. And you stated in your report that
15 bimolane is an established cause of APL, correct?

16 A. I did.

17 Q. But as you sit here today, you're not
18 able to cite for me a single quantitative
19 epidemiological study finding a correlation between
20 bimolane exposure and APL, correct?

21 A. I'm not able to point you to a
22 quantitative epi study, I agree with that, and would
23 change the wording of this paragraph or change the
24 wording of this sentence. I just had not read those
25 studies carefully enough. I mean, it's pretty

1 compelling data, the number of cases that they saw;
2 but you are correct, it is not a quantitative study.

3 Q. Based on those -- well, I guess, 15
4 individual cases, would you say it's sound enough
5 evidence to reach a conclusion about causation as to
6 bimolane and APL?

7 MR. GOTTLIEB: Object to form.

8 A. I would say that it's -- it's consistent
9 with our understanding of that drug, and those two
10 reports are very consistent. It actually -- it's kind
11 of like what you were asking me about earlier, it's
12 going to be hard to repeat it, because bimolane is not
13 used anywhere else other than in China. And once
14 these case reports or studies came out, that was
15 sufficient for the medical community in China to stop
16 using this drug to treat psoriasis. So it was
17 certainly compelling enough evidence for them, but you
18 -- you are correct in your question.

19 Q. Okay. Let's move along to paragraph 17.

20 A. Okay.

21 Q. You state in your report at paragraph 17
22 that "There is no reliable scientific evidence that
23 the (15;17) translocation is related to benzene or any
24 other occupational exposure," correct?

25 A. Yes.

1 Q. And have you considered all of the
2 relevant scientific literature on the topic of the
3 t(15;17) and its possible relationship to benzene
4 exposure?

5 A. I think I've considered all of the
6 scientific data. I mean, I can always be proven
7 wrong, but I think I've looked at everything that has
8 to bear on that topic.

9 Q. Okay. And do you agree with the
10 statement that benzene is clastogenic and is capable
11 of breaking and rearranging chromosomes?

12 A. Well, I certainly agree with the
13 statement that benzene is clastogenic. And by
14 benzene, we're all talking about the metabolites.
15 That's fine. I mean, I certainly agree with that.
16 And that has been known for as long as we've known
17 about human chromosomes. And the breaking part seems
18 to be pretty clearly documented. The last part of
19 your question, the translocations, that's a little
20 harder to answer; and there's certainly a lot less
21 data to support that.

22 Q. I think I heard you mention this earlier,
23 but I'll ask you now just to make sure. Are you
24 familiar with the substance called topoisomerase II?

25 A. Yes, very familiar with that.

1 Q. Okay. And can you explain what it is and
2 what its function is inside the cell?

3 A. Topoisomerase II is an enzyme. It's
4 found in the nucleus. It's involved in the -- the DNA
5 is wound up pretty tightly when it's inside of
6 chromosomes. The double helix, which everyone knows
7 about, and then it's wrapped around histones and -- it
8 doesn't matter, but it's wound up very tightly, so
9 tightly that it's not possible to replicate the DNA
10 when it's in that state. So it has to unwind the DNA
11 in order for the DNA to replicate and in order for the
12 cell to divide. In order to divide, it has to
13 replicate the DNA. And topoisomerase is the enzyme
14 that clips the DNA, allows it to unwind during the
15 replication process, and then reanneals the two ends
16 so that you then have a solid DNA strand again. So
17 it's an important enzyme in DNA replication and
18 cellular division. Does that help?

19 Q. Yes. Are you familiar with the group of
20 substances known as topo II inhibitors?

21 A. Yes, sir.

22 Q. And can you explain what they are and
23 what they do?

24 A. Well, topo II inhibitors -- it's a broad
25 classification, but essentially you're talking about

1 drugs that -- chemicals that inhibit the enzyme
2 topoisomerase II and prevent the cell from replicating
3 its DNA and, therefore, prevents the cell from
4 dividing. So topo II inhibitors will cause cells to
5 die that are trying to divide in its presence.

6 Q. Now, is there actually -- there are two
7 kinds of topo II inhibitors, is that correct, or two
8 classifications? Would that be correct?

9 A. There are at least two.

10 Q. Okay. And from what I've seen, there are
11 -- there's a group called catalytic inhibitors and
12 then also a group called topo II poisons?

13 A. That's correct.

14 Q. Okay. Can you explain the difference
15 between those two?

16 A. In general terms, catalytic inhibitors
17 means that it's inhibiting the enzyme in a catalytic
18 fashion. It seems to happen before the enzyme has an
19 opportunity to bind to DNA. So it doesn't allow for
20 the formation of cleavable complexes, which is a side
21 effect of this process, whereas topo II poisons do
22 allow for the formation of these cleavable complexes
23 and poisons the enzyme wherever it is in its catalytic
24 cycle, is my understanding.

25 Q. Are you aware of any studies that show

1 that topo II inhibitors induce APL?

2 A. There are a class of topo II inhibitors
3 of which bimotox is an example that are thought to be
4 able to cause the (15;17) translocation and cause APL.

5 Q. Okay. So I think you've answered that
6 question also. The next question I was going to ask,
7 are you aware of any studies linking exposure to
8 topo II inhibitors linking those to that translocation
9 (15;17)? And I take it your answer to that question
10 would be yes?

11 A. Well, they are the same. (15;17) is APL.
12 APL is (15;17), so they are essentially synonymous.

13 Q. Now, you mentioned this before, but just
14 to be clear, would you agree that it's not generally
15 believed in the scientific community that benzene
16 directly triggers DNA damage, but, rather, it acts
17 through a series of metabolites?

18 A. It has been very well-established through
19 a series of nice experiments that benzene has to be
20 metabolized in order to be toxic, however you want to
21 define toxicity.

22 Q. Okay. And are you aware of any studies
23 that show benzene metabolites act as topo II
24 inhibitors?

25 A. Let me just add one other thing to the

1 earlier question.

2 Q. Sure.

3 A. High-dosage exposure to benzene has
4 narcotic effects, just like any type of organic
5 solvent. By high dose, I'm talking thousands of ppm.
6 And that probably is independent of any type of
7 metabolism.

8 Q. Okay.

9 A. So when I said it has to be metabolized
10 to be toxic, that wasn't complete. All right. Then
11 the next question is various phenolic metabolites of
12 benzene have been reported under very controlled
13 experimental conditions to inhibit topoisomerase II.

14 Q. Okay.

15 MR. KIWALA: And, Teresa, if you could go
16 ahead and mark the last document.

17 (Deposition Exhibit 7 was marked.)

18 MR. DETHERGE: What is Exhibit 7, Ryan?

19 MR. KIWALA: Why don't we hand it to --

20 A. This is a paper I published with Rich
21 Irons and David Kroll where we were looking at the
22 mechanism by which benzene metabolites could inhibit
23 this enzyme.

24 THE DEPONENT: Would you mind if I just
25 take a really quick break? It won't take but just two

1 minutes. Is that okay?

2 MR. KIWALA: We can take a two-minute
3 break.

4 (Recess taken, 12:29 p.m. to 12:31 p.m.)

5 THE DEPONENT: So did I answer your -- is
6 there a question pending or where are we?

7 Q. (BY MR. KIWALA) I think you answered
8 what the article is, right, and what it is is an
9 article that you co-authored with some other
10 individuals a few years back, correct?

11 A. Yes, specifically dealing with
12 metabolites of benzene and its ability to inhibit
13 topoisomerase II.

14 Q. Okay. If you take a look at -- it's
15 marked as page 832 on the top left-hand corner.

16 A. The gels, the actual data?

17 Q. Well, I just want to make sure you've got
18 the correct page.

19 A. Yeah, I'm on page 832, top left are three
20 gels.

21 Q. And I want you to take a look at actually
22 the second-to-last paragraph before you get to the
23 acknowledgment.

24 A. Okay.

25 Q. First -- the first sentence of that

1 paragraph.

2 A. Okay.

3 Q. And it says, "In contrast to these topo
4 II poisons, benzene metabolites and their
5 peroxidase-activated congeners appear to inhibit
6 topo II via a distinct and upstream mechanism."

7 Does that mean that you include benzene
8 in that first group the catalytic inhibitors?

9 A. In what first group?

10 Q. Well, we mentioned there are two kinds of
11 topo II inhibitors, the catalytic inhibitors and then
12 the topo II poisons, correct?

13 A. Generally speaking, yes. And I think the
14 answer to your question would be that that is somewhat
15 debatable in the scientific literature; but, yes, that
16 is -- that seems to be the case.

17 Q. At any rate, is that what you say in --
18 in the article here?

19 A. Well, I don't -- yes, classified as
20 catalytic inhibitors of topo II similar to those
21 described as these other drugs.

22 Q. Are you aware of any studies done in the
23 literature that show -- are you aware of any studies
24 in the literature that show metabolites of benzene to
25 be topo II poisons?

1 A. Oh, I think that's what Neil Osheroff
2 said. I mean, he basically said that we had -- based
3 on these clearly defined or specifically defined
4 experimental conditions, we had too much of a reducing
5 agent in our assay, and that's why we didn't see the
6 cleavable complex formation, and that he was able to
7 demonstrate cleavable complexes in his assay. So I
8 think that's what Neil Osheroff said, but I'm not --
9 I'm not positive. I know that David Eisman, early --
10 and he was the first one that kind of got into this
11 area back in the '80s. I know that's what he believed
12 is that it was acting just like a topocide.

13 Q. All right. Let's move on to paragraph
14 18. And you mention there the concept of comparative
15 inhibition.

16 A. Yes, sir.

17 Q. Can you explain what that concept is?

18 A. It is a well-characterized phenomenon.
19 It occurs with lots of chemicals. But for this
20 particular instance, since benzene has to be
21 metabolized in order to be toxic, it's being
22 metabolized. Its first oxidation step is occurring
23 through an enzyme called cytochrome P450 2E1. And if
24 you are exposed through other chemicals that are also
25 being oxidized by that enzyme, then the enzyme is busy

1 basically metabolizing the other chemicals and it is
2 less efficient at metabolizing benzene.

3 So by co-exposure to toluene or xylene or
4 any aromatic hydrocarbon that's going through the 2E1
5 pathway, ostensibly that will reduce benzene's
6 metabolism and, therefore, reduce benzene's toxicity.

7 Q. Okay. And in preparing your report
8 today, have you considered all of the available
9 literature on the topic of competitive inhibition
10 specifically as to toluene's competitive inhibition
11 metabolism of benzene?

12 A. I'm very familiar with that literature.
13 With regard to -- yes, I've -- I've evaluated that
14 literature.

15 Q. Okay. Are you aware of any studies that
16 have shown that low-dose levels of exposure, toluene
17 exposure, can enhance the metabolism of benzene?

18 A. I'm not aware of any that shows that
19 low-dose exposure to toluene enhances the metabolism
20 of benzene, no.

21 Q. Well, let me rephrase that question.
22 Low-dose levels -- let's say -- and, obviously, you
23 would have to have a mixture of both toluene and
24 benzene, or whatever you're being exposed to. Given
25 that situation, low-dose levels of such a mixture that

1 the toluene, you know, in the solution actually
2 enhances the metabolism of benzene or increases the
3 metabolism of benzene?

4 MR. GOTTLIEB: Object to form.

5 A. Yeah, I don't know of any that would
6 indicate that toluene would change the metabolism rate
7 of benzene.

8 Q. (BY MR. KIWALA) Let's move to paragraph
9 21 on Exhibit 3.

10 A. Okay. And before I move on, what I meant
11 by change the metabolism of benzene, increase it the
12 way that you were --

13 Q. Okay.

14 A. -- you were asking your question, because
15 we were just talking about how well it could be
16 changed going the other direction. All right.
17 Paragraph 21.

18 Q. Now, in this paragraph, you mention there
19 is -- there's some older literature that suggests that
20 toluene was toxic to the -- I'm going to mess it up
21 again -- hematopoietic system and bone marrow, but the
22 same toxic effect has not been found in more recent
23 studies. Is that correct?

24 A. Yes.

25 Q. And you also mention a possible

1 explanation of the -- there have been significant
2 reductions in the benzene concentrations in toluene
3 and other petroleum-based solvents. Do you see that?

4 A. Yes.

5 Q. What specifically do you rely on for your
6 statement that there have been significant reductions
7 in the benzene concentration in toluene and other
8 petroleum-based solvents?

9 A. Well, that's pretty general knowledge,
10 but which ones do I have here? Significant reduction
11 of benzenes --

12 Q. Is there anything that documents that,
13 anything in the literature that you can rely on?

14 A. The ATSDR tox profile for toluene.
15 That's one that I relied on. IARC, that Volume 69.
16 The toxicology of toluene. The ones that I put in
17 here, and that's just -- everyone knows that. And the
18 levels of toluene -- the levels of benzene that were
19 in toluene in the '50s and '60s in some of these
20 cruder preparations are -- there's orders of magnitude
21 more benzene in those than with the better
22 distillation processes. In the hydro treatment of
23 toluene in today's refineries, there's virtually no
24 benzene left in the toluene. So that's a pretty
25 commonly accepted premise.

1 Q. Do you have any expertise in refining
2 processes?

3 A. I don't know. What do you mean by
4 expertise? I'm familiar with what they do. I've
5 visited a couple. I'm not a refinery petroleum
6 engineer. I know you can look at the MSDS sheets for
7 any toluene that you can purchase now and you can
8 compare those with the historic levels that were
9 reported back in the '60s. And it's clear that there
10 is much less benzene in that product than there used
11 to be.

12 Q. But as far as -- as far as anything
13 reported in the literature that you're citing in
14 support of this statement, there aren't any statements
15 that effect --

16 MR. DETHERGE: Asked and answered. He
17 just gave you the support for it, Ryan.

18 MR. KIWALA: I'm asking him if there's
19 anything that he cited in this literature.

20 MR. DETHERGE: He referenced the
21 literature. If you want to go back and pull out those
22 studies and go line by line through them or those
23 references.

24 MR. KIWALA: I'm just asking if he knows
25 if it makes any mention.

1 A. I'm --

2 MR. DETHERGE: Without going back to the
3 document, you're asking if you by memory he can
4 remember a particular line or phrase in there?

5 A. I don't have the ATSDR documentation for
6 toluene, but I could get it. And my recollection is
7 it -- it discusses this very topic.

8 Q. (BY MR. KIWALA) And that's the ATSDR for
9 toluene?

10 A. Correct.

11 Q. Okay. Okay. Let's move along. Are you
12 familiar with the IARC evaluation of formaldehyde?

13 A. IARC's evaluation of formaldehyde? I've
14 read it. I mean, I don't have it memorized, but I've
15 read it.

16 Q. Do you happen to have that with you in
17 the materials that you brought with you today?

18 A. It's possible. Hold on. No, I brought
19 all of the epidemiology. I have another binder that
20 has the regulatory documents for formaldehyde, and I
21 didn't bring that. I have all of the studies, but not
22 that particular document.

23 Q. Well, in your report -- I believe it's in
24 the second declaration, the one dated July 9, if you
25 could go ahead and take a look at that.

1 A. Okay. I have it.

2 Q. And in there, you note that "There are
3 numerous studies of embalmers, anatomists,
4 pathologists and other professions where formaldehyde
5 was used. These studies reported increases, decreases
6 or frequently no effect on the risk of leukemia
7 associated with these various occupations."

8 A. Correct.

9 MR. GOTTLIEB: Ryan, where are you
10 reading?

11 THE DEPONENT: First page.

12 MR. KIWALA: First page.

13 THE DEPONENT: First paragraph, six lines
14 down.

15 A. Yes.

16 Q. (BY MR. KIWALA) Okay. Now, do you know
17 how many of those studies found excess mortality for
18 leukemia?

19 A. A number? No, not without going back and
20 counting them up.

21 Q. Okay. And one of your criticisms of the
22 studies is generally that there's almost complete
23 lack-of-exposure information, correct?

24 A. Well, I'm not sure that I would call that
25 a criticism. It's just an observation. That's just

1 what they were doing. It would only be a criticism if
2 someone was trying to say that the findings in these
3 studies are specific to formaldehyde. That would be a
4 reach.

5 Q. Okay. And in your declaration, you
6 mention three particular large cohort studies that you
7 identify as being of some importance, correct, on the
8 discussion of whether or not formaldehyde is capable
9 of causing leukemia or APL?

10 A. I'm -- where are you?

11 Q. Well, I would look at the top of --

12 A. Page 2?

13 Q. -- page 2.

14 A. The large cohorts. Okay. Yeah, to date,
15 there have been three. Yes, okay, I'm with you.

16 Q. Okay. And one of the studies you
17 mentioned is -- well, you mentioned there's the NCI
18 study and its update, the NIOSH study of the garment
19 workers and its update, as well as the MRC study of
20 British chemical workers. Those are the three cohort
21 studies, right?

22 A. Correct.

23 Q. Do you know in the -- in the NCI study,
24 what -- what was the exposure information that was
25 supplied in that study?

1 A. I don't understand your question.

2 Q. How could they -- the -- the people --
3 individuals that were reviewed in that study, in that
4 cohort, how were they assigned, you know, a level of
5 exposure?

6 A. Which -- I mean, I've got them here.
7 They basically looked at several different exposure
8 metrics. They looked at peak, they looked at
9 cumulative, intensity. I think those were the three
10 big ones. Average intensity, peak exposure.
11 Cumulative is in there somewhere. Yeah, those were
12 the three. I think that's true for both of them,
13 Hauptmann as well as the Beane-Freeman update. Is
14 that your question?

15 Q. Well, what I'm -- I guess what I'm trying
16 to get at, how did they assign -- my understanding of
17 that study of the cohort, they assigned each
18 individual a particular level of exposure; is that
19 correct?

20 A. I -- I don't -- I don't know that much
21 detail about it. I mean, I suspect that would be
22 discussed in the methods, if you'd like to find it;
23 but I can't answer that just sitting here.

24 Q. Okay. Would the same be true for the
25 NIOSH study, the garment workers?

1 A. How they went about attributing --

2 Q. Attributing the level of exposure for any
3 individuals in that study.

4 A. At that level of detail, yes, I would
5 have to go back and specifically read to find that.
6 Yes, I didn't put it in my report.

7 Q. And when -- would the same be true of the
8 MRC study, the British chemical worker, you don't
9 know, as you sit here today, how they went about in
10 that cohort to assign a particular level of exposure
11 for the individuals who were in that cohort?

12 A. No.

13 Q. Okay. Are you familiar with IARC's
14 conclusion about the -- whether or not there is a
15 causal association between occupational exposure to
16 formaldehyde?

17 A. You cut out there.

18 Q. I'm sorry. Are you aware of what -- I'm
19 sorry. I'm getting a significant back -- let me go
20 ahead and restate it.

21 Are you aware of what IARC concluded
22 about the causal association between occupational
23 exposure to formaldehyde and leukemia? Are you
24 familiar with what their conclusion was in the
25 evaluation?

1 A. Not word for word, no.

2 Q. Okay. Can you tell me generally what
3 they stated?

4 A. As I recall, I believe they said that
5 there was evidence of an association, but the lack of
6 biologic plausibility rendered them unable to -- I
7 don't -- I mean, they said there was some evidence,
8 but the lack of a biologically plausible mechanism
9 didn't make sense to them. So that's a big
10 paraphrase.

11 Q. If their conclusion was that there is
12 strong evidence of causal association with
13 insufficient evidence of causal -- a strong but
14 insufficient evidence of a causal association between
15 occupational exposure to formaldehyde and leukemia,
16 would you agree with that statement?

17 MR. GOTTLIEB: Object to form.

18 A. I -- what do you mean? Would I agree
19 that that's true or would I agree that that's what's
20 in the IARC document --

21 Q. (BY MR. KIWALA) Let's just take it as a
22 general statement. Would you agree that there is
23 strong but insufficient evidence of a causal
24 association between occupational exposure to
25 formaldehyde and leukemia?

1 A. Well, there is certainly suggestive
2 evidence. So I mean it's not uniformly negative,
3 which is why it is still an ongoing issue.

4 The studies, for example, the NCI, which
5 are probably the most important, are very inconsistent
6 with a lot of the other literature, and really even
7 inconsistent within themselves. And the terminology
8 leukemia is a very general classification. And that
9 makes it really hard to try to -- to understand what
10 this data is telling you. When they break out the
11 various forms of leukemia, then those associations
12 become even weaker. In fact, in the latest one, the
13 strongest association was with multiple myeloma and
14 Hodgkin's lymphoma and not leukemia at all. So, no, I
15 don't think I would agree with that -- that
16 interpretation of the literature as it stands right
17 now.

18 Q. In your opinion, would it be
19 scientifically unsound or speculative to conclude from
20 all of the available scientific literature that
21 formaldehyde exposure is capable of causing leukemia?

22 MR. GOTTLIEB: Object to form.

23 A. Leukemia as a general classification?

24 Q. (BY MR. KIWALA) Yes.

25 MR. DETHERGE: As in any type of

1 leukemia?

2 MR. KIWALA: That is correct.

3 A. I -- yes, I think that would be overly
4 speculative to take the position that formaldehyde can
5 definitively cause any type of leukemia. But like I
6 said, there is certainly some positive evidence in the
7 literature that something might be going on with some
8 form of hemopoietic malignancy, but there's just no
9 consistency there.

10 Q. (BY MR. KIWALA) Okay. So it would be
11 unsound and speculative to draw that conclusion from
12 the available scientific literature, correct?

13 MR. GOTTLIEB: Objection.

14 A. I didn't say it would be unsound.

15 Q. (BY MR. KIWALA) Oh, I'm sorry.

16 A. I think that the scientific literature,
17 as it exists right now, is insufficient to -- to form
18 a definitive opinion on causation.

19 Q. Okay. I'm going to ask you the same
20 question with regard to AML. Would it be
21 scientifically unsound or speculative to conclude from
22 the available scientific literature that formaldehyde
23 exposure is capable of causing AML?

24 MR. GOTTLIEB: Object to form.

25 A. Most of the studies don't even look at

1 AML, they look at myeloid leukemia. If you take the
2 classification of myeloid leukemia, which includes
3 chronic and acute myeloid leukemia, yes, I think that
4 would be a reach. I think that would be speculative.
5 I don't think the scientific evidence, as it exists
6 right now, is sufficient to say that formaldehyde can
7 cause myeloid leukemia in any person.

8 Q. (BY MR. KIWALA) Okay. Would -- and the
9 same question, finally, with regard to APL. Would it
10 be scientifically unsound or speculative to conclude
11 from the available scientific literature that
12 formaldehyde exposure is capable of causing APL?

13 A. Yes. That would be unsound and
14 speculative and purely hypothetical. There is no
15 evidence of that.

16 Q. Would reaching a conclusion that
17 formaldehyde exposure is capable of causing AML based
18 on the available scientific literature -- would that
19 be more or less speculative than reaching an opinion
20 about causation based on only case report?

21 MR. GOTTLIEB: Object to form.

22 A. I didn't -- sorry. I can't -- I didn't
23 understand that question.

24 Q. (BY MR. KIWALA) Well, you said it would
25 be a reach to conclude, based on the available

1 scientific literature, that formaldehyde exposure is
2 capable of causing AML, correct?

3 MR. DETHERGE: That mischaracterize.

4 MR. GOTTLIEB: Object to form.

5 MR. DETHERGE: I think he actually had
6 something more definitive to say than that.

7 A. Start again, please.

8 Q. (BY MR. KIWALA) Do you agree -- is it
9 your -- is it your testimony -- strike that. Is it
10 your testimony that it would be scientifically unsound
11 or speculative to conclude from the available
12 scientific literature that formaldehyde exposure is
13 capable of causing AML?

14 MR. GOTTLIEB: Object to form.

15 A. We -- we've already done that question,
16 haven't we? Well, what was my answer?

17 Q. (BY MR. KIWALA) I believe your answer --

18 A. I was asking the court reporter to read
19 it back.

20 (The question and answer referred to were
21 read back as follows:

22 Question: "I'm going to ask you the same question
23 with regard to AML. Would it be scientifically
24 unsound or speculative to conclude from the available
25 scientific literature that formaldehyde exposure is

1 capable of causing AML?"

2 Answer: "Most of the studies don't even look at AML,
3 they look at myeloid leukemia. If you take the
4 classification of myeloid leukemia, which includes
5 chronic and acute myeloid leukemia, yes, I think that
6 would be a reach. I think that would be speculative.
7 I don't think the scientific evidence, as it exists
8 right now, is sufficient to say that formaldehyde can
9 cause myeloid leukemia in any person.")

10 A. I like that answer.

11 Q. Okay. So based on -- there was a lot in
12 that answer, but the -- would you agree that the short
13 answer to that question was yes?

14 MR. GOTTLIEB: Object to form.

15 MR. DETHERGE: Asked and answered. He
16 gave you the answer.

17 A. I did. And I can't -- I mean, your
18 question was really long, so I had a long answer. I
19 think that's appropriate. I don't -- I don't know how
20 to shorten it. We can try again, if you'd like.

21 Q. Okay. But you -- I believe you said that
22 such a conclusion would be speculative, correct?

23 MR. GOTTLIEB: Among other things.
24 Objection.

25 MR. DETHERGE: Same objection. I mean,

1 he answered the question.

2 Q. (BY MR. KIWALA) Go ahead and answer it,
3 if you can.

4 A. I did. I answered the question. I don't
5 think the literature supports an association between
6 formaldehyde exposure and myeloid leukemia. There is
7 practically no data that would allow you to even
8 evaluate the relationship between formaldehyde
9 exposure and acute myelogenous leukemia, and no data,
10 zero data that would allow you to evaluate the
11 association between formaldehyde exposure and APL.
12 Does that help?

13 Q. Yes. In light of all that, if one
14 reached a conclusion that formaldehyde exposure was,
15 indeed, capable of causing AML, would that conclusion
16 be more speculative or less speculative than reaching
17 an opinion about causation based on only case reports?

18 MR. DETHERGE: Object.

19 MR. GOTTLIEB: Object to form.

20 MR. DETHERGE: Object lack of foundation.
21 I'm not sure what it means to be more or less
22 speculative. It's like more or less pregnant, isn't
23 it?

24 A. Yeah, I don't -- I don't know how to
25 answer that.

1 Q. (BY MR. KIWALA) Well, let me -- let me
2 ask you this: You cite in your report that bimolane
3 is an established cause of APL, correct?

4 A. Yes.

5 Q. And that was based on case reports,
6 correct?

7 MR. DETHERGE: Objection,
8 mischaracterizes.

9 A. It was based on one or two case reports
10 and then a large case series. And my understanding of
11 the scientific and medical communities in China is
12 that they stopped using bimolane as a result of those
13 studies. But I did agree with you that I probably
14 should have caveated that sentence with -- I mean,
15 unless -- I thought there was a cohort study. I
16 thought there was a quantitative epidemiological
17 evaluation done. And I'm still not 100 percent
18 convinced there's not. If there is, I'll send it to
19 you. If there's not and it's just those studies and
20 the response that the Chinese community had to those
21 studies, then I would have worded that a little
22 differently.

23 Q. (BY MR. KIWALA) But at any rate, you do
24 agree that there were -- as far as you know, there are
25 no quantitative epidemiological studies showing

1 consistent positive findings associating exposure to
2 bimolane and APL, correct?

3 MR. GOTTLIEB: Objection, asked and
4 answered multiple times.

5 MR. DETHERGE: Ryan, it just
6 mischaracterizes what he just told you.

7 Q. (BY MR. KIWALA) Go ahead and answer, if
8 you can.

9 A. I agree. We can go back and have the
10 court reporter read it again, if you'd like.

11 Q. So just to be more specific, would a
12 conclusion based on the available scientific
13 literature that formaldehyde exposure is capable of
14 causing AML, would that conclusion be more speculative
15 or less speculative than reaching an opinion about
16 causation whether or not bimolane is capable of
17 causing APL based on just case reports?

18 MR. GOTTLIEB: Objection.

19 MR. DETHERGE: Same objection. You've
20 asked -- it's been asked and answered, and it lacks
21 foundation for the same reasons we've discussed
22 before.

23 Q. (BY MR. KIWALA) Go ahead and answer, if
24 you can.

25 A. You're -- the question doesn't make much

1 sense to me, but I'll try. I mean, the -- these two
2 issues are very different. And you're asking me to
3 compare them with regard to their speculativeness, and
4 I don't know exactly how to do that.

5 In the bimolane and APL, to my knowledge,
6 those two studies -- maybe there's another one that
7 I've forgotten about, but I'm not sure, so that might
8 be it. That is the sum total of the literature. And
9 as I've told you earlier, that was sufficient for
10 bimolane to basically be taken off of the list for
11 treatment of psoriasis. I mean, it made a big deal in
12 the Chinese medical community. That's how I heard
13 about it. So it was established.

14 With regard to formaldehyde and myeloid
15 leukemia, you don't have two case reports. You have a
16 long list of epidemiological studies, quantitative and
17 otherwise, going back 40 and 50 years. You've gotten
18 embalmer studies and funeral directors, plus all of
19 these cohort studies that are in existence right now.

20 So this collectively, this body of
21 literature does not support an association between
22 formaldehyde exposure and AML in my opinion. Now, I
23 can't rank it in terms of speculativeness. I don't
24 know how to do that.

25 Q. Okay. Last question. Dr. Pyatt, what's

1 the hourly rate that you charge for your expert
2 services?

3 A. \$300 an hour.

4 Q. Okay. Is that the same for deposition
5 and for trial testimony?

6 A. Yes. I don't differentiate one from the
7 other.

8 Q. And for the time that you spend preparing
9 or researching issues or preparing reports, is it
10 still the same rate?

11 A. It's all the same, correct.

12 Q. Okay.

13 MR. KIWALA: Thank you very much,
14 Dr. Pyatt. Those are all the questions I have.

15 THE DEPONENT: Okay.

16 WHEREUPON, the within proceedings were
17 concluded at the approximate hour of 1:06 p.m. on the
18 11th day of August, 2009.

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* * * * *

I, DAVID W. PYATT, Ph.D., do hereby
 certify that I have read the above and foregoing
 deposition and that the same is a true and accurate
 transcription of my testimony, except for attached
 amendments, if any.

Amendments attached () Yes () No

 DAVID W. PYATT, Ph.D.

The signature above of DAVID W. PYATT,
 Ph.D., was subscribed and sworn to before me in the
 county of _____, state of
 _____, this _____ day of
 _____, 2009.

 Notary Public

My commission expires

Andrew Wolfe and Denise Wolfe 8/11/09 (tc)

1 REPORTER'S CERTIFICATE

2 STATE OF COLORADO)
) ss.

3 CITY AND COUNTY OF DENVER)

4 I, TERESA COOGLE, Shorthand Reporter and
Notary Public, State of Colorado, do hereby certify
5 that previous to the commencement of the examination,
the said DAVID W. PYATT, Ph.D., was duly sworn by me
6 to testify to the truth in relation to the matters in
controversy between the parties hereto; that the said
7 deposition was taken in machine shorthand by me at the
time and place aforesaid and was thereafter reduced to
8 typewritten form; that the foregoing is a true
transcript of the questions asked, testimony given,
9 and proceedings had.

10 I further certify that I am not employed by,
related to, nor counsel for any of the parties herein,
11 nor otherwise interested in the outcome of this
litigation.

12
IN WITNESS WHEREOF, I have affixed my
13 signature this 12th day of August, 2009.

14 My commission expires May 8, 2010.

15
16 X Reading and Signing was requested.

17 Reading and Signing was waived.

18 Reading and Signing was not required.

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