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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

Brian K. Milward and Linda J. Milward	*	
v.	*	Civil Action
	*	No. 1:07-cv-11944-GAO
Acuity Specialty Products Group, Inc., et al.	*	

Deposition of David H. Garabrant, M.D., M.P.H.
Wednesday, February 18, 2009
Nixon Peabody LLP
100 Summer Street
Boston, Massachusetts 02110

---------- J. Edward Varallo, RMR, CRR ---------
Registered Professional Reporter
HG LITIGATION SERVICES ~ DALLAS, TEXAS
1-888-656-3376

Present for Plaintiffs:
Steve Baughman Jensen, Esq.
Allen Stewart, P.C.
Republic Center
325 North St. Paul Street - Suite 2750
Dallas, Texas 75201
214.965.8700 ~ Fax 214.965.8701
sjensen@allenstewart.com

Present for Radiator Specialty Company:
Brian R. Birke, Esq.
Adler Pollock & Sheehan, P.C.
175 Federal Street - 10th Floor
Boston, Massachusetts 02110
617.482.0600 ~ Fax 617.482.0604
bbirke@apslaw.com

Present for The Clorox Company:
Charles K. Mone, Esq.
Campbell Campbell Edwards & Conroy, P.C.
One Constitution Center - 3rd Floor
Boston, Massachusetts 02129
617.241.3000 ~ Fax 617.241.5115
cmone@campbell-trial-lawyers.com

Present via telephone for Berryman Products, Inc.:
Brian P. Voke, Esq.
Campbell Campbell Edwards & Conroy, P.C.
One Constitution Center - 3rd Floor
Boston, Massachusetts 02129
617.241.3000 ~ Fax 617.241.5115
bvoke@campbell-trial-lawyers.com

Present for The Sherwin-Williams Company; Henkel Corporation:
Kevin R. Powers, Esq.
Cetrulo & Capone LLP
World Trade Center East
Two Seaport Lane - 10th Floor
Boston, Massachusetts 02210
617.217.5500 ~ Fax 617.217.5200
kpowers@cetcap.com

Present for WD-40 Corporation:
Christopher G. Betke, Esq.
Coughlin Betke, LLP
175 Federal Street - 9th Floor
Boston, Massachusetts 02110
617.988.8050 ~ Fax 617.988.8005
cbetke@coughlinbetke.com

Present for The Sherwin-Williams Company:
James R. Miller, Esq.
Dickie McCamey & Chilcote, P.C.
Two PPG Place - Suite 400
Pittsburgh, Pennsylvania 15222-5402
412.281.7272 ~ Fax 412.392.5367
jmiller@dmclaw.com

Present for United States Steel Corporation; Aristech Chemical Corporation; USX Corporation:
Tim Gray, Esq.
Forman Perry Watkins Krutz & Tardy, LLP
City Centre Building - Suite 100
200 South Lamar Street
Jackson, Mississippi 39201
601.960.8600 ~ Fax 601.960.8613
tgray@fpwk.com

Present via telephone for Sunnyside Corporation:
Leslie A. Sheehan, Esq.
Gordon & Rees LLP
633 West Fifth Street - Suite 4900
Los Angeles, California 90071
213.576.5000 ~ Fax 213.680.4470
lsheehan@gordonrees.com

Present for Rust-Oleum Corporation:
Matthew P. Zayotti, Esq.
Keegan Werlin LLP
265 Franklin Street - 6th Floor
Boston, Massachusetts 02110
617.951.1400 ~ Fax 617.951.1354
mzayotti@keeganwerlin.com

Present for Nu-Calgon Wholesaler, Inc.
Eileen P. Kavanagh, Esq.
Litchfield Cavo, LLP
6 Kimball Lane - Suite 200
Lynnfield, Massachusetts 01940-2682
781.309.1500 ~ Fax 781.246.0167
kavanagh@litchfieldcavo.com

Present for Boyle-Midway, Inc.
William R. Covino, Esq.
McDonough Hacking & Lavoie, LLC
One Washington Mall - 9th Floor
Boston, Massachusetts 02108
617.367.0808 ~ Fax 617.367.8307
wcovino@mhlattys.com

Present for Acuity Specialty Products Group, Inc.;
The Steco Corporation:
Curtis L.S. Carpenter, Esq.
Morrison Mahoney LLP
250 Summer Street
Boston, Massachusetts 02210
617.439.7500 ~ Fax 617.439.7590
ccarpenter@morrisonmahoney.com

Present for CRC Industries, Inc.:
Joseph J. Leghorn, Esq.
Nixon Peabody LLP
100 Summer Street - 25th Floor
Boston, Massachusetts 02110
617.345.1000 ~ Fax 617.345.1300
jleghorn@nixonpeabody.com

Present for The Steco Corporation:
Christopher Sullivan, Esq.
Sullivan & Collins, LLC
500 W. Cummings Park - Suite 4000
Woburn, Massachusetts 01801
781.939.5840

Present via telephone for American Grease Stick Company:

Syd A. Saloman, Esq.
Tucker Heifetz & Saltzman, LLP
100 Franklin Street
Boston, Massachusetts 02110
617.557.9696 ~ Fax 617.227.9191
saloman@ths-law.com

Present for NCH Corporation (Chemsearch Division):

Wesley A. Weathers, Esq.
Weathers Riley & Sheppeard, LLP
4848 S.W. 21st Street - Suite 202
Topeka, Kansas 66604
785.273.2020 ~ Fax 785.273.4662
wes@wrslaw.net

Also Present:

Vic Houston Henry, Esq.
Henry Oddo Austin & Fletcher, P.C.
1700 Pacific Avenue - Suite 2700
Dallas, Texas 75201
214.658.1900 ~ Fax 214.658.1919
vhhenry@hoaf.com

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(ORIGINAL EXHIBITS DELIVERED TO ATTORNEY JENSEN)

MORNING SESSION

9:17 a.m.

DAVID H. GARABRANT, M.D., M.P.H.,

having been first duly sworn on oath,

was examined and testified as follows:

EXAMINATION

BY MR. JENSEN:

Q. Good morning, Dr. Garabrant.

A. Good morning.

Q. We were introduced earlier this morning, but I'm Steve Jensen and I'm here on behalf of the plaintiffs today to ask you some questions.

And I apologize to everyone. I have not brought extra copies of my materials this morning, but I don't believe I'm going to mark anything that isn't part of reliance materials or reports, so everyone should have copies available to them.

Marking as Exhibit 1 two pages that I believe is a list of your legal testimony since November 2004. Take a look at that and see if that's correct, Doctor.

A. I believe it is.

Q. And do you have your own copy of that or

do you need to look at it?

A. No, I do not.

Q. Okay. Taking a look at that list on Exhibit 1, Dr. Garabrant, are there any of those cases that are listed on Exhibit 1 in which you were engaged to testify by plaintiff's counsel in a personal-injury case?

A. I don't believe so.

Q. And approximately how many cases -- Strike that.

Were there any of the cases that are listed on Exhibit 1 which involved litigation other than personal injury litigation, to your knowledge?

A. I'm not sure I know the definition of personal injury litigation. Some of these are workers' compensation cases, so I'm not sure how to answer that.

Q. Fair enough.

In each of those cases, were you asked to provide opinions as to the extent to which an exposure to a particular toxic substance is capable of causing a particular disease?

MR. LEGHORN: Object to the form.

A. I am not sure I understand that question. As I hear it, the answer would have to be no.

Q. And why is it no?
A. Well, I'm not sure what you mean by an exposure to a toxic substance is capable of causing particular disease. That's the part that I'm not sure what you mean.
Q. Okay. And how would you in your own words describe in general terms the areas of testimony in which you have provided opinions in the cases described in Exhibit 1 or listed in Exhibit 1?
A. (Pause) Well, many of those cases have to do with chemical exposures and whether the plaintiffs' alleged exposures caused them to have various illnesses.
Q. And were you -- Let me back up for a second. If I use the term general causation, does that have any significance to you? Do you understand what that means?
A. I believe so.
Q. And if I use the term specific causation, does that have some meaning for you?
A. I believe I understand that.
Q. Okay. In those cases listed in Exhibit 1, were you always providing opinions going to general causation?
A. I would say in most of these cases, yes.

I'm not sure that it was always true, but certainly in most of them it was true.

Q. Were there also cases in which you provided both a general causation opinion and a specific causation opinion?

A. Yes.

Q. Can you recall looking at the list which of those cases that was true for?

MR. LEGHORN: Object to form.

A. That I provided both general and specific causation opinions?

Q. That's my question, yes.

A. Not from memory, no.

Q. From memory, is it possible for you to look at this list and identify what toxin or toxins or alleged toxin or toxins were at issue in each of those cases?

A. I could do most of them from memory; not all.

Q. In approximately how many of those cases was the toxin at issue asbestos?

A. When you say the toxin at issue was asbestos, are you referring to cases involving friction products?

Q. I am referring to any case listed on

Exhibit 1 in which you provided opinions and the allegation by the plaintiff was that they had become ill with some disease as a result of asbestos exposure.

A. Well, there are a substantial number of cases here where the allegation was that exposure to friction products has caused them to become ill, and I would estimate that that's perhaps half of the cases listed here.

Q. And am I correct that the allegation by the plaintiff in those cases was that the friction product contained some amount of asbestos to which the plaintiff was exposed and which contributed to their injury. Is that correct?

A. Those cases involved allegations of chrysotile asbestos in friction products.

Q. Let me take a quick look at that list, please. Thank you.

Is it true that some of the cases listed on Exhibit 1 involved allegations of injury from benzene exposure?

A. Yes.

Q. Can you identify those cases?

A. (Pause) I think the one listed as Garcia v. Allied Diagnostic; Henricksen v. Chevron. And

the third one I'm not sure, Baker v. Chevron. I can't recall whether the allegation included benzene or not. I know it had to do with petroleum-based fuels such as diesel fuel and gasoline, but I don't remember whether there was an allegation of benzene exposure.

Q. In the Garcia v. Allied Diagnostic case, do you recall what the injury was of the plaintiff, or injuries, that was at issue?

A. I believe Mr. Garcia had a non-Hodgkin's lymphoma.

Q. And do you recall what the substance of your opinions in the case were in Garcia?

A. Mr. Garcia was a printer and it was my opinion that his work as a printer did not cause his non-Hodgkin's lymphoma.

Q. And is it your opinion generally that exposure to organic solvents is not capable of causing non-Hodgkin's lymphoma?

MR. LEGHORN: Object to the form.

A. It is my opinion that there is not sufficient scientific evidence to reach a conclusion that exposure to solvents causes non-Hodgkin's lymphoma.

PHONE VOICE: I'm having a little trouble

hearing Dr. Garabrant.

MR. LEGHORN: Try to keep your voice up.

MR. SULLIVAN: We're having difficulty down here at the end of the table too, Dr. Garabrant.

THE WITNESS: I will speak more loudly.

MR. SULLIVAN: Thank you.

BY MR. JENSEN:

Q. Is it also your opinion, Doctor, that the scientific evidence is insufficient to conclude that benzene specifically is capable of causing non-Hodgkin's lymphoma?

MR. LEGHORN: Object to the form.

A. It's my opinion that the scientific evidence is not adequate to support a conclusion that benzene causes non-Hodgkin's lymphoma.

Q. And were both of those opinions part of the opinions you delivered in the Garcia case?

A. I'm not sure I recall exactly what my opinions were in Garcia, but I think that's roughly correct.

Q. Turning to the Henricksen versus Chevron case, do you recall what the injury alleged in Henricksen was?

A. I am not sure, but I believe it was acute

myelogenous leukemia. I could be wrong, though. From memory I'm not sure.

Q. All right. Do you recall what the substance of your opinions in that case were?

A. Mr. Henricksen worked as a fuel truck driver, to the best of my recollection, and it was my opinion that his exposure to motor fuels, including gasoline and diesel fuel, did not cause his AML.

Q. And was your opinion in that regard based on the lack of evidence of sufficient exposure?

A. It was based on the scientific evidence that fails to show that either gasoline or diesel fuel is causally associated with increased risk of AML.

Q. So am I correct in understanding that you were providing a general causation opinion in that case? Is that correct?

A. Yes. And I believe I also provided a specific causation opinion.

Q. And with respect to your general causation opinion, your general causation opinion was tied to the specific kinds of products and materials that Mr. Henricksen alleged exposure to. Correct?

A. Yes, my opinion was tied to the alleged

exposures of the plaintiff.

Q. Did the plaintiff allege that the benzene in the gasoline was the cause of his injury?

A. I don't recall offhand.

Q. Do you recall what type of AML Mr. Henricksen had?

A. No.

Q. Do you recall what injuries were at issue in Baker versus Chevron?

A. There were four plaintiffs in the Baker versus Chevron case. They suffered from monoclonal gammopathy of unknown significance, or MGUS; a chronic lymphadenopathy that persisted for years but in which no cancer diagnosis was reached; AML that was successfully treated, I believe. And I take that back. I don't recall if there was an AML. There was a case of Hodgkin's disease that was successfully treated with radiation therapy and the plaintiff subsequently developed breast cancer in the radiation field; and one of the plaintiffs also had a monoclonal gammopathy.

Q. So there were two monoclonal gammopathies in the group of four?

A. That's correct. So one of the plaintiffs had two diagnoses. Actually, and another one of

them had a diagnosis of Hodgkin's disease and then subsequent breast cancer.

Q. Do you recall what substances the plaintiffs alleged were causing these various diseases?

A. The allegations revolved around a refinery in which alleged contamination of groundwater under the neighborhood where these plaintiffs lived had caused their disease.

Q. Where was that case?

A. In southern Ohio. I'm blocking out the name of the town. Hooven, Ohio.

Q. And Exhibit 1 indicates that you testified both in a deposition and in a Daubert hearing in that case. Is that correct?

A. Yes.

Q. Do you know what the outcome of the Daubert hearing was?

A. I do not.

Q. As far as you can recall, do any of the cases listed in Exhibit 1 involve allegations of APL from exposure to benzene or benzene-containing materials?

A. Not to my recollection.

Q. You have also provided testimony in legal

cases before November of 2004. Is that correct?

A. Yes.

Q. As best you can recall, have any cases in which you have ever testified involved allegations of acute promyelocytic leukemia from exposure to benzene or benzene-containing materials?

A. I don't believe so.

Q. Do you recall when was the first time you ever provided legal testimony in litigation?

A. I believe it was in the mid 1980s.

Q. Have you ever provided testimony at the request of a plaintiff's counsel in a personal-injury case?

A. Yes.

Q. Do you know how many times?

A. Offhand I do not know.

Q. And what kinds of cases, if you can recall?

A. Well, the first time I gave testimony in the mid 1980s had to do with a plaintiff who had colon cancer in which he alleged it was caused by asbestos exposure and I testified on behalf of the plaintiff.

Q. Any other examples of testifying on behalf of the plaintiff in a personal-injury case that you

can recall?

A. There have been numerous cases where people have alleged injury from various chemicals causing asthma, chronic dermatitis and other conditions where I've testified on their behalf.

Q. Aside from the example of a plaintiff alleging that his asbestos exposure was related to his colon cancer, can you recall other examples of cases in which you've testified on behalf of a plaintiff who alleged that a chemical caused him to develop cancer? Or her.

A. (Pause) There may well have been. I can't recall any from memory, though.

Q. All right. Is it fair to say that of the cases listed on Exhibit 1, that the vast majority if not all of them involve allegations by a plaintiff that they have developed cancer as a result of one or more chemical exposures?

A. No.

Q. That's not fair to say?

A. No.

Q. Please identify for me the cases listed on Exhibit 1 which involved injuries other than cancer and, to the best of your recollection, what those allegations of injury were.

A. I'm not sure I can do that for each and every case. I will do my best, however.

Essenmacher versus Orkin Exterminating Company, I believe the plaintiff alleged multiple chemical sensitivity from pesticides.

Jerry Ward versus Albion Personnel Services was not a cancer case. I don't remember what Mr. Ward had.

MDL Docket 1535, Welding Rod Products, had to do with allegations that welding caused Parkinson's disease.

Presler versus Lincoln Electric involved allegations that welding caused Parkinson's disease.

Karen Brown versus Christus Spohn Health System had to do with a woman who received a barium enema and they perforated her colon and she got barium in her peritoneum and alleged that she had barium poisoning.

I could go on, but that's out of the first maybe eight or nine, about half of them had nothing to do with cancer, and I think that that pattern is true probably throughout the entire exhibit.

Q. I have put an exhibit sticker marking as Exhibit 2 what I believe is a copy of your report in this case, Dr. Garabrant, if you would verify that

that's true.

A. Yes.

Q. Have you done additional work in this case since you prepared the report marked as Exhibit 2?

A. Yes.

Q. What additional work have you done?

A. I have reviewed Dr. Martyn Smith's supplemental declaration. I have reviewed additional scientific literature. I have reviewed the declarations prepared by Dr. Pyatt and Dr. Bennett, and I have reviewed Dr. Martyn Smith's deposition testimony.

Q. Have you formed additional opinions that are not reflected in Exhibit 2?

MR. SULLIVAN: Excuse me, counsel. Could you just identify Exhibit 2 by the date of the report?

MR. JENSEN: It's dated November 19, 2008.

MR. SULLIVAN: Thank you.

A. I have formed opinions regarding statements made by Dr. Smith in his supplemental declaration and in his deposition testimony.

Q. What opinions are those?

A. We would have to go through his declaration and his deposition in order to identify

all of them.

Q. Dr. Garabrant, have you brought with you today copies of Dr. Smith's original declaration and supplemental declaration?

A. Yes.

Q. At the time you prepared Exhibit 2, you had already reviewed Dr. Smith's original declaration. Is that correct?

A. I believe I had.

Q. Do you have any opinion today relating to Dr. Smith's original declaration that you did not express in your report marked as Exhibit 2?

A. I believe Exhibit 2 contains all of my opinions regarding Dr. Smith's original declaration.

Q. All right. If you could put in front of you Dr. Smith's supplemental declaration, please. And for the record, I will mark a copy of that as Exhibit 3. And let me verify that Exhibit 3 is indeed the same thing as what we're talking about, Dr. Smith's supplemental declaration.

A. Yes, I believe that to be the supplemental declaration.

Q. Okay, thank you.

Can you tell me what opinions you have developed relating to Dr. Smith's supplemental

declaration that are not reflected in your report which is Exhibit 2?

A. Well, okay, I'll do my best. The first is at Smith's paragraph 2 where he claims defense experts make the error that because of this unique clinical standing, it is also a unique etiological or causal entity, and there he's referring to APL. I don't think that I made any such error. There is simply good scientific evidence that the etiology of APL has nothing to do with benzene, which makes it different than some of the other forms of AML.

At paragraph 6 Dr. Smith says "Thus, common environmental causes are likely for these leukemias and may include low-level benzene exposure, quinone compounds in our diet, ionizing radiation and chemicals producing oxidative stress." I believe he is simply wrong on that with respect to APL. There is not evidence that benzene is a risk factor for APL.

Dr. Smith reiterates a similar view at the top of the next page, and I would again respond with the point I just made.

At paragraph 7 Dr. Smith comments "If APL were really so different from AML, why is it not listed as a separate cause of death on death

certificates and why are there no epidemiological studies which focus only on APL and benzene exposure?" He then goes on to say "The problem is that death certificates and case referrals in epidemiology studies consider AML as one disease or in our analogy as a car, independent of the color."

Dr. Smith seems to have forgotten that he has identified a substantial body of epidemiological literature which looks specifically at APL and benzene and which fails to show any association, so it's odd that he would question the existence of that literature when he has reviewed it.

Secondly, death certificates in epidemiology do not always consider AML as one disease. There are many studies which consider different forms of AML and Dr. Smith has done some work to identify those studies.

At paragraph 8 he comments that "Because APL is seen in studies of workers exposed to benzene where the subtypes of AML have been separately analyzed," I would comment that he has just contradicted his previous point that there are no studies that have done that, and he goes on to say, quote, "and has been found at higher levels than expected with an odds ratio that exceeds 2." There

are no studies that show an odds ratio that exceeds 2 for APL and benzene, and Dr. Smith has failed to show any.

At paragraph 12 Dr. Smith comments on the study by Golomb, G-o-l-o-m-b, and having reviewed that myself, Dr. Smith has not counted up the number of cases properly and has not calculated the odds ratios properly, and there is no incidence of APL that is approximately two times higher in those patients with probable benzene exposure than in unexposed patients, as Dr. Smith claims.

At paragraph 14 Dr. Smith says he has used this information to calculate an odds ratio for APL in the Chinese cohort study that is in excess of 2. And I believe he has made errors in the assumptions behind his calculations as well as in his methods of calculating.

At paragraph 16 Dr. Smith comments regarding my critique, quote, "Overall, his critique could have some validity if APL were a separate disease, which it is not." I believe Dr. Smith in paragraph 2 indicated that, quote, "I do not dispute that APL is a unique therapeutic entity among the myeloid leukemias," so I am perplexed by his contradiction of his earlier paragraph.

He then goes on to say at paragraph 16, quote, "My point is that we know benzene causes AML and that the Travis study shows that a significant proportion of these AMLs, four of nine cases analyzed, see below, are APL cases." I disagree that we know that four of the nine are APLs because of deficiencies in the diagnostic information in the Travis report.

At paragraph 19 Dr. Smith attributes a statement to me at lines 3 through 7 that I don't believe I ever made. He then goes on to make an error in claiming that the proportion of acute leukemias that were APL is 28.6 percent. That's not correct and the literature that Dr. Smith claims to have read shows it's not correct, so I don't know how he arrived at that conclusion.

He then calculates an odds ratio -- I'm still at paragraph 19, at the top of page Smith 000704 -- he claims he calculated an odds ratio. In fact he did not calculate an odds ratio; he is wrong. His calculation is not based on any reliable methodology. Moreover, he did not calculate any test of statistical significance or any confidence interval regarding his measure of association, which he incorrectly calls an odds ratio, and therefore he

has no basis for saying at the bottom of paragraph 19, quote, "Thus, one can say to a reasonable degree of scientific probability that the odds ratio for APL associated with benzene exposure in the Chinese cohort is more likely than not greater than 2."

At paragraph 20 Dr. Smith makes a comment that my calculations have no validity because the proportion of APL among AML cases in China appears to be much higher than among AML cases in the U.S.; and two, the Chinese cohort is a group of healthy workers that is not representative of the general population, making direct comparisons to other population incidence untenable. He is simply wrong. There's no basis for those claims.

At paragraph 21 Dr. Smith claims that both Dr. Bennett and I ignore the difficulties of performing research in China in the time period before 1987. He's wrong about that; I don't ignore that. I simply pointed out that the diagnoses of APL were not reliable and were not based on the diagnostic materials that are essential in order to reach those diagnoses.

Dr. Smith then goes on to address a number of responses to the declaration by Dr. David Pyatt. Although I do not agree with a number of things he

has said there, I will not address those since those are really directed at Dr. Pyatt's opinions.

Q. Starting with your opinion in regard to paragraph 2 of Exhibit 3, Dr. Smith's supplemental declaration at paragraph 2, as I recall, you told me that your opinion is that there is good evidence that the etiology of APL has nothing to do with benzene exposure. Is that correct?

A. I don't think that's what I've said.

Q. Okay. The record will reflect what you've said. Here's my question about what you've said. Are you basing your opinion in regard to paragraph 2 on any evidence other than epidemiological studies?

A. Yes.

Q. What evidence besides epidemiological studies?

A. Well, first let me comment on the role of the epidemiological studies. The epidemiological studies provide a direct test of the hypothesis that APL is causally associated with benzene and they fail to show that association, and so they provide the strongest evidence in response to Dr. Smith's allegation that APL is not a unique etiological or causal entity with respect to benzene.

Secondly, I rely on more general concepts

derived from my education, training and experience in medicine that goes to the issue of how do we actually differentiate one disease from another. In other words, why is rheumatoid arthritis different from systemic lupus erythematosus? Why is rheumatoid arthritis different from osteoarthritis? Why is tuberculosis different from other mycoplasmal diseases?

The history of medicine provides a firm foundation for the overall process of differentiating diseases based on seeing that they have different clinical presentations, different clinical courses, and different treatments, as well as different etiologies. And so over the history of medicine we have split broad diagnoses into more clearly defined and differentiated diseases. At times we have taken diseases that appeared to be different and then realized that they were different manifestations of the same underlying disorder, and so on.

What I believe is clear for APL, and particularly since cytogenetics and immunophenotyping has been brought into widespread use in the diagnosis of leukemias, is that not only is it a distinct clinical entity, but to the extent

that we have been able to examine the association of that distinct entity with various putative causes, it has different causes than some of the other forms of AML.

Q. Will you be providing any opinions in this case dealing with the cellular origins for APL or any other form of leukemia?

MR. LEGHORN: Object to the form.

A. No.

Q. Will you be providing any opinions in this case relating to the natural history of how APL develops?

MR. LEGHORN: Object to the form.

A. I'm not sure I know exactly what you mean by that question. If that question includes how it develops with respect to etiology, yes.

Q. Will you be providing any testimony in this case relating to what is going on at the cellular, subcellular, genetic level that is causing APL to develop?

MR. LEGHORN: Object to form.

A. I have not been asked to cover that area and at the moment I have no plans to testify in that area.

Q. Moving on to paragraph 6 of the

supplemental declaration of Dr. Smith, which is Exhibit 3, the first sentence of paragraph 6 says "Common genetic variants in a gene called NQ01 for NAD(P)H:quinone oxidoreductase, one, confer susceptibility to AML and two studies in England and China show that this is strongest for de novo AML cases harboring translocations and inversions, including t(15;17) in APL." Do you have any opinions as to whether that sentence is correct?

A. I do not have any opinions regarding whether that sentence is correct.

Q. I won't read the second sentence but I'll ask you the same question about the second sentence. Do you have any opinions as to whether the second sentence of paragraph 6 is correct?

A. I do not.

Q. Am I correct, Dr. Garabrant, that your opinions regarding paragraph 6 of Dr. Smith's opinion are really relating to the third sentence of the paragraph, which says "Thus, common environmental causes are likely for these leukemias and may include low-level benzene exposure" and he goes on from there. Is that right, your opinions are addressed at that sentence?

A. Well, my opinions are addressed at the

hypothesis that Dr. Smith has that since he has a possible mechanism by which environmental causes might cause APL, he then makes a conclusion that common environmental causes are likely. And I think that his conclusion is not borne out by the available evidence. He's got a hypothesis that does not have proof.

Q. The fourth sentence of paragraph 6, Dr. Garabrant, says "Further, in a recent epidemiological study of childhood AML, we separated the, quote, good prognosis, close quote, AMLs with translocations and inversions from other forms of AML and found a strong association between parental exposure to solvents and increased risk of these specific forms." Then he gives a citation. Up to that point in the sentence, do you have any opinions as to whether what I've read so far is correct?

A. I don't have an opinion regarding that sentence. This litigation is not about childhood AML and so I don't know the relevance of Dr. Smith's reference to that.

Q. Well, the rest of the sentence after the citation says "Again suggesting a common cause for APL and other AMLs harboring translocations and inversions." I assume you disagree with that

portion of the sentence. Am I correct?

A. Well, again Dr. Smith is talking about childhood AML. This is not a case about childhood AML. The childhood leukemias are different than the adult leukemias in many ways, and I do not know the literature on childhood AML and parental exposure to solvents in depth and I didn't review it with respect to this case, and so I can't comment on the validity of his claim without having actually explored that area in detail. All I can say is I think he is invoking something of marginal or no relevance to the case at hand.

Q. And your view that the evidence he is invoking is of marginal or no relevance is based on the fact that it in this particular instance comes from a study relating to childhood AML which you believe is of marginal or no relevance to an adult AML. Is that correct?

A. Well, there is a large literature on childhood leukemia looking at parental exposures to solvents, benzene, pesticides, incense, parental occupations, and Dr. Smith is referring to a single study pulled out of that large body of literature and reaching a conclusion based on that single study. And my comment is if we're going to talk

about childhood AML, that is a very large area that needs to be examined rigorously and systematically. You cannot reach a valid conclusion by citing to a single study that has a finding that you like, without considering all of the rest of the body of literature.

This case is not about childhood AML and neither Dr. Smith nor I have done a rigorous examination of that large body of literature, and so I think it is irrelevant to simply pick a single study and to say "See, this supports me."

Q. Do you have any knowledge as you sit here today, Dr. Garabrant, as to how many other studies, if any, have looked at comparing translocations and inversions of AMLs that have the so-called good prognosis with other forms of AML in childhood AMLs?

A. Again, as I have already stated, I have not reviewed the literature on childhood AML in preparation for this case. I think it is of marginal or no relevance to the case, but if Dr. Smith wants to bring that up, I'd be happy to review it and provide opinions regarding childhood AML and what we know about its etiology. Dr. Smith has not done that. He has cited to a single study.

Q. Turning to paragraph 12 of Dr. Smith's

supplemental declaration, you indicated that it was your opinion that Dr. Smith had not correctly counted the cases from the Golomb study. Is that right?

A. I believe so.

Q. How do you believe the Golomb cases should be counted?

A. (Pause) In the 58 unexposed patients in the Golomb study, there are five patients who have APL. Dr. Smith counts four and he then uses that erroneous count to calculate an odds ratio of 2.1. So he's counted wrong.

Q. Other than the four should have been a five, are there any other errors in the calculation that Dr. Smith made that is reflected in paragraph 12, in your opinion?

A. From memory, I don't know exactly how he made his calculation, so I would have to repeat that calculation in order to verify whether he has done his arithmetic properly.

Q. Well, without pulling out a calculator to do the arithmetic, what I'm asking you is whether you have any methodological criticism of the way that that calculation was done as it is described in paragraph 12?

A. Again, without working back through what he has described, I can't comment. I'd be happy to do that, but I can't do that without sitting down and working back through his logic and doing the arithmetic.

Q. So it is fair to say as you sit here today you have not developed any opinions beyond what you've already told me regarding any errors that Dr. Smith may have made in paragraph 12. Is that correct?

MR. LEGHORN: Object to the form.

A. Well, no. I've already told you that he's counted wrong. There are five cases; he only counted four of them, and therefore his calculation is in error.

Q. My question intended to encompass that criticism, Doctor. But besides the counting four cases when he should have counted five, as you sit here today you have identified no other methodological errors that Dr. Smith made in his calculations at paragraph 12. Is that correct?

MR. LEGHORN: Object to the form.

A. No. In fact, to the extent I understand what he's done, he chose to exclude one of those five cases because there were not confirmed or I

should say because cytogenetic testing was not done or was not reported in the Golomb paper. He is inconsistent in his methods when he comes to the Travis paper where he specifically includes cases that have no confirmed cytogenetic abnormalities. So in Golomb he excludes the one where there's no confirmed cytogenetic abnormality; in Travis he specifically includes them. That is a methodologic inconsistency that is inconsistent with rigorous and carefully done science.

Q. Again, that criticism goes to how many APL cases are reflected in Golomb that should have been counted in his calculation. Is that right?

MR. LEGHORN: Object to the form.

A. No. It goes to his methods and it goes to the reliability of his thinking.

Q. Besides the number of APLs that are used in the calculation in paragraph 12, as you sit here today you have no other criticisms related to that calculation. Is that correct?

MR. LEGHORN: Object to the form. It has been asked and answered.

A. As I have already answered, in order to determine whether I have other criticisms I would need to check his arithmetic.

Q. Which you have not done as we sit here. Correct?

A. I have not done it as I sit here. I did work through his arithmetic previously, but I don't have it and I don't recall whether I found any other errors.

I should also mention that Dr. Smith fails to provide any test of statistical significance or any confidence interval with his calculated odds ratio, and as a consequence of that, it is unclear whether that odds ratio is reliable or not. Let me rephrase that: It is unclear whether that odds ratio is reliably different than 1.0 or not.

Q. Is it your view, Dr. Garabrant, that an epidemiological study that shows an odds ratio or a relative risk or a standardized mortality ratio or whatever the equivalent measure of association is for that type of study which is not statistically significant but is above the odds ratio of relative risk, whatever is above 1, that such a study provides no evidence of an association?

MR. LEGHORN: Object to the form.

A. Well, the evidence of association from an epidemiological study is whatever is calculated by the SMR or odds ratio or whatever other measure of

association one calculates. The issue is whether that measure of association is meaningfully different from the value 1.0, which means there is no association.

Q. Right. And my question for you is: If the association calculated is not statistically significant, is it your opinion that such a study, regardless of whatever else its findings or data show, provides no meaningful evidence of an association?

A. It is my opinion that when you have measures of association that are not statistically significant, the data are reasonably compatible with there being no association whatsoever.

Q. And if the data are reasonably compatible with there being no association whatsoever, is it your opinion that any such data should not be considered as evidence of an association?

A. It's my opinion that good scientists consider all reliable and relevant data, which is what I think Dr. Smith systematically does not do in his supplemental declaration.

Q. Let me pose a hypothetical to you, Doctor. If there were ten epidemiological studies all looking at the issue of whether benzene exposure may

cause APL and each of those studies found an elevated relative risk above 2.0 but the confidence interval for each of those studies encompassed 1.0, so all ten of them come up with similar results, none of them are statistically significant but all of them have a relative risk that is calculated at above 2.0. Would it be your opinion that the data is insufficient to conclude that more likely than not benzene exposure causes APL in that circumstance?

MR. LEGHORN: Object to the form.

A. Your hypothetical isn't adequate to reach any such conclusion one way or the other.

Q. I would add to the hypothetical that's the only epidemiological evidence that was available that was specific to both APL and benzene exposure.

MR. LEGHORN: Object to the form.

BY MR. JENSEN:

Q. Does that make any difference to you?

MR. LEGHORN: Object to the form.

A. No. The hypothetical still is not sufficient to reach any meaningful conclusion one way or the other.

Q. In your opinion, is it ever appropriate to reach an opinion that a particular chemical causes a

particular disease in the absence of statistically significant epidemiological evidence that supports that proposition?

MR. LEGHORN: Object to the form.

A. It is my opinion that when epidemiological evidence exists, you must consider it.

Q. That wasn't my question. Do you need me to repeat the question?

A. No. If your question is whether you can reach a conclusion of causation in the absence of epidemiological evidence, my answer is that's not the instance we're in. We have a case here where there is a substantial body of epidemiological evidence which must be considered. There are many settings where we can conclude causation in the absence of epidemiology, such as gunshot wounds, such as falling out of airplanes when your parachute doesn't open. You don't need epidemiology. But when you have situations such as low-level chemical exposures and the development of diseases years or decades later and there is epidemiologic evidence, you have to consider it and you have to consider it fully.

Q. Is it your view, Dr. Garabrant, that the available epidemiological evidence that exists with

respect to acute promyelocytic leukemia and benzene exposure establishes that benzene exposure cannot cause APL?

MR. LEGHORN: Object to the form.

A. As Dr. Smith himself pointed out, you cannot prove the null hypothesis. I agree with that statement. He got that one right. The epidemiologic evidence that we have regarding benzene and APL fails to prove the alternative hypothesis.

Q. Am I correct, Dr. Garabrant, that because in your view the epidemiological evidence with respect to APL and benzene fails to prove the alternative hypothesis, it is your view that it is unnecessary to look to other bodies of evidence such as biological mechanism evidence to determine the question of whether benzene is capable of causing APL?

MR. LEGHORN: Object to the form.

A. I am a strong adherent of Austin Bradford-Hill's comments on causation. And consistent with Hill's comments, I believe that one has to look for evidence of an association when the purpose is to determine whether an environmental exposure is causally associated with a disease such as APL. One

has to look for evidence of an association and that if one does not find evidence of an association, then most of the other considerations that Hill discusses are rendered moot. In other words, when there's no association, you can't look for dose response because there's no dose response when there's no association. You really can't look at specificity when there's no association. You can't really judge coherence of the literature -- Well, I guess you can when there's no association and when you see a coherent picture of lack of association, you can say "You know? There's really no association."

So your comments about biological plausibility I think go to the issue of, well, should you look for biological plausibility when you can't find evidence of an association? And my comment to that would be I've spent my career as a scientist, and smart scientists can come up with a biologically plausible explanation for almost any hypothesis. That's not hard. The issue is whether you have empirical evidence that supports that the hypothesis is correct in the first place.

Q. And in your view the only type of evidence that counts as empirical evidence to support the

hypothesis with respect to environmental exposures and latent disease are human epidemiological studies. Is that correct?

A. No. My opinion is that when human epidemiological studies exist, you can't ignore what they may say, and that's the instance we're in here. We have a substantial body of literature which Dr. Smith has largely identified which is directly relevant to whether there is an association between benzene exposure and APL. You can't ignore it.

MR. JENSEN: Let's take a quick break.

MR. LEGHORN: I was going to say, before we go to another paragraph, it would be a good time for a break.

(In recess 10:38 a.m. to 10:51 a.m.)

BY MR. JENSEN:

Q. Turning to paragraph 19 of Dr. Smith's supplemental declaration, I believe you testified that it was your opinion that Dr. Smith's statements about the proportion or assumptions about the proportion of APLs in the Chinese population is wrong. Am I correct that that was your opinion or that is your opinion?

A. Let's read back exactly what I said about that, because I don't think that's what I said.

Q. Well, I don't want to quibble with you about what your opinion is, so I'll ask you: What is your opinion with regard to the proportion of APLs and what Dr. Smith has to say about that in paragraph 19?

A. Well, my first opinion is that I can't see any reason in the world why you would calculate something based on proportions when the data is available to actually compare incidence rates. So Dr. Smith chose to do a calculation that has the potential to have many sources of bias instead of doing a calculation that would be much more reliable. So, again, his fundamental approach is just wrong.

Q. Do you have an opinion about whether his statement in paragraph 19 -- it's the third sentence, I believe -- that begins "Thus, four cases of APL in fourteen cases of acute leukemia would be equal to the general representation of APL in the Chinese population, i.e., 4/14 equals 0.286 or 28.6 percent." Do you have an opinion about whether the statement in that sentence is correct?

A. Well, it's wrong. We know from the Yang paper that the correct proportion is not 28.6 percent. Now, that's a paper that Dr. Smith read.

So why would he choose to make an assumption that's wrong when the actual proportion is in the paper? That's the sort of incorrect methodology that we see recurring in Dr. Smith's opinions.

Q. What is the proportion reflected in the Yang paper of APLs to the total ANLL incidence in China?

A. Well, the more important question is why would you bother to use proportions when you can actually use the actual incidence rates? Here's the problem with proportions. When one disease is overrepresented, the proportions of all others are underrepresented; and conversely when one disease is underrepresented, the proportions of all other diseases are overrepresented. So proportions by their very nature are a less reliable measure than are actual incidence rates.

So I cannot think of a reason why any reliable scientist would use proportions when he has access to the underlying rates. It's just the wrong thing to do.

Q. What is the proportion of APL in ANLL as reported by the Yang paper?

A. 18.7 percent.

Q. Besides what you've already testified to,

do you have any other specific criticisms of paragraph 19 and the approach that Dr. Smith took in his paragraph 19?

A. Yes. One of the principles of science is that a good scientist considers all relevant and reliable data. Dr. Smith chose not to do that in paragraph 19. So by choosing to make an erroneous calculation based on proportions and ignoring the far more reliable and relevant incidence rates, he has not followed good scientific procedure. He has ignored good data and chosen to do something that is highly likely to give an unreliable answer, and in fact the proportion he chose was based on a poorly documented statement at the very end of the Travis paper where Dr. Travis says the proportion of APL in de novo ANLL was similar to that in the general population.

So he took that and said, well, it's really the same, it's 28.6, when it wasn't the same; it was actually, in my opinion, not even very similar. And my underlying opinion is I wouldn't even use that approach because it's not a good approach. The Yang paper gives tell you incidence rates. You can calculate an incidence ratio.

Q. What is the healthy worker effect?

A. The healthy worker effect is a term that really is an umbrella term for the commonly observed phenomenon in the occupational epidemiology literature coming from the United States and Western Europe that in many cohort studies of working populations, the workers are in general healthier than the general population.

Q. Does the healthy worker effect, in your opinion, play any role with respect to analysis of the Travis et al. papers and series of studies by Travis, Yin, Hayes et al.?

A. I think it deserves careful consideration.

Q. How did you consider the healthy worker effect and what role did it play in your opinions in this case?

MR. LEGHORN: Object to the form.

A. The Travis paper reports on hematopoietic malignancies among benzene-exposed workers in China. If we go back to some of the earlier reports from that population, we find that the Yin paper published in 1989 gives us the ability to evaluate whether there is a healthy worker effect among benzene-exposed workers in China. And what we find is that the all-cause-of-death mortality rate in the benzene-exposed workers is roughly double that in

the nonexposed workers.

So not only is there not a healthy worker effect in the population under study in the Travis paper, it goes the other way. It's a twofold increase in risk. So if Dr. Smith were really interested in adjusting for the healthy worker effect, he's got it backwards. In fact, that working population has double the all-causes mortality of the general population. And if he's going to adjust for it, then he should have adjusted the other way. That's point number one.

So he has invoked something in a manner where he's actually done it backwards.

Number two, to my recollection Dr. Smith objected to using the incidence rates in the general population of China derived from the Yang paper as we've discussed and he chose to use the proportion of APLs among AMLs instead of using the incidence rates. And in part he did that because he said there was a healthy worker effect in using the population reported in the Yang paper.

His comment suggests that although he's read the Yang paper, he didn't read it very carefully, because many of the populations studied in the Yang paper were working populations. They

came from the Daqing Oil Field, the Changchun Automobile Company, the Yanju Forestry Farm, the Baotou Steel Company, the Pingdingshan Coal Mine, the Kailuan Coal Mine, the Fengfeng Coal Mine, et cetera.

So in fact those rates to which he objected using were largely derived from working populations and so it would have been perfectly appropriate to have compared the rates derived from the Yang study, the cancer incidence rates, to the cancer incidence in the Chinese benzene cohort. Perfectly appropriate to do.

Q. Does the Yang paper indicate what proportion of the people from which the incidence rate for APL is calculated are workers as opposed to nonworkers?

A. They didn't tabulate it or they didn't give the summaries, but that could easily be derived from Table 1.

Q. With respect to your statements regarding the Yin 1989 paper, did I hear you correctly that Yin was calculating all cancer mortality of the exposed worker population by comparing it with an unexposed worker population?

MR. LEGHORN: Object to the form.

A. That's not what I said. I was talking about all causes of death. You were talking about cancer.

Q. I'm sorry. But Yin did calculate all causes of death in the exposed population by comparing it with an unexposed population of workers. Is that right?

A. Yes.

Q. So both populations were workers with respect to the calculations made by Yin. Right?

A. That's correct.

Q. Isn't comparing an exposed worker population to an unexposed worker population one of the methods that epidemiologists commonly use to avoid any impact of the healthy worker effect?

A. Yes. And that's why Dr. Smith should have carefully looked at the Yin paper. He would have realized that there's no healthy worker effect in the benzene-exposed cohort. In fact, their all-cause-of-death mortality is double that in the unexposed population.

Q. Well, in order to measure the healthy worker effect, if any, don't you have to compare a worker population to a nonworker population?

A. If you want to measure the healthy worker

effect, yes, you have to.

Q. So there could be a number of different reasons besides any healthy worker effect or lack thereof for the mortality in the exposed workers described in Yin to be higher than the unexposed workers. Right?

A. Yes. And the most likely reason is far better disease surveillance in the benzene-exposed than in the unexposed. In other words, what this really suggests is that there is systematic difference in the way they're doing their surveillance in the benzene-exposed population compared to the unexposed. I mean, a doubling of mortality is extraordinary. We never see that. Never. It's absolutely extraordinary.

Q. Another contributor could be that the exposures themselves are causing mortality. Correct?

A. I think that's extremely unlikely here. What exposures could you hypothesize that would double mortality across all causes of death? I can't think of any. There are no chemicals that cause increases in cardiovascular disease, cerebrovascular disease, renal disease, pulmonary disease, all causes of cancer, diabetes, infectious

diseases, accidents, suicides, psychiatric disease, neurologic disease. There aren't any.

Q. Exhibit 2, which is your report of November 19, at page 3 -- Are you with me, Doctor?

A. Yes.

Q. Okay. The first full paragraph there on page 3 discusses the Travis study and your analysis of Dr. Smith's opinion of the Travis study. Is that right?

A. Well, the first paragraph is what it is.

Q. And in that paragraph it says "If we use Dr. Smith's estimate of three to eight cases of APL per one million person-years," that estimate that you're describing there is an estimate based on incidence in the United States. Is that correct?

A. I don't recall where Dr. Smith got that estimate, but that's his estimate.

Q. And you were comparing in that paragraph an incidence rate that derives from a general population with the incidence in the benzene-exposed group discussed in Travis. Is that correct?

A. Well, I'm using Dr. Smith's own estimate of the incidence rate to make an estimate of the expected number of cases you'd see in Travis.

Q. And I'm asking you whether you even know

if that incidence rate that is estimated, you say, by Dr. Smith at about three to eight cases of APL per year, is that an incidence rate for a worker population or for a general population?

A. I don't recall where Dr. Smith got that number. To the best of my recollection, he never said. Or, I should say, the range.

Q. So I take it, then, that it doesn't make any difference to you whether or not the incidence rate that Dr. Smith is using of three to eight cases of APL per one million person-years is an incidence rate derived from a general population or a worker population for purposes of your analysis?

A. Well, it does matter. And in fact it is entirely consistent with the incidence rate of APL in what I was referring to as the Yang study, it's actually Yang Chongli, in the Chinese Medical Sciences journal. In that study, which is largely derived from working populations in China, the incidence rate is 3.5 per million person-years, so it is entirely consistent with Dr. Smith's estimates.

Q. Dr. Garabrant, have you ever published any article, textbook chapter or any other publication in which you've expressly discussed the issue of

whether benzene exposure is capable of causing acute promyelocytic leukemia?

A. I don't believe so.

Q. Have you ever published a study of benzene-exposed workers and leukemia risk?

A. I'd have to look at my C.V. I don't recall any. I know my colleagues and I published a study of childhood leukemia looking at parental exposures where we specifically looked at benzene and other solvents. I would have to look back through my C.V. to see if there's anything else. I know I've done research that is not published that has looked at that issue.

Q. Is the paper you describe on childhood leukemia the Buckley et al. paper of 1989?

A. Yes.

Q. What unpublished work have you written with respect to benzene and leukemia?

A. We did a large cohort mortality study of auto industry workers where we looked at each and every one of about ninety causes of death, including leukemias, and over a hundred different exposures. In that list of exposures we included many different types of solvents, oils, lubricants, greases, machining fluids, petroleum distillates, paint

thinners. So these were auto industry workers and we looked at leukemia mortality.

Q. In that cohort of workers, were there any measured air concentrations of benzene that were available for purposes of exposure analysis?

A. We did not have any at the time we did this study. I am aware that there is some information regarding industrial hygiene data from the plants we studied, but it was not incorporated into our research.

Q. Was that study commissioned by one or more of the auto companies?

A. No. It was commissioned by the United Auto Workers-Ford Motor Company National Joint Committee.

Q. What were your findings with respect to benzene and -- Excuse me. What were your findings with respect to solvent petroleum exposures and leukemia in that study?

A. To the best of my recollection, I don't think we found any significant associations.

Q. Are you familiar generally with Dr. Smith's work in the field of benzene toxicology?

A. I have seen some of it. I wouldn't say I'm generally familiar with it.

Q. Do you have an opinion as to whether Dr. Smith is considered a highly respected benzene toxicology researcher?

MR. LEGHORN: Object to the form.

A. I don't know whether he is a highly respected benzene toxicology researcher. I do believe he's a highly respected scientist.

Q. Did you read either or both of Dr. Cranor's reports in this case?

A. I read Dr. Cranor's report dated October 9, 2008.

Q. Dr. Cranor issued a supplemental report on December 9, 2008. Did you have the opportunity to review that?

A. I don't believe so.

Q. In paragraph 6 of his supplemental report Dr. Craner states, quote, "As a part of a review of the science, whether for assessing claims in physics or human health, scientific judgment is critically involved not only for drawing the ultimate conclusions but also for a number of steps along the way," close quote. Do you agree with that statement?

MR. LEGHORN: Object to the form.

A. I've never read the report. Could I see

it and read that section of it? (Pause) Okay, what's your question?

Q. If I may have it back, I'll repeat the question.

A. Well, I need it. Do you want me to read that sentence back?

Q. Yes. The sentence that I read to you, and my question was simply whether you agreed with that sentence.

A. I would say yes, I agree with that sentence, and I strongly agree with the preceding paragraph in which Dr. Cranor says "A scientist in reviewing and assessing all the scientific evidence for a conclusion such as whether benzene exposure can cause APL must consider and integrate all the available relevant evidence." And that is of course the critical issue that Dr. Smith has not done. He has not properly looked at the incidence rates of APL in China. He has relied on calculations that are not reliable, choosing them over calculations based on much more reliable evidence. He has invoked a healthy worker effect where none exists as a potential objection to comparing incidence rates in the benzene-exposed cohort in the Travis paper compared to incidence rates in other populations in

China.

If he were to integrate and evaluate all the relevant evidence, I think he would find that his conclusions are not well-supported by the data.

Q. And in your opinion, biological mechanism evidence is not relevant in this instance. Correct?

A. That is not my opinion.

Q. It is your opinion that because the epidemiology in your view fails to show an association between benzene and APL, that consideration of biological mechanism evidence is unnecessary. Isn't that true?

MR. LEGHORN: Object to the form.

A. That is not my opinion. It is my opinion that the epidemiology provides a critical test of whether hypotheses derived from mechanistic evidence are borne out by the experience of the human population, and in this setting they appear not to be borne out.

Q. Is it your opinion that biological mechanism evidence with respect to environmental exposures and latent disease is never sufficient of itself to establish that exposure causes the disease?

MR. LEGHORN: Object to the form.

A. That is not my opinion. It is my opinion that when you have epidemiologic evidence as we have in this case, you must consider it, and it provides a test of whether your mechanistic hypothesis is or is not correct.

Q. And it is your view that regardless of the limitations on that epidemiology, to the extent that epidemiology fails to itself show an association, that it renders the mechanistic evidence incapable of reaching the conclusion of causation. Isn't that right?

MR. LEGHORN: Object to form.

A. That is not my opinion. My opinion is that you have or I should say Dr. Smith has a mechanistic hypothesis. The epidemiology provides a real test of whether populations exposed to benzene are at increased risk of APL; it does not support a conclusion that they are.

Q. And the flip side is, Doctor, that you've admitted that the epidemiological evidence also cannot prove the null hypothesis. Correct?

A. That is correct, and that is a widely accepted principle of scientific inference across all branches of science.

Q. So the epidemiological evidence with

respect to benzene and APL in your opinion neither proves that benzene does cause APL nor does it prove that benzene does not cause APL. Correct?

MR. LEGHORN: Object to the form.

A. The issue is this. In science if you have a hypothesis that some agent causes a disease, let it be the hypothesis that benzene causes APL, the burden of proof is on the person who forms the hypothesis to show that their hypothesis is correct. We largely endorse the approach written by Karl Popper, the idea of refutation of hypothesis, that what most scientists do is try to refute hypotheses that have been proposed.

So we are in a setting where Dr. Smith has hypothesized that low-level benzene exposure causes APL, and it is appropriate that the epidemiology evidence and other forms of scientific evidence be examined carefully and systematically to determine whether they provide proof of Dr. Smith's hypothesis or whether they fail to provide it. In other words, do they refute it or do they provide data that are inconsistent with his hypothesis? The answer is they provide data that fails to support Dr. Smith's hypothesis.

What that means then is he has a

hypothesis that lacks proof.

Q. I am going to repeat my question which you didn't answer. Isn't it your opinion that the epidemiological evidence with respect to benzene exposure and APL is neither sufficient to show that benzene exposure can cause APL nor is it sufficient to show that benzene exposure cannot cause APL?

MR. LEGHORN: Object to the form, asked and answered.

A. As Dr. Smith testified, you cannot prove the null hypothesis. That is widely agreed across all areas of science. So your question has a presumption in it that somehow I should be forced to do something that we all agree can't be done. In science we seek to prove alternative hypotheses such as that benzene causes APL and, failing to do so, which is the situation we're in, we are left with the conclusion that there is not adequate evidence to conclude that benzene causes APL, period.

Q. Based on the human epidemiology studies. Right?

A. Based on a consideration of all the evidence.

Q. Well, Doctor, if the human epidemiology studies themselves can't prove the null hypothesis,

then how can they be affirmative evidence that benzene exposure does not cause APL?

MR. LEGHORN: Object to form, argumentative.

A. I've already answered that question.

Q. Is there any circumstance in which you would find that biologic mechanism evidence itself is sufficient to reach a conclusion scientifically that more likely than not exposure to agent A causes disease B?

MR. LEGHORN: Object to the form.

A. There are numerous instances where that could be true. If you had a gunshot wound to the head and you explored the anatomy of what had happened as the bullet passed through the head, I think you could easily invoke mechanistic evidence that would say that was the cause of death; you don't need epidemiology.

Q. I'll try it again. Is there any circumstance in which you would find based on mechanistic evidence in the absence of epidemiology evidence that an exposure to an environmental agent causes a particular disease following some latency period?

MR. LEGHORN: Object to the form.

A. I would be reluctant to accept mechanistic evidence as the sole basis for a conclusion that an environmental agent caused a disease such as cancer with an appreciable time lag between exposure and disease and in the setting where there were other known or unknown causes of that disease. That approach, I believe, is entirely consistent with for example the International Agency for Research on Cancer, which uses a set of rules in which they are almost invariably unwilling to reach a decision that a chemical agent is known to cause human cancer in the absence of sufficient epidemiologic evidence. They consider mechanistic evidence as a far less important form of support for reaching those conclusions than do they consider the epidemiologic evidence.

If I were to try to apply the logic and rules that IARC uses to the setting of benzene and APL, it would be quite clear that the epidemiologic evidence is inadequate to support a conclusion that benzene causes APL. Whether you have mechanistic evidence or not, I do not think you could sustain a conclusion that benzene is known to cause APL in humans.

Q. In fact, IARC has a classification for

whether something is a known carcinogen and whether something is a probable carcinogen as well. Correct?

A. I believe they use the terms known, probable, possible, and not classifiable. They also have a fourth classification for known not to cause. There's only one chemical that's ever been classified in that last category.

Q. And IARC will classify agents as probably carcinogenic to humans in circumstances when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. Correct?

A. I believe that's correct. And I am not aware that we have sufficient evidence in animals for benzene and APL and I believe we do not even have limited evidence in humans. I doubt this would be IARC class 2A. It would probably be IARC category 3.

Q. IARC also classifies a carcinogen or possible carcinogen as 2A as a probable carcinogen when there is inadequate evidence of carcinogenicity in humans, sufficient evidence of carcinogenicity in animals, and strong evidence that carcinogenesis is mediated by a mechanism that also operates in

humans. Is that right?

A. I believe that's one of the set of criteria by which they will classify a chemical as a 2A or probable carcinogen. But I don't believe that we've satisfied those conditions.

Q. Would you agree that the human epidemiology studies that have examined benzene exposure and acute nonlymphocytic leukemias as a group have shown a strong association between benzene and ANLL?

MR. LEGHORN: Object to the form.

A. The epidemiology studies that have examined that have shown that there is a strong association between benzene exposure at levels that exceed 40 to 50 ppm-years in some studies, in some more than 200 ppm-years and increased risk of ANLL.

Q. And that association in the studies between benzene and ANLL has also been a consistent association. Would you agree?

MR. LEGHORN: Object to the form.

A. I'm not sure what you mean by consistent association.

Q. I mean it has been consistently found in a number of different cohorts and a number of case-control studies that there is an association between

ANLL as a group and benzene exposure.

MR. LEGHORN: Object to the form.

A. There is a body of well-done epidemiology that I believe supports the conclusion that benzene exposures greater than 40 to 50 ppm-years are causally associated with increased risk of ANLL.

Q. And those studies show or many of them show an increase in the risk with increased dose. Correct?

MR. LEGHORN: Object to the form.

A. I would not characterize it as many. It's actually a few have adequate exposure information to be responsive to your question.

Q. And taken as a whole, the body of literature, epidemiological literature looking at benzene exposure and ANLL shows a coherent picture. Would you agree?

MR. LEGHORN: Object to the form.

A. You would have to define what you mean by coherent. The previous series of questions I think were more consistent with the concept of replication rather than coherence.

Q. How do you interpret coherence as it relates to the set of considerations described by Sir Austin Bradford-Hill?

A. Let's use Hill's own description of it. He says "Coherence. On the other hand, the cause-and-effect interpretation of our data should not seriously conflict with the generally known facts of the natural history and biology of the disease." He goes on to say "Thus, in the discussion of lung cancer, the committee finds its association with cigarette smoking coherent with the temporal rise that has taken place in the two variables over the last generation and with the sex difference in mortality, features that might well apply in an occupational problem. The known urban/rural ratio of lung cancer mortality does not detract from coherence, nor the restriction of the effect to the lung."

And so Hill is actually talking about the overall pattern of the findings whereas I think your previous questions were talking about replication of findings. Clearly, with respect to benzene and APL, there's no coherent picture. There's none whatsoever. We don't have the characteristics such as Hill just described for smoking and lung cancer where you have time trends that lag the prevalence of smoking, where you have a sex ratio that reflects the difference in smoking patterns between men and

women, where you have an urban/rural difference. In other words, that's a coherent picture. We don't have that for benzene and APL.

Q. Do you have a coherent picture for benzene and ANLL?

A. I think we do. I might mention on that, one of the important elements in that coherent picture is the evidence that only the exposures within about ten to fifteen years of diagnosis convey risk. So not only do we have evidence of dose response where the risk is clearly increased at exposure levels above 40 to 50 ppm-years, but we also have evidence that distant past exposures don't matter. And that is really a picture that has become coherent in the past ten years.

MR. JENSEN: Counsel, I think that I have less than thirty minutes of questioning left. I don't know for sure, but that's what I think.

MR. LEGHORN: Do you want this on the record?

MR. JENSEN: Either way. I don't care. We're getting close to lunchtime. I think it should be the doctor's decision primarily what we do in terms of whether to take a lunch break or not. But if we were to take a short bathroom break now, I

could organize my thoughts and probably finish within thirty minutes. It's up to you.

THE WITNESS: I would prefer to finish without taking a lunch break.

MR. JENSEN: All right. Let's take a very short break now.

(In recess 11:43 a.m. to 11:53 a.m.)

BY MR. JENSEN:

Q. Dr. Garabrant, is it true that for purposes of your opinion in this case, you have not done any review of the literature relating to the issue of the extent to which topoisomerase inhibitors can and do cause APL?

A. No, actually I have looked at some of that literature.

Q. But you are not offering any opinion on that subject. Is that correct?

A. That's correct. It is my understanding that Dr. Pyatt is addressing that issue.

Q. And you are not offering any opinion on the subject of the extent to which benzene exposure inhibits topoisomerase II. Is that correct?

MR. LEGHORN: Object to the form.

A. I have no intention of offering opinions regarding the extent to which benzene inhibits

topoisomerase II. I have not been asked to do that.

Q. I have just put an exhibit sticker, Exhibit 4, on a collection of binder-clipped articles that were left for me at my hotel when I arrived last night. And I would ask you to take a quick look, Doctor, and see if you recognize those articles.

A. (Pause) Yes.

Q. Did you recently identify those articles as articles that you wished to rely on for purposes of your opinions in this case?

A. I believe these are articles I assembled since submitting my report on November 19, 2008, although -- Let me restate that. These are articles I have reviewed since submitting my report in November of 2008, although some of them are already cited in my report and I had reviewed them prior to submitting my report in addition. I mean, I don't know how to answer these things I recently accumulated. Some of them I've had for years; some of them I've cited in my report; some of them I re-reviewed; some of them were new since submitting my report.

Q. My understanding from counsel is that you have recently been out of the country. Is that

correct?

A. Yes.

Q. And after you got back from your trip, you identified the set of articles that have been marked as Exhibit 4 as materials that you wished to rely on to defense counsel in this case. Is that correct?

A. I'm not sure that's exactly correct. These are articles for which I provided defense counsel with copies just yesterday. Some of them are cited in my report of November 19 and I assume that everybody has had copies of them since November or had copies prior to that. Some of them are articles that I looked up and read in response to Dr. Smith's supplemental declaration. So it's a combination of factors. The common theme is that I gave copies of these electronically to Mr. Leghorn yesterday. So some of them are old, some are new, some are in response to Dr. Smith's work, some are ones that I had reread looking now at some new aspect of them.

Q. Okay, thank you.

MR. JENSEN: And just for the record, to the extent that the articles in Exhibit 4 include materials that were previously referenced in Dr. Garabrant's original report, we certainly don't

have any objection to his reliance on them. To the extent that they're new, we do have an objection. That can be resolved however it will be resolved. Thank you.

BY MR. JENSEN:

Q. Dr. Garabrant, who compiles for you your list of legal testimony as reflected by Exhibit 1?

A. I do.

Q. You do. How do you do it?

A. I try to keep track of all the times I have been deposed or testified in court.

Q. And the reason I ask is because I'm aware of at least one area or one instance of testimony that doesn't seem to be reflected, which is trial testimony you gave in the case of Turner versus Chevron. You've got your deposition testimony reflected but no trial testimony.

A. If I've omitted it, it isn't by intent. That list, I believe, reflects that that was prepared on November 18. I don't remember when I testified in Turner, whether it was just before that or just after that. It was sometime last fall, so I may have missed it or it may have been brand-new; I don't know.

Q. Does anyone besides yourself check the

accuracy of the list?

A. No.

Q. If you will turn with me to Dr. Cranor's report of October 9 at page 10, there is a subparagraph iii in the middle of page 10 and the third sentence of that paragraph says "As both medical and legal commentators put the point, 'In the final analysis, assessment of evidence and causal inferences depend on accumulating all potentially relevant evidence and making a subjective judgment about the strength of the evidence'." Do you agree with that statement?

MR. LEGHORN: Object to the form.

A. I would have to go back and read reference 39, which is footnoted at the bottom Kassirer & Cecil, Annals of Internal Medicine, before I would comment on what Dr. Cranor is concluding there.

Q. Do you have an opinion as to whether the following sentence after that sentence is true, which says "When professional judgment is so central to the drawing of inferences, professionals may disagree at various stages of reasoning in an inference to the best explanation, and thus may have disagreements about their overall view of the scientific conclusions"?

A. Well, I mean, I think what Dr. Cranor is saying there is nothing more than people can disagree on their view of what a body of evidence says. So I don't think there's any content to that statement. We know that people can disagree, and of course what we try to do is to explore why they disagree and try to uncover whether they have looked at all of the evidence, whether they have considered it properly, whether they have made their calculations properly, whether they have followed the rules of science that are widely accepted and so on.

So I don't think there's much content to Dr. Cranor's sentence. People can disagree.

Q. Outside the context of litigation, scientists disagree with one another about scientific propositions all the time. Is that true?

MR. LEGHORN: Object to the form.

A. The essence of the scientific method is based on the idea that every scientist has a responsibility to be skeptical of everyone else's work and to try to refute it. That's what we do as scientists, and that's not limited to medicine or epidemiology or physics or biology. That's part of the method. And when we can refute other people's

conclusions with evidence, then their conclusions should not be trusted as reliable.

Q. Well, oftentimes scientists have competing inferences and competing conclusions based on the same evidence. Isn't that true?

MR. LEGHORN: Object to the form.

A. I would have to say no because of your use of the word "often." Largely scientists live in a world where we agree to the vast body of evidence and disagree only around the fringes. Once in a while that's not true. As Cranor points out, Newton's laws of motion were widely accepted until Einstein came along and showed that at very high velocities, newtonian physics don't really -- aren't supported by real evidence, by data or by theory. But largely we live in a world where bridges don't fall down; where when you turn your furnace on it heats your house; where when you hit the brakes in your car, it stops; where when you have a blood test done, the results mean what we all agree they mean. The methods of science have turned out to provide an extraordinarily broad and reliable body of evidence that has allowed mankind to move forward and to make great progress in almost every realm of life.

And so when you say we often disagree, my

answer is no. Overwhelmingly we agree. It's only around the fringes of discovery where the pattern of evidence is unclear that we disagree. And that is of course what is going on in this case. Is there evidence that benzene causes APL? And the answer is: not nearly enough to conclude that there is. And as we've discussed, Dr. Smith has simply looked at the epidemiology improperly and failed to consider the epidemiology that is directly relevant to his opinions and that is a direct test of his hypothesis and doesn't support it.

MR. JENSEN: I will let you close with your closing argument. That's all the questions I have.

MR. LEGHORN: Thank you.

(Deposition concluded at 12:10 p.m.)

COURT REPORTER'S CERTIFICATE

I, J. Edward Varallo, RMR, CRR, Registered Professional Reporter and Notary Public in the Commonwealth of Massachusetts (my commission expires 12/24/2015), hereby certify that the deposition of David H. Garabrant, M.D., M.P.H. taken on February 18, 2009, in the matter of Brian K. Milward and Linda J. Milward v. Acuity Specialty Products Group, Inc., et al. was recorded by me stenographically and transcribed; that before being sworn by me, the deponent provided satisfactory evidence of identification as required by Executive Order 455 (03-13) of the Governor.

I certify that the deposition transcript produced by me is true and accurate to the best of my ability.

I certify further that I am not counsel, attorney, or relative of any party litigant, and have no interest, financial or otherwise, in the outcome of this suit.

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DATED: 2/25/2009 J. Edward Varallo

WITNESS: David H. Garabrant, M.D., M.P.H.
DATE: February 18, 2009
CASE: Brian K. Milward and Linda J. Milward v. Acuity Specialty Products Group, Inc., et al.

DISTRIBUTION TO COUNSEL The original signature page/errata sheet was sent to Joseph J. Leghorn, Esq., to obtain signature from the deponent. When signed, please send original to Steve Baughman Jensen, Esq., who will supply a copy of the signed errata sheet to other counsel present at the deposition.

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SIGN AND DATE THE ERRATA SHEET and return it, along with the transcript, to your counsel.