

NO. B-176,114

|                           |                            |
|---------------------------|----------------------------|
| RICHARD E. NOLEN          | * IN THE DISTRICT COURT OF |
| AND NITA NOLEN            | *                          |
|                           | *                          |
| VS.                       | * JEFFERSON COUNTY, TEXAS  |
|                           | *                          |
| E.I. DU PONT DE NEMOURS & | *                          |
| COMPANY, ET AL            | * 60TH JUDICIAL DISTRICT   |

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ORAL AND VIDEO DEPOSITION OF  
DR. RICHARD IRONS  
FEBRUARY 4, 2010

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ORAL AND VIDEO DEPOSITION OF DR. RICHARD IRONS, produced as a witness duly sworn by me at the instance of the Plaintiff, taken in the above-styled and numbered cause on February 4, 2010, from 10:10 a.m. to 1:24 p.m., before STACY AMY BAKLIK, CSR, Certified Shorthand Reporter No. 2680 in and for the State of Texas, at the Hotel Boulderado, 2115 13th Street, Boulder, Colorado, pursuant to the Texas Rules of Civil Procedure and the provisions stated on the record or attached therein.

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APPEARANCES

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ALSO PRESENT:

Complete Litigation Support  
Videographer

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1 THE COURT REPORTER: What are the agreements?

2 MS. PARKS: By the Rules.

3 DR. RICHARD IRONS,

4 having been first duly sworn to testify the truth, the whole  
5 truth, and nothing but the truth, testified as follows:

6 (10:10)

7 EXAMINATION

8 BY MS. PARKS:

9 Q. Good morning, sir.

10 A. Good morning.

11 Q. Would you state your full name for the record.

12 A. Richard D. Irons.

13 Q. And Dr. Irons, what is your business address?

14 A. I have two. One is Boulder, Colorado; and the  
15 other is Shanghai, China.

16 Q. In the Boulder, Colorado, area, what is the actual  
17 address of your office?

18 A. We use a mailing address, and we have a separate  
19 office address.

20 Q. Okay. What is the mailing address?

21 A. Mailing address is 4800 Baseline Road, Colorado.

22 Q. How long have you had offices in Boulder?

23 A. Since 2007.

24 Q. How long have you had offices in China?

25 A. In one form or another, since 2001.

1 Q. Dr. Irons, you understand today that I'm here, and  
2 I've introduced myself right before we started. My name is  
3 D'Juana Parks. I represent Mr. Nolen, Richard Nolen, and his  
4 wife, Nita Nolen, in an action we have filed against several  
5 oil companies and also a company called Univar alleging that  
6 his exposures to benzene and the products at those facilities  
7 was a cause of his myelodysplastic syndrome. Do you  
8 understand that I'm here to talk to you about your opinions  
9 that you've given in this case?

10 A. Yes.

11 Q. Prior to your deposition today, we sent a notice  
12 for your deposition, and attached to that was a subpoena  
13 duces tecum. I have represented to counsel, Mr. Scott, today  
14 that you received a prior notice but it actually had the  
15 wrong name on it. It wasn't Richard Nolen. That's been  
16 changed on this notice that I'm going to mark as  
17 Exhibit No. 1 to your deposition. Have you seen the prior  
18 notice which contained the same subpoena with the one  
19 exception that the name Richard Nolen was John Thompson on  
20 that notice?

21 A. I believe I saw it for the first time this morning.

22 (AT THIS TIME, DOCUMENT WAS MARKED FOR  
23 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 1.)

24 Q. And did you just see the -- the John Thompson  
25 notice this morning?

1       A.    Yes.

2       Q.    When you looked through the notice and the  
3 subpoena, were there areas that you recall that you did not  
4 provide the documents requested in the subpoena?

5               MR. SCOTT: D'Juana, can I just jump in here?  
6 Apparently my office is filing some objections to the notice  
7 although in my review I didn't think there were very many  
8 things, not so much in the way of objection, but we have had  
9 a practice in this case and others with your firm that the  
10 experts do not bring textbooks and large volumes of things  
11 which are clearly requested by my subpoenas and yours. So,  
12 he has not done that. And there is one Paragraph 12 that  
13 asks for payments from the defendant's counsel, and it's not  
14 limited to the Nolen case. So, there may be consulting  
15 relationships in all of that that you-all would assert under  
16 similar circumstances as well as we would. So, you can  
17 question him about those things, but I know he's not brought  
18 any of those. In fact, I'm not positive that's brought  
19 billing records on this file. He may have.

20       Q.    Have you, in fact, brought billing records,  
21 Dr. Irons?

22       A.    Yes, I have.

23       Q.    Let me go ahead, while we are at it, you have a  
24 notebook in front of you, a black notebook in front of you.

25       A.    Yes.

1 Q. And you have a small manilla folder?

2 A. Yes.

3 Q. You also have another black notebook that I see.

4 Are those the two notebooks that you have that contain  
5 literature or whatever you are going to rely on in the  
6 opinions that you are giving today with the exception of  
7 textbooks?

8 A. Yes.

9 Q. All right. Would you just generally describe what  
10 is contained within each of the black notebooks?

11 A. The black notebooks contain the references that I  
12 cite in my report in this case as well as, I believe, a  
13 couple of other references that I brought with me this  
14 morning. That's basically what is included in the  
15 notebooks.

16 Q. Is that what is included in both of the  
17 notebooks?

18 A. Yes. It's just too big to conveniently put in one  
19 binder.

20 Q. Are they separated out with any particular manner,  
21 or are they just specifically all the references that you've  
22 relied upon?

23 A. It's references I relied upon, and they are in  
24 order of citation of discussion in my report and it just  
25 continues from the end of the first notebook into the

1 second.

2 Q. All right. We are going to mark the notebooks as  
3 2a and 2b just to show that you've produced them in two  
4 different notebooks. 2a is going to be the larger notebook.  
5 2b will be the smaller.

6 Dr. Irons, the court reporter is going to be making  
7 a copy of all of the references that you used. Is it all  
8 right with you if we mark it on the outside of the notebook,  
9 put the sticker there?

10 A. Yes.

11 Q. I'm going to mark 2a as your big one here and 2b as  
12 your smaller one.

13 (AT THIS TIME, DOCUMENTS WERE MARKED FOR  
14 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NOS. 2a and 2b.)

15 Q. You've also brought a manila folder that has some  
16 information or documents in it. Can you tell us what is  
17 included in the manila folder?

18 A. The manila folder is my file in this case. It  
19 includes items that I believe are responsive to some of the  
20 items in the subpoena duces tecum. It contains my CV, my  
21 summary of Mr. Nolen's history, a list of recent testimony  
22 that I've given in deposition.

23 Q. Why don't we mark your CV as Exhibit No. 3.

24 A. Okay.

25 (AT THIS TIME, DOCUMENT WAS MARKED FOR

1 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 3.)

2 Q. Let's mark your listing of previous depositions as  
3 Exhibit No. 4.

4 (AT THIS TIME, DOCUMENT WAS MARKED FOR  
5 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 4.)

6 Q. Is this a listing of all depositions you've given  
7 or deposition and trial testimony that you've given?

8 A. Both over the last five years.

9 Q. And does it include a complete listing of all  
10 depositions and/or trials that you've testified in over the  
11 last five years?

12 A. I believe so.

13 Q. And by the looks of it, it appears that you've only  
14 testified at one trial in San Francisco. That was Shelby  
15 versus ExxonMobil; is that correct?

16 A. I believe so.

17 Q. And that was in 2008?

18 A. Yes.

19 Q. Have you given any depositions in 2009?

20 A. I don't believe so.

21 Q. And is this the first deposition that you've given  
22 in 2010?

23 A. Yes.

24 Q. We are going to attach as Exhibit No. 5 your  
25 billing. Is that the billing records that you brought?

1       A.    Yes.

2               (AT THIS TIME, DOCUMENT WAS MARKED FOR  
3 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 5.)

4       Q.    What are you charging, Dr. Irons, for your work in  
5 this case?

6       A.    I charge \$600 an hour for my time. The company has  
7 different rates for different services. My professional  
8 services bill out at \$600 an hour.

9       Q.    Is that a straight \$600 for you testifying at  
10 deposition or at trial?

11       A.    Preparation, basically anything, anything that I  
12 do.

13       Q.    I also see on here there is something that says  
14 professional services, 22.5 hours at \$150. Why is that  
15 different from the \$600?

16       A.    That doesn't refer to me. That refers to my staff,  
17 and they bill out at different rates.

18       Q.    What are the names of the staff members who have  
19 provided 22.5 hours work on the Richard Nolen case?

20       A.    That would be Dr. Patrick Kerzic, K-e-r-z-i-c.

21       Q.    All right. And who else?

22       A.    If it's billed out at 150 an hour, that would be  
23 him.

24       Q.    Okay. Does Dr. Kerzic work in Boulder or in  
25 China?

- 1       A.    China.
- 2       Q.    Is Dr. Kerzic an American?
- 3       A.    Yes.
- 4       Q.    And he is a doctor.  Is he a medical doctor?
- 5       A.    He is a Ph.D. toxicologist.
- 6       Q.    Where did he get his degree, if you know?
- 7       A.    University of Colorado.
- 8       Q.    And how long has he had his degree in toxicology?
- 9       A.    Approximately five years.
- 10      Q.    Did he study under you at the University of
- 11 Colorado?
- 12      A.    Yes, he did.
- 13      Q.    And were you his professor in different courses?
- 14      A.    Yes.
- 15      Q.    How long has he been working for you?
- 16      A.    He's been working with me since 2000 -- I believe
- 17 2002.
- 18      Q.    Has all of the work he has performed for you been
- 19 done in China?
- 20      A.    Yes.
- 21      Q.    What specifically did you ask Dr. Kerzic to do in
- 22 the Richard Nolen case?
- 23      A.    I asked him to compile some references, to do
- 24 specific searches for individual papers, to do some summaries
- 25 of information from various records.

1 Q. When we look at the notebooks which are attached as  
2 Exhibit No. 2a and 2b, would you be able to tell me which  
3 references you obtained versus the references Dr. Kerzic  
4 obtained for you?

5 A. No.

6 Q. My question would also be in 2a and 2b, would  
7 Dr. Kerzic have obtained all of those references, or did you  
8 obtain some of them?

9 A. Obtained some of them. He obtained some of them.

10 Q. Would you be able to give me any idea of a  
11 percentage of the references that you obtained versus those  
12 that Dr. Kerzic obtained?

13 A. He spent more time searching for specific articles,  
14 retrieving articles, than I did, quite a bit more. Most of  
15 the articles that I requested were specific. As I recall, I  
16 also asked him to look for material that was not material I  
17 specifically requested, also to obtain articles cited by  
18 other experts in this case.

19 Q. By other experts, do you mean plaintiff experts or  
20 defendant experts?

21 A. Certainly plaintiff's, probably both.

22 Q. When you asked him to do a specific search, what  
23 did you ask him to look for?

24 A. Usually a specific paper.

25 Q. Okay. You gave him the name of a paper or the

1 author?

2       A.    Yes, and the author, year, whatever information I  
3 could recall.

4       Q.    Did you do any independent search on a  
5 computer-based program or data base?

6       A.    No.

7       Q.    The articles that you obtained, were those articles  
8 already within your file either here in Colorado or in  
9 China?

10      A.    The vast majority of them, yes.

11      Q.    You also said today you brought with you two  
12 additional studies this morning that are not in the  
13 notebooks. What studies are those?

14      A.    I brought some papers that I didn't cite in my  
15 report that just deal with risk factors and myelodysplastic  
16 syndromes and --

17      Q.    When did you obtained those two additional articles  
18 or studies?

19      A.    In the last month.

20      Q.    And did you obtain them yourself or did you have  
21 Dr. Kerzic or were they provided to you by someone else, if  
22 you know?

23      A.    I think -- I don't know specifically where -- how I  
24 obtained these. I may have requested these from Mr. Scott  
25 and may have asked Dr. Kerzic.

1 Q. All right. Let me ask you this. Did you obtain  
2 those additional articles before or after you wrote your  
3 report in this case?

4 A. After.

5 Q. Did those articles that you obtained change or  
6 alter any of the opinions that you've given in this case?

7 A. No.

8 Q. I'm going to mark the articles separately so we'll  
9 know that they were given -- provided to you or you obtained  
10 them later.

11 (AT THIS TIME, DOCUMENT WAS MARKED FOR  
12 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 6.)

13 Q. The first article marked as Exhibit No. 6 is Risk  
14 Factor for Myelodysplastic Cases. It's a case-control study  
15 in Greece.

16 MR. SCOTT: Will you tell us the lead author,  
17 too?

18 Q. The lead author is Maria Dalamaga. Do you know  
19 Ms. Dalamaga?

20 A. No, I don't, haven't had the pleasure.

21 Q. Do you know whether or not this specific article  
22 looks at benzene as a risk factor specifically for  
23 myelodysplastic syndrome?

24 A. No.

25 Q. No, it does not?

1       A.    It does not.

2       Q.    Article -- the next article that we are marking as  
3 Exhibit No. 7 is entitled Tobacco Smoking and Risk of  
4 Hematological Malignancies in Adults.

5               (AT THIS TIME, DOCUMENT WAS MARKED FOR  
6 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 7.)

7       Q.    Again, this was an article you received after your  
8 report, correct?

9       A.    Yes.

10      Q.    Does this article look at benzene as a risk factor  
11 for hematological malignancies?

12      A.    No, it doesn't.

13               MR. SCOTT: I'm sorry. Do you mind telling us  
14 the title and the lead author?

15               MS. PARKS: I wish you wouldn't have asked me  
16 that. The lead author's name in this particular case is  
17 Paolo Pasqualetti.

18               MR. SCOTT: 1997 British Journal of  
19 Hematology.

20      A.    Pasqualetti.

21      Q.    All right. Do you know Mr. Pasqualetti?

22      A.    No, I don't.

23      Q.    Do you know where this was done, this article?

24      A.    I believe it's Canada.

25      Q.    I would think so.

1       A.    Yes.

2       Q.    All right.  And did this confirm some specific  
3 opinion you had in this case?  In other words, was this  
4 instrumental in confirming an opinion you've given here?

5       A.    These three articles -- there has been a great deal  
6 of literature that has associated the risk of smoking with  
7 hematopoietic neoplasms, MDS and acute myelogenous leukemia,  
8 AML, often indiscriminately.  And I requested these papers in  
9 order to confirm and to distinguish between the risk that's  
10 been associated in the literature between MDS and AML  
11 indiscriminately or nonspecifically with specific risks  
12 associated with MDS.

13      Q.    In the articles that you have and you brought with  
14 you, let me go ahead and mark Exhibit No. 8 which is entitled  
15 Smoking and Myelodysplastic Syndromes.  The first author is  
16 Jonas Bjork, B-j-o-r-k.

17                   (AT THIS TIME, DOCUMENT WAS MARKED FOR  
18 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 8.)

19      A.    Yes.

20      Q.    In any of these three articles does it discuss the  
21 risk of smoking and a specific subcategory of myelodysplastic  
22 syndrome?

23      A.    Can I take a look?

24      Q.    Absolutely.

25                   MR. SCOTT:  D'Juana while he's doing that,

1 those are -- I just happen to know that those are articles  
 2 that on January 22nd Dr. Irons asked -- apparently there is  
 3 some problem in getting some of these articles while he's in  
 4 China just because of their internet service or something.  
 5 And, so, he had asked one of my paralegals to get those three  
 6 articles, Pasqualetti, the '97, article Bjork, the 2000  
 7 Dalamaga, the 2002 article on January 22 and it looks like  
 8 she did provide them to him on January 25th. So, that's  
 9 where those came from.

10 Q. So, Dr. Irons, they were provided to you by  
 11 Mr. Scott's office, correct?

12 A. That's very likely.

13 MR. SCOTT: He asked for them by name and  
 14 author and journal.

15 Q. And if you asked them for them by name, Dr. Irons,  
 16 would you have asked for them or would it have been  
 17 Dr. Kerzic that requested those specific articles?

18 A. I would have done it.

19 Q. And was it in preparation of this report that you  
 20 decided you wanted to look at these articles?

21 A. To be perfectly forthcoming about it, I would have  
 22 asked for them anyway because I think that the question that  
 23 I raised, specific issue is one that I wanted to have  
 24 documentation of.

25 Q. Do you believe that smoking is a risk factor for

1 myelodysplastic syndrome?

2 A. Yes.

3 Q. What category, what subcategory of myelodysplastic  
4 syndrome?

5 A. In particular, smoking -- where, in fact, there has  
6 been subtype discrimination, I think that there is evidence  
7 to suggest a risk specifically for refractory anemia and  
8 refractory anemia with ring sideroblasts.

9 Q. Can you show me the article or articles that show  
10 that there is an increased risk of myelodysplastic syndrome,  
11 refractory anemia, caused by smoking?

12 A. I think maybe I can.

13 MR. SCOTT: While he's looking for that, there  
14 is one other subject I wanted to raise with you-all. We  
15 provided -- because he was in China we provided the medical  
16 records to him electronically in PDF form. He's never  
17 printed them off I learned this morning. So, he's got them  
18 electronically but not here.

19 MS. PARKS: I don't ask him to produce them  
20 again.

21 MR. SCOTT: He's got summaries, his notes from  
22 reviewing the articles. Since we had the subpoena out there,  
23 I wanted to be clear what was being produced and what  
24 wasn't.

25 Q. Okay. Dr. Irons, did you find one?

1       A.    Yes.

2       Q.    What is the title of the article?

3       A.    Risk Factors in Myelodysplastic Syndrome,  
4 Case-control Study.

5       Q.    It's a case-control study?

6       A.    Yes.

7       Q.    Would you mind pulling it out of there and letting  
8 me see it for just a moment, please, sir? Do you know what  
9 compound or chemical in cigarette smoke is thought to be  
10 causative for the myelodysplastic syndrome?

11      A.    I think that's completely unknown. There are  
12 numerous theories, including some of my own, but that's by no  
13 means an established --

14      Q.    What are your theories of the causative agent in  
15 cigarette smoke?

16      A.    There are a number of agents that are associated  
17 with hematopoietic toxicity. Benzene is in cigarette smoke.  
18 I personally don't think that the amount of benzene in  
19 cigarette smoke is sufficient to account for virtually any of  
20 the risks associated with cigarette smoke and MDS or other  
21 hematopoietic neoplasms. The substituted quinone catechols  
22 that are present in cigarette smoke independent of benzene  
23 dwarf the amount of benzene present. And, so, I think that  
24 it's more likely that other reactive quinones and catechols  
25 in cigarette smoke play a role.

1 Q. Can you tell me specifically which quinones those  
2 would be that play a significant --

3 A. Hydroquinone, catechol. There are a variety of  
4 other substituted quinones.

5 Q. Have you seen any studies on hydroquinone as being  
6 a risk factor for MDS in cigarette smoke?

7 A. Specifically, no.

8 Q. Have you seen any studies specifically stating that  
9 catechol is a contributing factor to MDS that's in cigarette  
10 smoke?

11 A. If you are talking about epidemiologic studies  
12 demonstrating an independent risk demonstrated through these  
13 compounds, no. If you look at the sum total of the  
14 literature that has studied the pathogenesis of hematopoietic  
15 diseases and potential role of compounds in cigarette smoke,  
16 there are numerous that have been based upon one hypothesis  
17 or another, have looked at potential mechanisms that --  
18 associated with these compounds. I've published a lot of  
19 those in the past, and there are numerous ones that at least  
20 based on that premise provide a rationale.

21 But with respect to independent epidemiology  
22 studies demonstrating specific risks associated with those  
23 compounds independently, there isn't any.

24 MS. PARKS: I'll object to everything after  
25 the word no, the first no.

1 MR. SCOTT: As nonresponsive?

2 MS. PARKS: Yeah. A little too responsive.

3 MR. SCOTT: I don't agree with you. I just  
4 want to be sure since that's only one of the objections we  
5 can make, I thought I'd be clear.

6 Q. Dr. Irons, in this particular -- oh, this is the  
7 Strom article. In the Strom article, do you know whether or  
8 not the subcategory of -- the supposed subcategory of MDS 5q  
9 was even included in this case-control study? And we are  
10 going to mark that as exhibit -- I don't want to pull it out  
11 of your book. So, what I'm going to do is -- it is behind  
12 your Index No. 40. So, we will identify the Strom article as  
13 2a, Index Tab 40.

14 MR. SCOTT: If there is a question out, I  
15 object to form of it.

16 Q. Dr. Irons, let me try to make counsel a little  
17 happier with the question. In there do they look  
18 specifically for 5q myelodysplastic syndrome as it relates to  
19 the causative agent?

20 A. They discuss it, but it's not clear to me whether  
21 or not, based upon their description of case assignment,  
22 whether or not they included it in their analysis or not.

23 Q. Do you have any explanation for why a subcategory,  
24 if it is indeed a subcategory, would not be included in an  
25 analysis of myelodysplastic if you are actually breaking it

1 out into subcategories?

2 A. It has to do -- it has to do with the change in the  
3 criteria for diagnosis of MDS and the different  
4 classification schemes that were in place at a given time.

5 Q. Pardon me. Go ahead.

6 A. In this particular case, because they were  
7 evaluating a series of cases that began before the adoption  
8 of the WHO 2001 diagnostic criteria, they were employing the  
9 old FAB criteria.

10 Q. Do you see any reason why they couldn't go back and  
11 employ the WHO 2001 criteria?

12 A. It would be very difficult to do that. They give a  
13 fairly good, concise description of the limitations in their  
14 methodology for classification.

15 Q. Is it your testimony that it would be impossible to  
16 go back and apply a different classification such as the WHO  
17 2001 to something -- and what is the date of that article,  
18 sir?

19 A. The date is 2005.

20 Q. 2005. Which is after the WHO 2001 classification  
21 was published, correct?

22 A. Yes, but the patients that they examined in this  
23 particular cohort were presented between 1999 and 2003.

24 Q. Which is also after the WHO 2001 classification,  
25 correct.

1       A.    Yes.

2                   MR. SCOTT:  Object to the form.  Parts of it  
3 are.

4       Q.    All right.

5       A.    You know, I think that the best thing I can do is  
6 read to you their description of why they did this.

7       Q.    Honestly, if you could just answer the question of  
8 they didn't do it.  That's all I want to know.

9       A.    For this particular series they did not do it.

10      Q.    Dr. Irons, we are probably -- and I'm probably the  
11 least fussy person that's going to ask you questions probably  
12 in your whole life.  But if you could just answer the  
13 questions -- it's going to make it lot longer.  If you need  
14 to explain it, that's fine.  Your counsel can go back later  
15 on.  But if there is something you need to explain, by all  
16 means do so.  But if you can answer my questions, just the  
17 question I'm asking, it will make this a little quicker.

18                   MR. SCOTT:  First, I'm not his counsel.  
19 Second, I'm Univar's counsel and I'm presenting him.  Second,  
20 I want to be sure that you are not instructing him to limit  
21 his answers and do anything but produce a complete and clear  
22 answer to the best of his ability.

23                   MS. PARKS:  Absolutely.  I just don't want to  
24 extra stuff, if possible.

25      Q.    Now speaking of which, Mr. Scott is not your

1 counsel, correct?

2 A. That's correct.

3 Q. You are working on behalf of Univar. Univar is  
4 paying you for your testimony here today. Is that correct?

5 A. That's correct.

6 Q. Are you also being paid by the entities that for  
7 lack of a better term I'm going to refer to as the Texaco  
8 entities?

9 A. As I sit here, I'm not certain.

10 Q. Let me just ask it this way. What is your  
11 understanding about the companies -- what companies have  
12 hired you to provide testimony in the Richard Nolen case?

13 A. I'm certain that I've been hired by Univar.

14 Q. And that's the only company you are certain of?

15 A. Yes.

16 Q. All right. Back to what we were speaking of. You  
17 were talking about smoking, and I asked you about a study  
18 specifically on refractory anemia. Do you have any specific  
19 epidemiological studies that reflect smoking as a risk factor  
20 for the subcategory refractory anemia with ring sideroblasts,  
21 I think you said?

22 A. I believe so, but it may take me awhile to find it.  
23 I'm not specifically -- as I sit here, I believe that there  
24 is a study on that, but I don't -- can't recall specifically  
25 which one it is.

1 Q. Dr. Irons, I'll give you maybe a break, you can  
2 look at that, but I believe you believe it is a study, one  
3 study, two studies, or do you know?

4 A. I don't recall specifically.

5 Q. I believe you stated that you believe that smoking  
6 is a risk factor for myelodysplastic syndrome, correct?

7 A. Yes.

8 Q. You've listed the two subcategories that you  
9 believe smoking is a risk factor for, correct?

10 A. Those specific categories I believe there is data  
11 that is relevant to this specific subtypes.

12 Q. And you know that we have the Strom study for the  
13 refractory anemia, and then you believe you may have another  
14 study for the refractory anemia with ring sideroblasts?

15 A. Actually, they are the same.

16 Q. They are the same, the Strom study?

17 A. Yeah.

18 Q. And, again, any other epidemiological reports?

19 A. I believe that there are.

20 Q. Do you have them with you today?

21 A. I believe so, but I have to -- I would have to  
22 spend some time to review them to look for that  
23 specifically.

24 Q. Did you put anything in your report about  
25 Mr. Nolen's smoking being a risk factor for his particular

1 myelodysplastic syndrome?

2 A. No, I did not.

3 Q. Do you believe that Mr. Nolen's myelodysplastic  
4 syndrome, that a cause of it was his smoking?

5 A. I believe that the epidemiologic literature does  
6 demonstrate a significant risk of smoking for the broad  
7 category of myelodysplastic syndromes. I think most of the  
8 studies do not resolve it into specific subtypes. The two  
9 that we've talked about or discussed this morning do provide  
10 evidence as it relates to specific subtypes. I am not aware  
11 specifically that there are studies demonstrating a selective  
12 risk associated with MDS 5q minus syndrome.

13 Q. Dr. Irons, do you agree that the overwhelming  
14 majority of epidemiological studies as it relates to MDS do  
15 not distinguish between the subcategories?

16 A. Oh, yes, absolutely.

17 Q. Do you believe that benzene is a risk factor for  
18 myelodysplastic syndrome?

19 A. Yes.

20 Q. How long have you held that opinion?

21 A. I've held that opinion for probably the better part  
22 of at least 15 years, and more specifically with respect to  
23 studies I've done demonstrating an epidemiologic association  
24 the last two years.

25 Q. What studies are you aware of that --

1 epidemiological studies that classify the myelodysplastic  
2 syndromes into separate subcategories?

3 A. Well, certainly our study.

4 Q. And when you say our study, for the members of the  
5 jury, what is the name of your study? We call it the  
6 Shanghai study, correct?

7 A. Yes.

8 Q. People in the general public?

9 A. Yes.

10 Q. But what is the true name of the study?

11 A. I'm looking to make sure I get the title right.

12 Integrating WHO 2001, 2008 Criteria for the Diagnosis of  
13 Myelodysplastic Syndrome, a Case-case Analysis of Benzene  
14 Exposure.

15 Q. And that study was published when?

16 A. It is -- it's in press. Its publication date is  
17 2009.

18 Q. When you say it's in press, what does that mean?

19 A. That means that it's been reviewed, accepted and is  
20 available online. It hasn't appeared in print.

21 Q. And when it appears in print, what publication will  
22 it be published in?

23 A. Chemico-Biological Interactions.

24 MR. SCOTT: Chemico, c-o, not chemical. You  
25 said chemico, but I was afraid everybody heard chemical.

1 Q. Chemico-Biological Interactions. And it's to be  
2 published this year, in 2010?

3 A. Yes.

4 Q. Are there any other epidemiological studies that  
5 you are aware of that distinguishes between subcategories of  
6 myelodysplastic syndrome as it relates to benzene exposure?

7 A. As it relates to benzene exposure?

8 Q. Yes.

9 A. Not specifically. There are -- there is at least  
10 one study that is consistent with but does not provide  
11 specific -- a specificity with respect to benzene exposure.

12 MS. PARKS: Object to everything after not  
13 specifically.

14 Q. Dr. Irons, do you dispute the diagnosis for  
15 Mr. Nolen?

16 A. If, in fact, the diagnosis is MDS 5q minus  
17 syndrome, no.

18 Q. Would you dispute the diagnosis if the diagnosis  
19 was myelodysplastic syndrome?

20 A. Well, myelodysplastic syndrome is a pleural.  
21 Certainly MDS 5q minus syndrome is one of the subtypes of  
22 myelodysplastic syndrome.

23 Q. What subtypes of myelodysplastic syndrome do you  
24 recognize? Name them for me.

25 A. Refractory anemia which has now been subsumed under

1 the category refractory cytopenia, unilineage dysplasia,  
2 refractory anemia with ring sideroblasts, refractory  
3 cytopenia multilineage dysplasia, RCMD, refractory anemia  
4 with excess blasts which is sometimes divided into two  
5 categories, RAEB 1, RAEB 2, refractory anemia or  
6 myelodysplastic syndrome unclassifiable, myelodysplastic  
7 syndrome 5q minus syndrome. There is also a separate  
8 category of MDS associated with therapy-related disease which  
9 is independently classified as TAML, TMDS.

10 Q. Do you also recognize childhood myelodysplastic  
11 syndrome as a separate subcategory?

12 A. That's correct, yes. It's a provisional category  
13 under the 2008 criteria.

14 Q. Of these subcategories which, if any, do you  
15 believe that benzene would be a risk factor for?

16 A. Well, certainly our studies demonstrate that  
17 myelodysplastic syndrome unclassifiable is a risk factor  
18 based upon the specific criteria that we've outlined in our  
19 studies. I believe that RCMD, refractory cytopenia with  
20 multilineage dysplasia, there is some potential risk for.  
21 Other subtypes in particular we have not been able to  
22 identify a significant excess.

23 Q. Have you identified any excess in any of the other  
24 categories? And let's start off -- I apologize, Dr. Irons.  
25 What do you consider to be a significant?

1       A.     Statistically significant.

2       Q.     And to you what is statistically significant? Did  
3 it have to be over 2.0?

4               MR. SCOTT: Object to the form of the  
5 question.

6       A.     Statistically significant in general -- as far as  
7 criteria for determining a -- the power of a study and the  
8 findings of a positive association requires that depending  
9 upon the statistical analysis that's used that the -- it  
10 meets 95 percent confidence interval. I don't believe that a  
11 relative risk of 2 is an absolute. Most epidemiologic  
12 studies that include a confidence interval that is  
13 significant are -- I think will demonstrate a relative risk  
14 of 2 or more, but that's not an absolute requirement. The  
15 important thing is that the confidence interval in the  
16 analysis basically does not include 1, that it's greater than  
17 1.

18       Q.     Have you ever had the opinion that a relative risk  
19 of over 1 would be statistically significant?

20       A.     Yes, and I think the most pressing example of that  
21 is cigarette smoking for which relative risks for many  
22 diseases do not exceed much greater than 1, 1.2, 1.5, but the  
23 numbers are so high that, in fact, there is statistically  
24 significant data to support it.

25       Q.     And by the numbers are so high, what do you mean by

1 that?

2 A. The power of the study is such that the confidence  
3 intervals -- and the confidence intervals are tight enough  
4 that, in fact, a relative risk of less than 2 is associated  
5 with a statistically significant.

6 Q. In other words, there is a whole lot of people in  
7 the study, correct, the numbers are so high?

8 A. Yes.

9 Q. Okay. What do you consider numbers high enough  
10 that you could have a relative risk of 1.123 that would be  
11 statistically significant?

12 A. There is no absolute way to answer that. It  
13 requires -- it requires an analysis of study design. Most of  
14 these studies involve meta-analyses where studies are  
15 combined which is a highly technical --

16 Q. The studies that you were talking about, the  
17 cigarette smoking where the relative risk is less than 2.0  
18 but you consider them statistically significant because the  
19 numbers are so high, how high were the numbers, how many  
20 people?

21 A. Why don't we take a look. With Bjork, this is a  
22 case-control study with 330 cases and 337 match controls.

23 Q. Do you consider that a large number?

24 MR. SCOTT: Object to the form.

25 A. This is actually a relatively small number, but the

1 odds ratio is, in fact -- it approaches 2 but it's not, it's  
2 1.8, and the confidence intervals are greater than 1 except  
3 for a couple of categories. Most of them are all greater  
4 than 1 So, the lowest value is greater than 1.

5 Q. All right. And really what I'm asking is, you told  
6 me there are 330 cases and 337, but you don't consider  
7 that --

8 A. This is -- this is a particularly powerful study  
9 for a small number.

10 Q. Small number. What I'm asking is the ones that  
11 there are a large number, what do you consider to be a large  
12 number?

13 A. Well, for example, the Pasqualetti study looked at  
14 1216 cases.

15 Q. Do you consider 1216 to be a large study?

16 MR. SCOTT: Object to the form.

17 A. It's a pretty good size study.

18 Q. Do you feel that the larger the study, the more  
19 powerful the study is in terms of being able to show relative  
20 risk?

21 MR. SCOTT: Object to the form.

22 A. In general the number of cases of disease in a  
23 study, size of a study, is an important factor for  
24 determining relative -- the reliability or the power to  
25 determine relative risk. Other issues are equally important

1 such as study design. You can have a large study that's not  
2 designed appropriately or, in fact, isn't designed  
3 specifically to answer the questions that you want to  
4 address. But in general the size with respect to the number  
5 of cases is important.

6 Q. Have you ever given an opinion that refractory  
7 anemia with excess blasts is benzene-related?

8 A. I'm sure I have.

9 Q. Is it your opinion today that benzene is a risk  
10 factor for the myelodysplastic syndrome that is known as  
11 refractory anemia with excess blasts?

12 A. I think if you -- I think if you look at the odds  
13 ratio in our study, the odds ratio is greater than 1, but the  
14 confidence interval does not include 1. So, there is a --  
15 there is a suggestion of a signal, but we do not have the  
16 power to see a significant difference with respect to  
17 refractory anemia.

18 Q. Pardon me. When you say you don't have the power,  
19 what do you mean by that?

20 A. That the size of the study -- certainly the power  
21 of the study cannot support the finding that there is an  
22 increased risk of refractory anemia with excess blasts  
23 associated with benzene.

24 Q. How much greater than 1 is the odds ratio for  
25 refractory anemia with excess blasts in your study?

1       A.    It was 1.4.

2       Q.    Do you consider 1.4, in your study to be  
3 statistically significant?

4       A.    No, not based upon the confidence interval.  The  
5 important factor is the confidence interval.

6       Q.    And what your confidence interval there?

7       A.    It was 0.19 to 11.1.

8       Q.    Did you review Richard Nolen's bone marrow  
9 slides?

10      A.    No, I did not.

11      Q.    Did you ask to review the bone marrow slides?

12      A.    No, I did not.

13      Q.    Did you rely upon any other defendant's expert in  
14 this case as far as their reading of the bone marrow slides?  
15 In other words, was there another expert for the defense that  
16 you are aware of that looked at the bone marrow slides?

17      A.    I don't recall whether Dr. Natelson reviewed the  
18 slides.  I did review Dr. Natelson's report.  I also reviewed  
19 the medical records provided to me and the pathology reports  
20 that were included in that, and that's the basis for my  
21 testimony in this case with respect to his disease.

22      Q.    Other than the two subcategories that we've  
23 mentioned here, those are the only two subcategories that you  
24 recognize or you feel that benzene is a risk factor for; is  
25 that correct?

1       A.   Based upon -- based upon our results, there is a  
2 significant excess of MDS unclassifiable, highly significant  
3 excess. There is unity with respect to refractory cytopenia  
4 with unilineage dysplasia, and for other subtypes we either  
5 have odds ratios less than 1 or nonsignificant.

6       Q.   And when you say your results, again, you are  
7 talking about the China study that you did in Shanghai?

8       A.   Yes, yes.

9       Q.   Can you point to any other studies that conclude  
10 that benzene is not a risk factor for certain subcategories  
11 of myelodysplastic syndromes?

12      A.   In general, I don't think any study -- you can't  
13 prove a negative. So, pointing to a study that says benzene  
14 is not a risk factor is basically not -- that's not something  
15 that as a scientist I can do.

16      Q.   So, in your own study would it be true that you are  
17 not going to give testimony that benzene is not a risk factor  
18 for Mr. Nolen's myelodysplastic 5q since you cannot prove a  
19 negative?

20               MR. SCOTT: Object to the form of the  
21 question.

22      A.   I am not going to say that it is not possible that  
23 benzene could be associated with the development of any MDS,  
24 including Mr. Nolen's. I am going to say that the evidence  
25 that supports a relationship between benzene and MDS is

1 confined to those types that we've been discussing this  
2 morning and certainly in our specific study a very clear  
3 association with the specific subtype and morphologic  
4 features.

5 Q. All right. I want to make sure I have your opinion  
6 very succinct. You are going to -- if I ask you at trial, if  
7 I say, Dr. Irons, can you say with probability that benzene  
8 was not a risk factor for Mr. Nolen's myelodysplastic  
9 syndrome, what are you going to tell me?

10 MR. SCOTT: Object to the form of the  
11 question.

12 A. If you ask me within reasonable scientific  
13 probability whether, in fact, benzene is a risk factor in  
14 Mr. Nolen's MDS, I'm going to say that it is not. If you ask  
15 me if I can say with certainty that there is no risk  
16 associated with the development of Mr. Nolen's disease and  
17 benzene, I can't say that.

18 Q. And when I ask you if it's based on scientific  
19 probability, you are going to say, all I can tell you is  
20 there are two groups that I can say are related to benzene,  
21 RCMD and myelodysplastic syndrome unclassified; is that true?

22 MR. SCOTT: Object to form.

23 A. I'm going to -- I can talk with respect -- I can  
24 opine with respect to what our study demonstrates in terms of  
25 the nature of that relationship between benzene and MDS

1 subtypes.

2 Q. So, my answer to that question would be yes, that's  
3 what you are going to tell me if I ask you?

4 MR. SCOTT: Object to the form of the  
5 question.

6 A. Could you repeat the question?

7 Q. Sure. If we are at trial and I sit there and I  
8 say, look, Dr. Irons, can you tell me within reasonable  
9 scientific probability the subclasses that you feel are  
10 related to benzene exposures, there are only two you are  
11 going to give me at trial; is that correct?

12 A. Yes.

13 Q. And those are based only on your study, Shanghai  
14 studies, correct?

15 A. That's correct.

16 Q. And if I say, Dr. Irons, based on the  
17 epidemiological data that you have seen, notwithstanding your  
18 study -- let's don't talk about your study -- have you seen  
19 epidemiological literature, scientific literature, that  
20 relates benzene exposures to myelodysplastic syndromes?

21 MR. SCOTT: Object to the form of the  
22 question.

23 A. That relates benzene exposures to myelodysplastic  
24 syndrome?

25 Q. Associates.

1       A.    Yes.

2       Q.    And is it just your opinion that you do not believe  
3 that it's related to other myelodysplastic syndromes as a  
4 whole?

5               MR. SCOTT:  Object to the form of the  
6 question.

7       Q.    In other words -- I guess, Dr. Irons, let me try to  
8 do it this way.  You don't believe you can have a  
9 myelodysplastic syndrome unless it's in one of these seven  
10 categories, correct?

11              MR. SCOTT:  Object to the form of the  
12 question.

13       Q.    You think every myelodysplastic syndrome can be put  
14 in all these categories, right?

15              MR. SCOTT:  Same objection.

16       A.    I wouldn't -- I wouldn't -- I wouldn't hazard that  
17 opinion.  The biology of MDS has been changing dramatically  
18 over the past ten years.  Over the past 20 years it's emerged  
19 from being nonexistent to being quite sophisticated.  It's  
20 changing since -- between 2001 and 2008 there have been  
21 generally agreed upon changes in guidelines and diagnostics.  
22 As we go forward into the future, I would not be at all  
23 surprised and, in fact, I expect we are going to see  
24 continuing changes and increased resolution and  
25 discrimination of MDS's.

1 Q. And by that do you mean you think you are going to  
2 have some more categories?

3 A. Yes.

4 Q. And are you continuing your work in Shanghai to see  
5 if benzene is going to be associated with some new  
6 categories?

7 A. No.

8 Q. Is your work in Shanghai finished?

9 A. My work with benzene in Shanghai is finished.

10 Q. Are you working with different chemicals now?

11 A. No longer -- at the present time I'm not doing any  
12 chemical studies, but I'm continuing to study MDS.

13 Q. And who is funding your continued studies on MDS?

14 A. Right now our funding comes from a variety of  
15 different sources, fee-for-service diagnostics, clinical  
16 trial work and consulting. None of it is focused on specific  
17 agents or etiologies in MDS.

18 Q. This fee-for-service diagnostics -- I'm sorry. I'm  
19 going to turn this off. Give me just a second. This  
20 fee-for-service diagnostics, is that a company?

21 MR. SCOTT: Object to the form.

22 Q. What is fee-for-service diagnostics?

23 A. It's simply diagnosis of hematopoietic and lymphoid  
24 diseases. The center that I run in Shanghai serves the  
25 Shanghai clinical community providing diagnostic services for

1 hematopoietic and lymphoid diseases.

2 Q. I guess what I really want to know is the center  
3 for services in Shanghai, who is paying for it?

4 A. The folks.

5 Q. Is it the same -- who?

6 A. The folks who are -- the clinicians and the  
7 patients that request the -- refer cases to us.

8 Q. Okay. Let me make sure I get that right. You are  
9 treating patients now specifically for myelodysplastic  
10 syndrome, correct?

11 MR. SCOTT: Object to the form of the  
12 question.

13 A. No. We are providing diagnostic services in  
14 esoteric diagnosis, hematopathology, cytogenetics, flow  
15 cytometry, morphology.

16 Q. Only for myelodysplastic syndrome?

17 A. For all hematopoietic and lymphoid diseases.

18 MR. SCOTT: D'Juana, I know you are trying to  
19 move quickly, but you are cutting him off.

20 MS. PARKS: I have a tendency to do that  
21 because I kind of, again, think the answers ought to be a  
22 little shorter, but I will be quiet.

23 MR. SCOTT: I object to the side bar. Let's  
24 let him answer fully and accurately the best he can the  
25 questions you ask.

1 Q. Go ahead, Dr. Irons.

2 A. We provide -- we provide routine diagnostic  
3 services for hospitals in China.

4 Q. Who pays your check?

5 A. Hospitals and patients.

6 Q. The patients are actually paying themselves now?

7 A. In China, patients pay most of the bill.

8 Q. When you did the Shanghai study in China, who  
9 funded the study?

10 A. The Benzene Health Research Consortium.

11 Q. I'm going to ask you some more about that in just a  
12 few minutes. It's called the Benzene Health Research  
13 Consortium?

14 A. It was, yes.

15 Q. We'll go back to that in just a few minutes. You  
16 told me about the categories that you feel benzene is a risk  
17 factor in, and I asked you in the past have you testified  
18 that refractory anemia with excess blasts, is benzene a risk  
19 factor. Has your opinion changed as it relates to refractory  
20 anemia with excess blasts?

21 A. Yes and no. And I have to answer it that way. I  
22 have to explain my answer in this case.

23 Q. Is it based on your study?

24 A. It's based partly on my study. It's also the  
25 biology associated with refractory anemia with excess blasts

1 which is not by origin specifically a necessarily a discreet  
2 form of MDS from refractory anemia, from refractory cytopenia  
3 with multilineage dysplasia, from refractory anemia with ring  
4 sideroblasts. Refractory anemia with excess blasts, in fact,  
5 can develop, evolve, from any of those other subtypes.

6 Q. Can it evolve from.

7 MR. BROWN: Object to responsiveness.

8 Q. Can it evolve from myelodysplastic syndrome  
9 unclassifiable?

10 A. Yes.

11 Q. Can it evolve from refractory cytopenia with  
12 multilineage dysplasia?

13 A. Yes.

14 Q. Had you finished your explanation?

15 A. Yes.

16 Q. Okay. If you have refractory anemia with excess  
17 blasts, are you able to determine whether or not it evolved  
18 from myelodysplastic syndrome unclassifiable?

19 A. It would depend on two things. One, previous  
20 medical history and/or pathology; and, two, upon the  
21 characteristics that present at the time that RAEB is  
22 diagnosed. To varying degrees it could be -- it could be  
23 possible to infer that it began as one of the other subtypes  
24 or the medical and pathology records will clearly demonstrate  
25 that it did.

1 Q. If you have a refractory anemia with excess blasts  
2 that you feel evolved from one of the two categories that you  
3 feel benzene is a risk factor for, if it evolved into  
4 refractory anemia with excess blasts, do you then change your  
5 opinion and say I do not believe benzene could be a risk  
6 factor for this?

7 MR. SCOTT: Object to the form.

8 A. The refractory anemia with excess blasts is not an  
9 independent category of MDS. It represents a stage in  
10 progression of MDS, and it relates to the number of blasts  
11 that are present which is in the definition. Technically any  
12 MDS subtype can evolve into refractory anemia with excess  
13 blasts. With respect to the 650 cases that we diagnosed,  
14 that were part of our study, if we look at exposure to  
15 benzene and the relationship between benzene exposure and the  
16 frequency of the diagnosis of refractory anemia with excess  
17 blasts, it was not statistically significant. There was no  
18 excess associated with benzene exposure. That does not mean  
19 benzene-induced MDS cannot become RAEB.

20 MS. PARKS: I'll object as nonresponsive to  
21 the question.

22 Q. When you say refractory anemia with excess blasts  
23 is not an independent category, do you now believe that it is  
24 not a subcategory of the myelodysplastic syndromes?

25 A. No, most certainly is.

1                   MR. SCOTT: I object to the form of the  
2 question because I don't think you stated what he said  
3 correctly.

4           Q.    Dr. Irons, on this WHO hand-out or chapter that  
5 Mr. Scott presented at, I believe, Dr. Infante's deposition,  
6 it's one chapter out of this, and have you reviewed this WHO  
7 classification system for myelodysplastic syndromes?

8           A.    Oh, yes.

9           Q.    And do you consider each of these on the first  
10 page, which we will go ahead and mark -- you probably have a  
11 copy with you, don't you, Dr. Irons?

12          A.    Yes.

13          Q.    We may have to mark your copy because I'm not  
14 seeing my extra one.

15                   MR. SCOTT: I brought one that I think we can  
16 mark instead.

17                   MS. PARKS: I hate to take yours out.

18                   MR. SCOTT: I don't care. I've got more.

19          A.    I think I can clarify this if you'll allow me to.

20          Q.    I certainly will. We are going to mark this as  
21 Exhibit No. 9.

22                   (AT THIS TIME, DOCUMENT WAS MARKED FOR  
23 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 9.)

24                   MR. SCOTT: And Exhibit No. 9 is Chapter 5 of  
25 2008 World Health Organization classification of tumors of

1 hematopoietic and lymphoid tissues.

2 MS. PARKS: Correct.

3 A. I'm going to hand this back to you. This is just  
4 the second page.

5 Q. All right.

6 A. And this is talking -- I'm using Table 5.01 to  
7 illustrate.

8 Q. All right. And if we'll look down there, for the  
9 members of the jury, that is actually Page 89 of this  
10 document; is that correct?

11 A. Yes, it is.

12 Q. All right. Go ahead. I'm with you.

13 A. So, it lists seven different categories for MDS on  
14 this particular table.

15 Q. Yes, sir.

16 A. RCUD, RARS, RCMD, MDSU and MDS associated with  
17 deletion of 5q minus are independent MDS subcategories with  
18 respect to the features and clinical characteristics of those  
19 diseases.

20 Q. Says who?

21 A. Says the WHO.

22 Q. And why does the WHO list additional categories in  
23 this chart on Page 89?

24 A. That's what I'm going to try to tell you.

25 Q. Okay.

1       A.    The definition of RAEB 1 is that there are -- that  
2 there are 5 to 9 -- you'll see in there 5 to 9 percent blasts  
3 in the bone marrow, as an example. And for RAEB 2, there are  
4 10 to 19 percent blasts in the bone marrow. If you look at  
5 the other categories, there are less than 5 percent blasts in  
6 the bone marrow. A case that presents with refractory  
7 cytopenia with unilineage dysplasia, RCUD, that has less than  
8 5 percent blasts, if that case progresses and has in the  
9 number -- the frequency of blast in the bone marrow exceeds  
10 5, between 5 and 9 percent, then that case will no longer be  
11 classified as RCUD. It be classified as RAEB 1. If that  
12 progresses and the frequency of blasts in the bone marrow  
13 rises to between 10 and 19 percent, then it will be  
14 classified as RAEB 2. So, an MDS case could present without  
15 any previous clinical history with an RAEB, but the diagnosis  
16 of RAEB 1 and 2 does not exclude that the patient presented  
17 with one of the other subtypes.

18       Q.    My question is very simple. How many subtypes do  
19 you consider to be in myelodysplastic syndromes? How many?  
20 Five, seven?

21               MR. SCOTT: Object to the form.

22       Q.    Do they overlap?

23       A.    Seven, eight. There are provisional categories  
24 that have been suggested. There are at least eight, and  
25 there are overlapping characteristics.

1 Q. And you did your study in China where you had,  
2 what, 640 cases of benzene --

3 A. 650, something like that.

4 Q. And you looked at only the WHO classifications as  
5 you related the 640 to see which ones had relative risks?

6 A. We classified all hematopoietic diseases which  
7 includes basically all of the WHO, both 2001 and 2008  
8 classifications.

9 Q. Did you have results for each of these that are  
10 listed on Page 89?

11 A. Yes.

12 Q. Okay. And of the categories listed on Page 89  
13 which there are, what, seven of them, seven categories, you  
14 found two that you felt showed that benzene was a risk factor  
15 for, correct?

16 A. Again, with respect to demonstration of a  
17 statistically significant excess, yes.

18 Q. Do you have Page 88 of this?

19 A. Yes.

20 Q. Okay. It's on the back. On Page 88, is that an  
21 overview of all myelodysplastic syndromes, overview?

22 A. It's an overview of myelodysplastic syndromes as  
23 classified by WHO at the particular time that the  
24 classification was published. This is the -- this is the  
25 primary body of data that supports the guidance for

1 classification and diagnosis of these diseases. It does not  
2 exclude other potential myelodysplastic syndromes or  
3 conditions. And, in fact, if you read elsewhere in the  
4 entire WHO classification tome, it will refer to other  
5 potential experimental and/or provisional classifications, at  
6 least one of which I know involves an MDS that it doesn't  
7 include in the overview.

8 Q. On Page 88, is this an overview of myelodysplastic  
9 syndromes as created by the WHO?

10 A. Yes, it is.

11 Q. Does that include all the classifications that are  
12 listed on Page 89?

13 A. It includes all the classifications listed on Page  
14 89, yes.

15 Q. Under the etiology on Page 88 for all of the  
16 myelodysplastic syndromes, in the third -- I'm still on Page  
17 88 -- in the third column under etiology, do you see where it  
18 says possible etiologies for primary MDS include benzene  
19 exposure at levels well above the minimum allowed by most  
20 governmental agencies.

21 A. Yes.

22 Q. Do you agree or disagree with that statement?

23 A. I agree with it.

24 Q. You also believe or have provided opinions that you  
25 feel there are subcategories of AML as well?

1 A. Oh, yes.

2 Q. How many subcategories of AML do you recognize?

3 A. There is a large number. I can -- again, we can go  
4 through the WHO classification if you wish.

5 Q. And do you -- is that the WHO 2008  
6 classification?

7 A. It's the most recent, yes.

8 Q. How many of those subcategories do you have an  
9 opinion for which benzene is a risk factor for? That's a bad  
10 question. Hold on. Let me strike that.

11 Of the subcategories of AML, which ones do you feel  
12 benzene is a risk factor for?

13 MR. SCOTT: Object to the form of the  
14 question.

15 Q. If any.

16 MR. SCOTT: Same objection.

17 A. Again, the results of Shanghai health study provide  
18 evidence to suggest that there is an increased risk that's  
19 associated with AML with recurrent genetic abnormalities,  
20 specifically translocation between chromosome 8 and 12 -- I  
21 mean 8 and 22.

22 Q. 8 and 22?

23 A. 8 and 21. Sorry.

24 Q. 8 and 21?

25 A. Yes.

1 Q. Any others other than the translocation of  
2 chromosome 8 and 21?

3 A. That was the only one that shows statistically  
4 significant.

5 Q. Again, that is in your study, correct?

6 A. Yes.

7 Q. So, is it your opinion that the only AML you would  
8 consider to be benzene-related would be if there was a  
9 translocation of the 8 and 21?

10 A. No, that's not what I'm saying. I'm saying that  
11 the evidence with respect to the risk between benzene and  
12 specific AML subtypes is -- at this point there have been  
13 assumptions and presumptions made with respect to the  
14 interpretation of previous studies, and the presumption of  
15 the association between the type or the types of AML  
16 associated with benzene exposure that would lead to the  
17 presumption that benzene would be associated with other  
18 subtypes. Our study which looks specifically at benzene  
19 exposure and resolved AML into the WHO -- the subtypes  
20 classified under WHO demonstrated a specific risk associated  
21 with t(8;21). It showed some evidence for an association  
22 between another translocation and that's t(15;17), but it  
23 wasn't statistically significant. For other subtypes, the  
24 risk between benzene exposure and other subtypes was not  
25 apparent.

1 Q. All right. My question is this. I'm asking for  
2 your opinion, Dr. Irons. Is it your opinion that AML, that  
3 benzene is only a risk factor for AML that is t(8;21)?

4 A. No, that's not my opinion.

5 Q. All right. What subcategories of AML do you  
6 recognize that benzene can be a risk factor for?

7 A. I've just told you what our data shows.

8 Q. Okay. You are telling me -- and we are just going  
9 over each other and we can do that, but it's not very  
10 productive. You are telling me that your study showed only  
11 the t(8;21). I'm asking you as a scientist are there any  
12 other subcategories that you believe there are other  
13 scientific studies or data that link benzene to those other  
14 subcategories? Just because you didn't find it, somebody  
15 else might have. That's what I'm asking.

16 MR. SCOTT: Object to the form of the  
17 question.

18 A. At this point in time I do not know of other  
19 studies that provide the same degree of resolution with  
20 respect to AML subtype analysis of our study. So, as I sit  
21 here today, I can't tell you whether or not -- certainly  
22 based upon our data which I believe is very surprising, even  
23 to me, that is a totally different pattern and risk  
24 association than has been suggested or inferred in the  
25 past.

1 Q. Let me ask it this way. If I have another client  
2 down in Jefferson County that ends up with AML t(15;17),  
3 would it be your opinion today that that AML is not related  
4 or -- not related to benzene exposure?

5 MR. SCOTT: Object to the form of the  
6 question.

7 A. If we are talking about specific causation of a  
8 case involving t(15;17), I believe that the evidence that we  
9 have suggests a potential but equivocal association of risk  
10 between benzene and t(15;17). I could not say as I sit here  
11 today that benzene exposure is not associated with t(15;17).  
12 The other issues that are important in reaching a conclusion  
13 involve exposure, they involve pattern of exposure, latency,  
14 all of which have to be evaluated in determining specific  
15 risk.

16 Q. In other words, you would look on it as a  
17 case-by-case basis to see what the benzene exposure was but  
18 would ultimately you would rely upon your study to say  
19 that you could not say within reasonable scientific  
20 probability that the t(15;17) is related to benzene  
21 exposure?

22 A. I think the data does not show a statistically  
23 significant risk, but it is marginal. It is close.

24 Q. Let me try it a different way. When you give an  
25 opinion in a case where a man has been exposed to benzene and

1 comes down with either myelodysplastic syndrome or AML or  
2 aplastic anemia or non-Hodgkin's lymphoma, do you rely only  
3 on your Shanghai study and the results that you found  
4 there?

5       A.   No. But I believe that the Shanghai health study  
6 informs with respect to disease specificity to a much greater  
7 degree than other previous epidemiologic studies and that the  
8 assumptions and presumptions that have been made by me and  
9 others with respect to what we can infer from previous  
10 studies have to be modified and reassessed in terms of the  
11 data that we now have.

12               MS. PARKS: I object to the responsiveness to  
13 everything after no.

14       Q.   All right. What level of benzene, in your view or  
15 opinion, is necessary to cause myelodysplastic syndrome?

16       A.   I cannot tell you what the threshold is. I  
17 certainly can tell you what the range of exposures are that  
18 were associated with MDS in our study.

19       Q.   And what was the range of MDS in your study?

20       A.   Exposures ranged basically between 67 milligrams  
21 per cubic meter to an excess of 100 to several hundred  
22 milligrams per cubic meter for periods of time ranging  
23 between six months and 13, 14 years. The median exposure  
24 duration was on the order of 12 years.

25       Q.   Do you have a quantitative estimate in parts per

1 million of the level of benzene exposure necessary to be  
2 associated with causing myelodysplastic syndrome, an opinion  
3 one way or the other?

4 A. The range for which we see -- the range that is  
5 associated with the MDS cases that we describe in our study  
6 is associated with very high level exposures, on the order of  
7 20 to greater than 100 parts per million for periods of time  
8 ranging between six months and, as I said, 12, 13 years.

9 Q. The same question, the level, quantitatively, in  
10 PPMs that you feel in your opinion is necessary to cause AML?

11 MR. SCOTT: Object to the form of the  
12 question.

13 A. I think that the quantitative epidemiologic studies  
14 that have been conducted in the past that have provided a  
15 quantitative estimate of exposure for AML in general show  
16 cumulative exposure associated with exposure -- or  
17 cumulative -- risk of AML associated with benzene in  
18 cumulative exposures ranging between 45 PPM years and greater  
19 than 200 PPM years.

20 Q. Do you have an opinion on the quantitative level of  
21 benzene exposure that Mr. Nolen, Richard Nolen, was exposed  
22 to?

23 A. No, I don't.

24 Q. Have you attempted to calculate a quantitative  
25 amount of Mr. Nolen's exposure to benzene?

1 A. No, I have not.

2 Q. Is it your opinion that because he has  
3 myelodysplastic syndrome 5q minus it's not related to benzene  
4 and you need to look no further about his exposure?

5 A. It's my opinion that MDS 5q minus syndrome has not  
6 been associated with exposure to chemicals.

7 Q. And I'm going to stop you right there. I need to  
8 stop you in little parts so I won't forget my question. Are  
9 you through yet on that? Go ahead. Go ahead and finish.

10 MR. SCOTT: I'm sorry. I've gotten lost. Can  
11 you tell us what the question was.

12 Q. Is it your because he has myelodysplastic syndrome  
13 5q minus it's not related to benzene and you need to look no  
14 further about exposures?

15 A. I believe that there -- it's my opinion that there  
16 are two issues with respect to determine specific causation  
17 and the probability that, in fact, Mr. Nolen's MDS is  
18 associated with exposure to benzene. One is the specific  
19 disease, and the other is the potential dose or exposure to  
20 benzene. With respect to the specific disease, I know of no  
21 evidence to suggest that myelodysplastic syndrome -- MDS 5q  
22 minus syndrome has been associated with exposure to benzene  
23 or other chemicals. So, that is one aspect of my opinion.

24 I have not been asked to ascertain the specific  
25 level of exposure to benzene that Mr. Nolen was exposed to.

1 I was asked to provide my opinion with respect to the -- the  
2 reliability and the cogency of the evidence and testimony in  
3 this case with respect to his exposure, specifically asked to  
4 address the issue of what's known about dermal exposure to  
5 benzene and to respond to the expert reports and opinions  
6 offered by plaintiff's experts. I was not asked to  
7 independently derive an exposure estimate for Mr. Nolen, and  
8 I didn't do so.

9 Q. Okey-doke. First issue, specific disease, in your  
10 opinion there is no evidence that his specific disease which  
11 is myelodysplastic, in your opinion, 5q minus, there is no  
12 evidence that benzene exposure is a risk factor for that  
13 disease. Do I have that right?

14 A. That's correct.

15 Q. And your opinion comes from your study, Shanghai  
16 study?

17 A. As my -- from the Shanghai study as well as other  
18 studies that have examined MDS and specific subtypes.

19 Q. What other studies?

20 A. Basically, any studies that I have reviewed with  
21 respect to MDS do not provide evidence to support a  
22 relationship between benzene or solvent exposure  
23 nonspecifically and the development specifically of MDS 5q  
24 minus syndrome.

25 Q. Every study that you have in front of you states

1 that benzene is not a risk factor for MDS 5q minus?

2 MR. SCOTT: Object to the form of the  
3 question.

4 A. No, ma'am, and that's not -- that's not what I  
5 said. I said -- you asked -- you asked -- you asked me to  
6 state the basis of my opinion, and what I'm saying, I cannot  
7 prove a negative. I do not know of any studies that  
8 demonstrate or show evidence that does associate specifically  
9 exposure to benzene or solvents and the development of MDS 5q  
10 minus syndrome. There are two studies that I'm aware of that  
11 specifically provide evidence relating to disease specificity  
12 and exposure to benzene or solvents. One is ours, and  
13 another one is a study by Vineis from Italy.

14 Q. The Vineis study, is that a case study --  
15 case-control study?

16 A. Yes.

17 Q. All right. The studies that you have in front of  
18 you, is there a study that specifically mentions MDS 5q  
19 minus?

20 A. Vineis provides -- provides -- indirectly provides  
21 evidence to say specifically the same thing.

22 Q. Does Vineis specifically say 5q minus syndrome?

23 A. No. It does specifically say that there were no  
24 cases involving Chromosome 5 involved in exposed cases.

25 MS. PARKS: I object to everything after no as

1 responsiveness.

2 Let's go off.

3 11:35

4 (WHEREUPON, THERE WAS A BREAK IN THE PROCEEDINGS,  
5 AFTER WHICH THE TESTIMONY RESUMED AS FOLLOWS:)

6 11:47

7 Q. (By Ms. Parks) Dr. Irons, we talked about the MDS  
8 5q minus, and you also stated that you were asked two issues  
9 on specific causation and concerning the potential dose. I  
10 believe you stated that you were not asked about specific  
11 exposures, not asked to give an opinion about that; is that  
12 correct?

13 A. That's correct.

14 Q. So, as we sit here today, you have not and do not  
15 intend to formulate any opinions about the level or a  
16 quantitative level of exposure to which Mr. Nolen would have  
17 been exposed?

18 A. I do not intend to formulate any opinions with  
19 respect to specific level that Mr. Nolen was exposed.

20 Q. I believe you also stated that you were asked to  
21 provide opinions with respect to the reliability and cogency  
22 of evidence and testimony with respect to exposures; is that  
23 correct?

24 A. That's correct.

25 Q. And what opinions do you have?

1       A.    I believe that I stated them in my report.  
2 Basically, my opinion is that the -- the literature with  
3 respect to the role of dermal exposure, relative importance  
4 of dermal exposure with respect to overall benzene exposure  
5 contributes relatively little to overall benzene exposure  
6 except under circumstances of extremely low exposure in which  
7 there is some evidence that dermal may play an increasing  
8 role, very little benzene exposure. But in general with  
9 occupational exposure to benzene, the relative role of  
10 dermal, the dermal route, is small.

11       Q.    When you say small, would you be able to give me  
12 that in percentages?

13       A.    Less than a percent, between maybe 1 and couple of  
14 percent total.

15       Q.    Have you reviewed the report of Dr. Paustenbach in  
16 this case?

17       A.    Yes, I have seen it.

18       Q.    Have you seen his opinion regarding dermal  
19 exposures in this case?

20       A.    Yes, I have.

21       Q.    Does he disagree, to the best of your recollection,  
22 or agree with you that dermal exposure would be less than 1  
23 percent?

24       A.    I said less than 1 percent to approximately 2 or 3  
25 percent. I believe, to the best of my recollection, that his

1 opinion is consistent with that, but as I sit here I don't  
2 recall specifically what precise numbers he stated.

3 Q. Would it surprise you if his estimates were greater  
4 than that 1 percent?

5 A. I said greater than -- less than 1 percent to 2  
6 percent, 3 percent, less than 5. Let's put it that way.

7 Q. Do you have a basis in the literature or your own  
8 study that dermal exposure plays a low impact on the disease  
9 development? In other words, do you have a specific study on  
10 which you rely?

11 A. Several. I can list them for you if you'd like.

12 Q. If you know which ones they are, sir, that would be  
13 greater. And perhaps you could just give me the number --  
14 that's in your index, correct?

15 A. Yes.

16 Q. You are now looking at, again, at Exhibit No. 2a, I  
17 believe?

18 A. Yes.

19 Q. And in the first part of Exhibit No. 2a, you have  
20 an index of your articles, correct?

21 A. Yes.

22 Q. What are the numbers of the articles that you feel  
23 provide a basis for your opinion regarding dermal exposure?

24 A. 51, 52, 53, 54, 55, 56, 57, 58, 59.

25 Q. Are these articles that you obtained yourself, or

1 are they articles that you had -- I apologize -- what is his  
2 name, doctor --

3 A. Kerzic.

4 Q. Kerzic obtain for you?

5 A. I've had these articles in my library for a dozen  
6 years or more with the exception of those that have been  
7 published more recently. So, I am either aware of them or  
8 have most of these. With respect to producing them for this  
9 case, I probably have had most of them obtained because of  
10 the nature of the logistics of getting my report completed  
11 and submitted from Shanghai. I don't have my references in  
12 Shanghai. But in terms of obtaining these as new studies  
13 that I have not reviewed before, the only ones that I haven't  
14 reviewed are those that are very recent such as 2008, in that  
15 range, in which case I have them specifically obtained.

16 Q. And I just want to make sure I understand that.  
17 Numbers 51 through 59, they were articles you already had  
18 within your files?

19 A. Vast majority.

20 Q. Unless it's 2008 or above?

21 A. Yes.

22 Q. And you feel that these are the articles that form  
23 the basis of your opinion that dermal exposure plays a low  
24 impact?

25 A. That's correct.

1 Q. All right. Again, going back to the question that  
2 you had answered previously that you were asked to provide  
3 opinions with respect to reliability and cogency of evidence  
4 in testimony, other than dermal exposure, was there anything  
5 else concerning dose or exposure you were asked to do?

6 A. I was asked to evaluate whether or not the  
7 testimony that I reviewed in this case with respect to the  
8 nature of Mr. Nolen's exposures were consistent with what I  
9 know about the acute toxicity of benzene, and my opinion is  
10 that they are not consistent with my knowledge of the acute  
11 toxicity of benzene.

12 Q. What testimony is inconsistent with your knowledge  
13 about the acute toxicity of benzene?

14 A. That the prolonged contact with pure benzene or  
15 high benzene content solvents directly with the skin, the  
16 solvent or saturated vapor for periods of time in excess of  
17 ten to 20 minutes repeatedly is consistent with -- whether  
18 it's possible. I don't believe it's possible. Acute  
19 exposure for even ten to 20 minutes at those levels even once  
20 is very likely to be associated with second degree burns,  
21 with sloughing of the skin, with very severe dermatitis; and  
22 certainly prolonged repeated exposure under those scenarios  
23 isn't consistent -- isn't consistent with long-term exposure  
24 to benzene.

25 Q. What is the basis for that opinion, sir? Was that

1 also the articles 51 through 59?

2       A.   No.  The data on acute benzene toxicity, the  
3 studies that have been published that look at acute benzene  
4 toxicity albeit are few but they do exist.  And there are  
5 notable cases of individuals who have been exposed at or less  
6 to concentrations and under conditions that are less severe  
7 than those that are described in the testimony from Mr. Nolen  
8 that are associated with extreme dermatopathology.

9       Q.   Where within the documents that you brought today  
10 is the data which you said there is just a few, but where is  
11 the data located regarding acute benzene toxicity?

12       A.   I provided a couple.  It would be 60 and 61.  There  
13 is also a textbook that I did not refer to that -- called  
14 Patty's Industrial Toxicology.

15       Q.   Is there a specific part of Patty's that you used  
16 to rely and provide a basis?

17       A.   Actually Patty's -- Patty's summarizes available,  
18 certainly at the time it was written, available acute  
19 toxicity data; and I believe that at least one of the  
20 references that I've cited supports Patty's.  So, I would say  
21 these are the primary references.

22       Q.   And they support your opinion that it was  
23 impossible to have the prolonged contact with pure benzene  
24 without burns or dermatitis?

25       A.   It's certainly inconsistent with the available

1 literature.

2 Q. What testimony do you recall that Mr. Nolen gave  
3 regarding the effects of the benzene on his skin, if any, if  
4 you recall?

5 A. I believe several references to defatting of the  
6 skin or drying, but the type of dermatopathology that's been  
7 associated with acute benzene exposure is far more severe  
8 than that.

9 Q. And, again, that would be found in your 60 and 61  
10 as well as Patty's?

11 A. That's correct.

12 Q. Did you see any photographs or pictures of  
13 Mr. Nolen's hands?

14 A. No, I did not.

15 Q. Did you ask to see such photographs or pictures or  
16 to see Mr. Nolen's hands?

17 A. No.

18 MR. SCOTT: Do those exist? If so, they  
19 haven't been produced.

20 MS. PARKS: No.

21 MR. SCOTT: I just wanted to be sure I haven't  
22 missed something here.

23 Q. Any other with respect to the reliability of the  
24 evidence and testimony with respect to exposure specifically  
25 on which you intend to opine?

1       A.    No.

2       Q.    And I believe you stated that you were also asked  
3 to review the expert reports of the plaintiffs?

4       A.    Yes.

5       Q.    And have you done so?

6       A.    Yes, I have.

7       Q.    What opinions, if any, have you come to as a result  
8 of reviewing the expert opinion of plaintiffs experts?

9       A.    Well, specifically with respect to Dr. Gardner and  
10 his description of pathogenesis of benzene-induced bone  
11 marrow damage, I feel in general that the -- his description  
12 of potential mechanisms is outdated and uninformed and I  
13 provided in my report statements to that effect and specific  
14 references in support of my opinion.

15      Q.    Does it say specifically in your report that you  
16 have issues with Dr. Gardner testimony in a specific part of  
17 your report?

18      A.    I don't believe -- I don't believe I commented  
19 specifically in reference to Dr. Gardner. I provided  
20 statements specifically related to the -- the findings or  
21 opinions and provided my own opinions. I did not, I believe,  
22 refer specifically to Dr. Gardner. I can't recall.

23      Q.    All right. And, Dr. Irons, you are not a medical  
24 doctor; is that correct?

25      A.    That's correct.

1 Q. And you not a hematologist?

2 A. I'm certainly not a clinical hematologist.

3 Q. Have you ever administered chemotherapy to a person  
4 with cancer?

5 A. No.

6 Q. Ever administered radiation?

7 A. No.

8 Q. Have you ever treated a person with cancer by  
9 providing treatments?

10 A. No.

11 Q. And you obviously have never treated Richard  
12 Nolen?

13 A. No.

14 Q. Are there experts on which you intend to state an  
15 opinion?

16 A. A great deal of my report focused on the  
17 methodology and the conclusions reached with respect to  
18 specific studies by Dr. Infante relating to methodology for  
19 use of an interpretation of appropriate epidemiology, and  
20 those references are provided in my reference list and I  
21 discuss them in my report.

22 Q. Is there a specific criticism you have of the  
23 methodology that Dr. Infante used in providing his opinions  
24 in this case?

25 A. I believe that in general Dr. Infante tends to mix

1 and match diseases with respect to specificity and providing  
2 evidence relating to quantitative risk and disease  
3 specificity. He also mixes and matches classification  
4 systems and schemes for the diagnosis of MDS using data that  
5 basically does not provide a specific indication of the risk  
6 of benzene exposure and MDS.

7 Q. In this particular case, what diseases do you  
8 believe that Dr. Infante mixed and matched when providing  
9 opinions?

10 A. Specifically AML and MDS, nonspecifically a variety  
11 of other myeloproliferative diseases that have been subsumed  
12 under the previous classifications of MDS. He, as I recall,  
13 has stated that the current criteria for classification and  
14 diagnosis of MDS is the 1982 FAB classification scheme which  
15 is outdated and hasn't been used for years, and, in fact, is  
16 not a -- is not considered a criteria for determination of  
17 disease specificity of MDS any longer.

18 Q. Where is there an article or a study or any  
19 document that says that the FAB is no longer used, outdated  
20 and not considered as criteria? Where is that published?

21 A. If you'll give me a couple of minutes I'll provide  
22 you with some cites. Well, certainly the WHO classification  
23 of tumors specifically references 10 and 11, also the  
24 independent validation of the WHO criteria in 12. These  
25 provide direct justification for the change in diagnostic

1 criteria and the literature that basically preceded the  
2 rationale for the change in diagnostic criteria and the  
3 separation of hematopoietic neoplasms into specific  
4 categories. In addition, a fairly good review demonstrating  
5 the diagnostic muddling of classification schemes is Ma, et  
6 al, which is 19.

7 Q. And that specifically refers to the WHO  
8 classification?

9 A. Ma refers to the WHO classification. It also  
10 refers to the specific ICD codes and FAB and the  
11 misclassification of MDS associated with studies using those  
12 different classification schemes.

13 Q. Have you reviewed or seen any articles,  
14 commentaries or studies in which hematologists or other  
15 scientists have criticized the WHO classification?

16 A. Yes, for specific reasons, not related to the  
17 diagnostic specificity.

18 MS. PARKS: I object to everything after  
19 yes.

20 Q. Do you believe Mr. Nolen was exposed to benzene?

21 A. I believe it's highly likely that Mr. Nolen was  
22 exposed to benzene. I think that it's a question of dose.

23 Q. Do you believe that Mr. Nolen was exposed to enough  
24 benzene to cause myelodysplastic syndrome?

25 A. I have seen no evidence -- reliable evidence that I

1 can use to ascertain what specific dose Mr. Nolen was  
2 exposed.

3 Q. Have any of the experts for Univar or Texaco  
4 provided you with any quantitative estimates of the exposures  
5 to the benzene that you agree Mr. Nolen would have been  
6 exposed to?

7 A. No.

8 Q. Have you seen any other quantitative evidence other  
9 than Dr. Nicas and Frank Parker's exposure estimates?

10 A. Those exposure estimates I have seen. I haven't  
11 seen any quantitative evidence of exposure in this case.

12 Q. Have you requested that Univar provide you with  
13 someone who has performed some quantitative estimate of the  
14 exposures that Mr. Nolen would have had to benzene?

15 MR. SCOTT: Object to the form.

16 A. I requested any information that Univar had with  
17 respect to Mr. Nolen's quantitative exposure to benzene.

18 Q. And when you requested that, what were you given?

19 A. Nothing.

20 Q. Would you agree that odor threshold is a way to  
21 estimate the airborne concentrations of benzene?

22 A. I think it's highly unreliable to the point of  
23 answering your question no. It's very unreliable.

24 Q. Are you aware of the published literature out there  
25 from the ACGIH and the EPA and the WHO that have published

1 findings showing odor thresholds for benzene?

2 MR. SCOTT: Object to the form of the  
3 question.

4 A. Oh, yes, I'm familiar with -- there is a great deal  
5 of data showing very conflicting and highly varied results  
6 with respect to odor threshold which is one of the reasons  
7 why I don't believe it's a reliable indicator of exposure.

8 Q. Have you seen the WHO publication or findings on  
9 odor threshold?

10 A. Can you specifically show me the cite?

11 Q. I can, and I will do it. Are you aware that WHO  
12 does have a published threshold for benzene?

13 MR. SCOTT: I need to object to the form of  
14 the question. Go ahead.

15 A. There are numerous published thresholds. I have  
16 seen a great many of them. I don't specifically recognize  
17 what you are referring to as WHO. So, I'd like to see it.

18 Q. I will put my hands on it at the next break, but  
19 I'm going to represent to you that there are -- there is  
20 documentation showing an odor threshold.

21 A. There are dozens that --

22 Q. Okay. Let me ask it this way. Does it surprise  
23 you that the WHO has a level which they consider to be odor  
24 threshold for benzene?

25 MR. SCOTT: Object to the form.

1       A.   No, that wouldn't surprise me.

2       Q.   If, in fact -- and I will find it because it's in  
3 my stack -- if, in fact, the WHO has published an odor  
4 threshold for benzene, you would disagree with that, correct?

5               MR. SCOTT:  Object to the form of the  
6 question.

7       A.   No, I did not say that.  I believe that there have  
8 been numerous various studies and publications that have  
9 attempted to characterize what the odor threshold for benzene  
10 is.  Many of them are mutually exclusive.  They are highly  
11 variable and that as a body of literature and evidence they  
12 indicate that the subjective analysis of an odor threshold  
13 for benzene is extremely unreliable and inaccurate.  It  
14 varies dramatically.

15       Q.   And you feel that any kind of information like that  
16 is extremely unreliable?

17       A.   As a method for estimating exposure to benzene I  
18 believe it's unreliable.

19       Q.   Do you make a distinction between 5q deletion and  
20 the arm of the 5q?

21               MR. SCOTT:  Object to the form.

22       A.   Could you please clarify that?

23       Q.   Sure.  5q minus, all right, that Mr. Nolen has, is  
24 that the deletion of the entire Chromosome 5 or just the arm  
25 of the chromosome?

1 MR. SCOTT: Object to the form.

2 A. It can be the arm of the chromosome or it can be a  
3 specific region between 5q13 -- and 5q13 and 33.

4 Q. Do you know which it is in Mr. Nolen's case?

5 A. Actually, it's in my notes. It's deletion 5q22  
6 q34. So, it is specific region of the chromosome bounded  
7 between q22 and q34.

8 Q. Have you given testimony in other cases previously  
9 that deletion of the 5 chromosome is benzene-induced?

10 MR. SCOTT: Object to the form.

11 Q. In certain --

12 A. Yes, I have in the past, based upon my presumption  
13 that, in fact, benzene-induced MDS AML was consistent with  
14 therapy-related disease in which that has been described as a  
15 finding; and that no longer is my opinion. With respect to  
16 specifically Mr. Nolen's disease it is significant that he  
17 was diagnosed with 5q minus syndrome as opposed to 5q minus  
18 associated with secondary MDS.

19 Q. In other words, he did not have secondary MDS,  
20 correct?

21 A. Not on the basis of his diagnosis.

22 Q. Have you given testimony in previous cases that the  
23 5q deletion being like chemotherapy type drugs, that that's  
24 similar to benzene?

25 A. I've given testimony in the past that I thought it

1 was highly likely that 5q minus and the deletion of the  
2 Chromosome 5 associated with secondary disease would be  
3 consistent with benzene exposure. Based upon the  
4 epidemiologic and clinical evidence that I now have I don't  
5 believe that that's the case.

6 Q. And how long has that been the case, that you've  
7 changed your opinion?

8 A. Over the course of the last year.

9 Q. And what happened to change your opinion?

10 A. The -- our analysis of the data that we have on 650  
11 MDS cases in China.

12 Q. Which was published in your 2009 article or will be  
13 published?

14 A. Yes.

15 Q. And prior to that, if we were to look at -- I  
16 believe it's your 2006 article.

17 A. Which one?

18 MR. SCOTT: Unique Form of Dysplasia?

19 MS. PARKS: I think so.

20 MR. SCOTT: That's 2005.

21 Q. 2005 article.

22 A. That one did not specifically address chromosome  
23 aberrations as I recall. The MDS study that we just  
24 published specifically characterized and analyzed chromosome  
25 aberration.

1 Q. Was there a reason that you added the chromosome  
2 aberration results in the 2009 one and not in the 2005 one?

3 A. They were different studies. The 2009 represents  
4 complete analysis of all of the hematopoietic cases that we  
5 reviewed and all of the diagnostic and molecular data that we  
6 had which included cytogenetic analysis. The paper  
7 characterizing benzene-induced dysplasia was characterization  
8 of those specific cases, and at that particular time --  
9 actually I can't recall whether we mentioned cytogenetics in  
10 that paper or not, but that wasn't the focus of that study.

11 Q. And as we sit here today you believe -- and what is  
12 the name of the study, the Prevalence of MDS Subtypes in  
13 Shanghai, China?

14 A. That one doesn't deal with benzene at all.

15 Q. Okay.

16 A. That one deals with a biological basis and  
17 prevalence of MDS subtypes in China.

18 Q. And also the clonal cytogenetic abnormalities?

19 A. Can I see it, please, make sure we are talking  
20 about the same paper?

21 Q. Sure.

22 A. Yes, yeah. Yeah, that one -- in this particular  
23 study we were characterizing the clinical findings for the  
24 series. We had not integrated or broken the code with  
25 respect to benzene exposure in that.

1 Q. When did you break the code?

2 A. The code was broken after the conclusion of case  
3 accrual which was June, 2007, and the code was basically  
4 then -- the case -- the case accrual was completed and the  
5 data sets analyzed by the respective investigators at that  
6 point.

7 Q. The investigators that analyze these data -- let's  
8 start over. The investigators that analyzed your data, who  
9 were the investigators? And I don't mean that specifically.  
10 I mean were they part of your Shanghai group?

11 A. They were part of the overall Shanghai group.

12 Q. In your Shanghai study, did you have any  
13 independent investigation or any independent analysis of your  
14 data?

15 A. Oh, yes. Data was peer-reviewed. The  
16 histopathology was independently reviewed by the secondary  
17 review of every case and a tertiary review in certain cases.  
18 The exposure analysis was reviewed by an expert group as well  
19 as scientific advisory panel and a group of industrial  
20 hygienists who were a subset of the scientific advisory  
21 panel.

22 Q. The scientific advisory panel was part of the  
23 scientific advisory panel of the Shanghai group?

24 A. Shanghai health study. They were external  
25 advisors. They weren't members of the actual study team.

1 Q. Were they members of petrochemical companies?

2 A. No.

3 Q. Were they members of the API?

4 A. No.

5 Q. Do you know who they did work for?

6 A. It depends. Jerry Rice is a professor at  
7 Georgetown. Richard Larson is a professor, hematologist, at  
8 University of Chicago. Harvey Checkoway is an epidemiologist  
9 at the University of Washington. Dick Albertini is a  
10 geneticist at -- I believe it's Dartmouth. There are several  
11 scientific investigators from -- clinical investigators from  
12 different organizations.

13 Q. And how was the scientific advisory panel paid?

14 A. I believe they were paid by the American Petroleum  
15 Institute. I don't know what those specific arrangements  
16 were.

17 Q. And what is your understanding of who makes up the  
18 American Petroleum Institute?

19 A. It's a trade organization that is made up of  
20 petroleum companies.

21 Q. I got a little off track, and I apologize. We were  
22 talking about some work you were asked to do in this case,  
23 and part of that was on testimony and you told me about  
24 Dr. Infante. Did you have other criticisms of Dr. Infante  
25 that we have not already covered?

1 MR. SCOTT: His report?

2 Q. Well, hey, let me ask it this way. Do you have any  
3 criticisms of Dr. Infante's credentials?

4 A. No.

5 Q. Have you ever worked with Dr. Infante on any  
6 study?

7 A. No.

8 Q. Have you ever worked for a governmental agency such  
9 as OSHA?

10 A. I've been an advisor to numerous governmental  
11 agencies, but I have not specifically been employed by one.

12 Q. Were you involved at all in the promulgation of the  
13 benzene standard?

14 A. No.

15 Q. All right. Now, the criticism of Dr. Infante's  
16 report, we talked about mix matched diseases, and I had asked  
17 you earlier, Dr. Irons, that the epidemiological data on  
18 benzene as a risk factor for leukemia and myelodysplastic  
19 syndromes, the overwhelming vast amount of that mixes the  
20 myelodysplastic syndromes with the AMLs; is that correct?

21 MR. SCOTT: Object to the form.

22 A. There is a great deal of muddling between those two  
23 and -- yes, there is a great deal of muddling between those  
24 two.

25 Q. Okay. What other criticisms do you have

1 specifically of Dr. Infante's opinions in this case?

2 A. Other than the methodology that he used and the  
3 conclusions that he reached based on that methodology,  
4 none.

5 Q. And when you talk about methodology, again, we are  
6 talking about mix and match, in your words, the diseases and  
7 mix and match the classification systems?

8 A. And exposure specificity and the conclusions that  
9 you can draw from the review of specific studies.

10 Q. When you say exposure specificity, what do you mean  
11 by that?

12 A. Exposure to benzene as opposed to exposure to other  
13 substances and/or mixtures and what conclusions you can draw  
14 from those.

15 Q. Do you know what evidence or testimony Dr. Infante  
16 relied upon in reaching his exposure opinions?

17 MR. SCOTT: Object to the form.

18 A. As I sit here today, no.

19 Q. All right. We talked about Dr. Infante. We talked  
20 about Dr. Gardner. Do you have any other specific opinions  
21 that you were asked to give as far as the reliability or  
22 credibility of the plaintiff's experts?

23 A. Only as I mentioned before, the issues related to  
24 dermal exposure and the modelling of dermal exposure.

25 Q. Have you ever done any modelling yourself?

1       A.    No.

2       Q.    Have you requested any modelling be done by any  
3 other expert in this case for Univar or for Texaco for your  
4 behalf?

5       A.    No.

6       Q.    Are there any other specific criticisms that you  
7 have of plaintiff's experts in this particular case?

8                   MR. SCOTT:  Object to the form.

9       A.    I don't believe so.

10      Q.    You are a toxicologist, correct?

11      A.    That's correct.

12      Q.    And it's your understanding also -- or is it your  
13 understanding also that Dr. Paustenbach is also a  
14 toxicologist?

15      A.    Yes.

16      Q.    Did you speak with Dr. Paustenbach,  
17 Mr. Paustenbach?

18                   MR. SCOTT:  Doctor.

19      Q.    Dr. Paustenbach.  Did you speak with  
20 Dr. Paustenbach at any time concerning your report or his  
21 report in this case prior to your report?

22      A.    No, I did not.

23      Q.    Have you read his report?

24      A.    Yes, I have.

25      Q.    Did you note in his report that he does not give an

1 opinion one way or the other regarding the MDS 5q minus?

2       A.    I didn't specifically -- it didn't cross my mind  
3 when I read it, but I don't believe I recalled that he  
4 rendered an opinion on 5q minus.

5       Q.    Would you expect -- let me ask it this way. As a  
6 toxicologist, one of the parameters of giving an opinion  
7 would be to review the relevant scientific and medical  
8 literature; is that fair?

9               MR. SCOTT: Object to the form of the  
10 question.

11       A.    It would depend -- it would depend upon what -- if  
12 you are talking -- if you are using me as an example, it  
13 would depend upon what I was asked to do and whether or not I  
14 felt it was within my range of expertise to reach an  
15 opinion.

16       Q.    Would you have expected Dr. Paustenbach to use your  
17 study, the Shanghai study, as a source for giving his  
18 opinions in this case?

19               MR. SCOTT: Object to the form of the  
20 question.

21       A.    I do not know -- I have no idea what  
22 Dr. Paustenbach was asked to do in this study and what  
23 opinions he was asked to provide, what data he was asked to  
24 analyze. So, I can't -- I don't know whether or not  
25 Dr. Paustenbach was asked to render an opinion on the

1 specific disease Mr. Nolen had.

2 Q. Have you ever as a toxicologist not been asked --  
3 serving as an expert witness are you always asked to render  
4 an opinion based on the disease the person has?

5 MR. SCOTT: Object to the form of the  
6 question.

7 A. In my case, that is often what I'm asked to do.  
8 But, again, over the course of my career I've been asked to  
9 do different things. Sometimes it involves evaluating the  
10 entire panoply of issues related to general and specific  
11 causation. Other times I've been asked to address specific  
12 issues. It depends on the -- depends on the case or the  
13 assignment that I've been asked to perform and that I've  
14 agreed to do.

15 Q. Have you ever had your testimony stricken in any  
16 court?

17 A. No.

18 Q. Are you aware that a West Virginia court did strike  
19 your testimony?

20 MR. SCOTT: Object to the form.

21 Q. Has anybody represented that to you?

22 A. That's a curious -- that was a curious case. My  
23 testimony as I understand it was not specifically stricken.  
24 The judge in that case asked me not to render an opinion that  
25 I did not hold and never gave, but he did not strike my

1 testimony.

2 Q. And what was the opinion that he asked you or told  
3 you you weren't going to render? Did it have to do with  
4 cytogenetics?

5 A. Yes, it did, as I recall.

6 Q. Did it have to do specifically asking you not to  
7 render any opinions regarding the deletion of the 5;7  
8 chromosomes?

9 A. No, I don't believe that's the case. I believe  
10 that the instruction I was asked -- and I wasn't asked  
11 specifically. I never actually saw it and there was never a  
12 hearing, but as I recall I was asked not to render the  
13 opinion that chromosome 5q minus could not be associated  
14 with -- could not be caused by benzene exposure. So, I was  
15 asked to render an opinion on a double negative which is not  
16 something I ever -- it's not an opinion I ever held.

17 Q. Did you render an opinion in that case, in the West  
18 Virginia case? Did you testify at trial or deposition?

19 A. I provided a deposition in that case.

20 Q. Did -- who was counsel in West Virginia that you  
21 worked for?

22 A. Joe Hollingsworth.

23 Q. And what was the disease? Was it myelodysplastic  
24 syndrome?

25 A. I don't believe so. I believe it was an AML, but

1 as I sit here I can't recall.

2 Q. Do you recall the name of the plaintiff?

3 A. Dean Hartley.

4 Q. Plaintiff's attorney?

5 A. Plaintiffs lawyer. Sorry.

6 Q. And when you were told -- and they don't ask you,  
7 Courts tell you -- when you were told you were not going to  
8 render an opinion based on the 5q minus, were you provided  
9 with an order from the Court, a copy of the order from the  
10 Court?

11 MR. SCOTT: Object to the form of the  
12 question.

13 A. No.

14 Q. Did you ask to see something in writing that the  
15 Court may have written regarding your testimony?

16 A. The first time was made aware, that was many months  
17 after the order was issued, and I never did receive it from  
18 counsel.

19 Q. Did you ever ask him again or just that one time?

20 MR. SCOTT: I'm sorry. Object to the form of  
21 the question.

22 A. I asked several times.

23 MS. PARKS: I said did you ever ask him again.

24 MR. SCOTT: Ask who again?

25 MS. PARKS: Counsel.

1 MR. SCOTT: For what?

2 MS. PARKS: For the order. That's what we are  
3 talking about, the order.

4 Q. You asked him several times?

5 A. Yes.

6 Q. Do you know what the basis for limiting your  
7 testimony was?

8 MR. SCOTT: Object to the form of the  
9 question.

10 A. No. I certainly don't believe it was my testimony  
11 because I never said -- I never said that.

12 Q. Have you worked for Mr. --

13 MR. SCOTT: Hollingsworth.

14 Q. Hollingsworth since this time?

15 A. No.

16 Q. Is that -- is the reason you have worked for him,  
17 does it have anything to do with the fact that this occurred  
18 with the -- your testimony?

19 A. I can't say one way or the other. But I certainly  
20 was not happy to find out about the evidentiary rulings in  
21 that case posttrial.

22 Q. I'm sorry. I apologize for interrupting you.  
23 Mr. Hollingsworth, who was he representing, what company?

24 A. I don't recall.

25 Q. Was it a chemical company?

1       A.    I believe it was a manufacturer.

2       Q.    And was the allegation in there that benzene caused  
3 the AML that you believe it was --

4       A.    I believe it was an AML.  I can't recall  
5 specifically.

6       Q.    And was the allegation benzene caused it?

7       A.    Yes.

8       Q.    I have some information, and I don't know if it all  
9 goes together, but it was provided to me with Bates stamps.  
10 Let me give this to you, and I'm going to mark it as  
11 Exhibit No. 10, and it's a compilation of documents.

12               (AT THIS TIME, DOCUMENT WAS MARKED FOR  
13 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 10.)

14               MR. SCOTT:  Did we give it to you?

15               MS. PARKS:  I really don't know where I got  
16 it.  I honestly don't.  It may have come with you-all's  
17 stuff.  I was looking through it.  It's got some of that  
18 stuff I've seen on his -- and it's Bates stamped.

19       Q.    Sir, let me ask you, Dr. Irons, do you recall a  
20 case that may have been MOC -- bates stamped with MOC and  
21 then numbers, a case you may have worked on?

22       A.    I have no idea what MOC stands for.

23               MR. SCOTT:  I think this came from Lance  
24 Lubel.

25               MS. PARKS:  It may have.  I don't know.  I

1 honestly don't.

2 MR. SCOTT: I just said that. I don't know.

3 Q. It's a compilation of items, and I've marked it as  
4 Exhibit No. 10, items that probably do not go together, but  
5 it came in all my benzene stack of stuff. Some of it has to  
6 do with -- well, it has to do with the Chinese Shanghai  
7 study, and they are pretty much in order Bates stamped which  
8 is why I think they went into something you must have worked  
9 on, but I couldn't totally wrong. I have some questions  
10 specifically, but if you'd like to just look through it for a  
11 second just to see if you recognize what case this may have  
12 come from.

13 A. I don't know which case this is from. All of the  
14 material -- well, I won't say all -- certainly there is  
15 information in here I'm familiar with. I am not familiar  
16 with the specific documents.

17 Q. Okay. All right. So, in other words, there is  
18 some of the information you've seen before, but put together  
19 it's not something that rings a bell?

20 A. No.

21 Q. Okay.

22 A. And, you know, I am intimately familiar with a lot  
23 of the information that's in here, probably not all of it,  
24 but I do -- I mean, it's familiar territory. It's the  
25 Shanghai health study.

1 Q. Okay. All right. I'm going to ask you about a few  
2 pages, if you don't mind, sir; and what I'll do is I'll refer  
3 to them by Bates stamps which are located at the bottom  
4 right-hand corner.

5 A. Okay.

6 Q. And first of all, there is one at the bottom that  
7 ends with the numbers 44364. It's not very far into that.  
8 This document starts off with Why China. Are you familiar  
9 with this document? Was it part of a Powerpoint that you did  
10 or that you've seen in the past?

11 A. Not that I'm aware of.

12 Q. Okay. And have you ever seen this particular  
13 document before? Again, I'm on 43 -- 44364.

14 A. You know, as I sit here, I can't tell you whether  
15 I've seen it or not. Mr. Lubel may have put this in front of  
16 me at some point or another, but I do not recognize the  
17 origin of this specific -- this looks like a Powerpoint.

18 Q. Does it to me, too.

19 A. It's not my Powerpoint.

20 Q. All right. Well, at any time was it your  
21 understanding that the Shanghai study that you conducted was  
22 done to prove or disprove the results of the National Cancer  
23 Institute, the Chinese Academy of Preventative Medicine  
24 study?

25 A. No, no.

1 Q. When you did your Shanghai study, did you look  
2 specifically at non-Hodgkin's lymphoma as well?

3 A. Yes. We looked at all blood and hematologic and  
4 lymphoid diseases.

5 Q. Did you find any excess risk of non-Hodgkin's  
6 lymphoma in benzene-exposed individuals?

7 A. The only excess risk that we saw was in a very  
8 small subset of follicular lymphomas. There were no other  
9 excess risks observed. And the risk associated with  
10 follicular lymphoma was surprising.

11 Q. So, you found no excess for non-Hodgkin's lymphoma.  
12 Is that what you are saying?

13 A. No. Follicular lymphoma is one of the subtypes of  
14 Hodgkin's lymphoma.

15 MR. SCOTT: Non-Hodgkin's.

16 A. Excuse me, non-Hodgkin's.

17 Q. Is it your opinion that benzene is a risk for  
18 non-Hodgkin's lymphoma?

19 A. Nonspecifically, no. For specific subtype, that's  
20 what the data shows.

21 Q. So, just as you've done myelodysplastic syndromes  
22 and AML, you have found subcategories and identified benzene  
23 exposures from that?

24 A. Yes, yes.

25 Q. How many subcategories of non-Hodgkin's lymphoma do

1 you recognize?

2 A. There are 23, 25, 30. I could count them for you,  
3 but there are a large number.

4 Q. And of those 23 whatever it is, there is only one  
5 for which you have found an excess --

6 A. There was only one for which we saw an excess.

7 Q. Will you go to 44374? Do you know Craig Parker?

8 A. Excuse me.

9 Q. I'm sorry.

10 A. These don't seem to be in an order that at least is  
11 consistent by the way I count.

12 Q. 44374.

13 MR. SCOTT: You mean two comes after one and  
14 three comes after two?

15 Q. Maybe they are not exact order. I'm giving them  
16 to you the way I got them. It's not very far through there.

17 A. I'm sorry.

18 Q. I don't want to look over you, but it's -- I copied  
19 yours straight from mine. So, it's very short in there. No,  
20 you are way too far away.

21 A. Okay. That would account for --

22 Q. 44374.

23 A. 371.

24 Q. 374.

25 A. No, I got 373. Then it jumps to 313. They are out

1 of order. I'm sorry.

2 Q. Okay. Well, I apologize. Evidently mine was.

3 Whoever copied yours didn't copy them right. How about I

4 just give you this one.

5 A. Okay.

6 Q. Do you know Craig Parker?

7 A. I don't believe so.

8 Q. Do you know what IPIECA stands for?

9 A. No.

10 Q. Have you ever seen what appears to also be a --

11 boy, yours is out of order -- what appears to be, again,

12 either a slide show or a Powerpoint?

13 A. I guess that it looks like it's probably generated

14 by a Powerpoint program.

15 Q. Okay. All right. And do you recall -- I hate to

16 do this to you, I'm just going to look -- the background of

17 significance of concerns to global petroleum industry that

18 the research would affect, are they talking about your

19 research, the Shanghai study?

20 MR. SCOTT: Object to the form of the

21 question.

22 Q. If you know.

23 A. Excuse me. What was the question again?

24 Q. Yes. Are they referring to your Shanghai study

25 when they are talking about describe the significant issues

1 of concern to global petroleum industry that this research  
2 would affect, are they talking about the Shanghai research?

3 MR. SCOTT: Object to the form of the  
4 question.

5 A. You know, I can't tell you as I sit here whether  
6 this is specifically -- in the context of what you have, I  
7 could only infer that. I don't know that for a fact.

8 Q. How about look up at the box above it. I found  
9 yours. It is all messed up. I found yours. Look at the  
10 project description in the box above it. It says, the  
11 proposed research is the investigation of the effects and  
12 dose response of hematological effects of benzene exposure --

13 A. Shanghai, China.

14 Q. Yeah, in Shanghai, China. Is there any other work  
15 going on in China that you are aware of doing what you are  
16 doing?

17 MR. SCOTT: Object to the form of the  
18 question.

19 A. No.

20 Q. So, would you agree that one of the issues of  
21 concern to global petroleum industry would include litigation  
22 alleging induction of various forms of leukemia and other  
23 hematopoietic diseases from exposure to petroleum derived  
24 benzene resulting in millions of dollars in expense to  
25 industry?

1 MR. SCOTT: Object to the form of the  
2 question.

3 A. Yes. I would agree that the whole issue of benzene  
4 causation of disease and specific disease is a health issue.  
5 It's also an economic issue, and it impacts litigation as  
6 well as any other aspect of society and business.

7 Q. In other words, it costs business money when they  
8 have to litigate cases like this where men are exposed to  
9 benzene and they file a lawsuit alleging their exposures  
10 caused their disease?

11 MR. SCOTT: Object to the form of the  
12 question. These are really improper of this witness.

13 MS. PARKS: It's really not.

14 Q. It's your study, isn't it, Dr. Irons?

15 MR. SCOTT: I'm not going to argue with you.  
16 Object to the form of the question. You need to talk to oil  
17 companies about that. Object to the form of the question.

18 MS. PARKS: I object to the side bar.

19 Q. Dr. Irons, this is your study, the Shanghai study,  
20 correct?

21 MR. SCOTT: Object to the form of the  
22 question.

23 A. I was principal investigator of the Shanghai health  
24 study, yes.

25 Q. And the Shanghai health study was paid for by oil

1 companies?

2 A. Yes.

3 Q. And also funded by the American Petroleum

4 Institute, correct?

5 MR. BAKER: Can we have an agreement that one  
6 objection is good?

7 MS. PARKS: Oh, yeah.

8 MR. SCOTT: I object to the form of the  
9 question.

10 A. Technically -- technically the American Petroleum  
11 Institute didn't pay for the study.

12 Q. When you say technically, did the money come from  
13 the oil companies to go through the API to go back to whoever  
14 got the money, or how did it work?

15 MR. SCOTT: Object to the form of the  
16 question.

17 A. Yes, but the API -- the API served as an  
18 administrator and management organization. The funding came  
19 through the Benzene Health Research Consortium.

20 Q. And the Benzene Health Research Consortium were oil  
21 companies?

22 A. Yes.

23 Q. Do you know which oil companies?

24 A. ExxonMobil, ChevronTexaco, BP Amoco, Shell  
25 Chemical, ConocoPhillips. Is that five? Did I leave anybody

1 out?

2 MR. SCOTT: I think you got five.

3 Q. Did you ever -- before your study ever began did  
4 you ever approach an oil company with your ideas of what you  
5 intended to do in China to see if you could get funding, you  
6 personally, whether you did it with a Powerpoint or just  
7 called them up and said, hey, I want to talk to you about a  
8 study I'm thinking about doing?

9 A. Well, the -- as I recall, that isn't how the study  
10 originated. And if you like, I can give you a brief  
11 description of how it originated which may answer your  
12 question; it may not.

13 Q. Well, I've got really specific questions and I'm  
14 happy to let you do that, but specifically did you ever talk  
15 with anybody at Shell regarding funding of your Shanghai  
16 study?

17 MR. SCOTT: Object to the form.

18 A. In the early days when the study was being reviewed  
19 as a possible project and during the design of the study, I  
20 made several presentations to -- originally it was in  
21 response to a request from the American Petroleum Institute  
22 and then later, once the five oil companies, petroleum  
23 companies, demonstrated an interest in funding it, there was  
24 a lot of discussion over the specific design and conduct of  
25 the project, and I gave several presentations.

1 Q. Do you feel there is any bias or prejudice that you  
2 did a study that was funded by the oil companies and came out  
3 with results that showed very little --

4 MR. SCOTT: Object to the form of the  
5 question.

6 Q. Relationship between exposures to benzene and  
7 various blood cancers?

8 MR. SCOTT: Object to the form of the  
9 question.

10 A. I'm not sure what you are referring to. Bias with  
11 respect to whom?

12 Q. The results of your findings.

13 A. If you look at the study design and you look how it  
14 was conducted and the safeguards that were in place,  
15 including blinding peer review and the overall design of the  
16 study, the actual -- I think it's fair to say that the design  
17 and conduct of the study is unprecedented with respect to the  
18 lengths we went to to eliminate bias which includes blinding  
19 of investigators from one part of the study to another, peer  
20 review and scrutiny. So, I think this study represents  
21 probably one of the most independent studies ever conducted  
22 of the magnitude that it is and its degree of independence  
23 from the study sponsors.

24 MS. PARKS: Objection, nonresponsive.

25 Q. How much was the total cost of the study itself?

1       A.    I've been asked that frequently.  I believe it was  
2 on the order, if you go -- talk soup to nuts from its very  
3 inception which includes the prestudy and design aspects, I  
4 believe I've heard numbers on the order of 35 million.

5       Q.    And is the study itself actually over now?

6       A.    Yes.

7       Q.    Are you going to be doing any follow-up studies?

8       A.    I'm not funded to do any follow-up studies.  So, at  
9 the present time I have no plans.

10      Q.    Do you intend to attempt to obtain funding for  
11 follow-up?

12      A.    If I'm asked, I would consider it.  I haven't been  
13 asked, and I can't tell you as I sit here whether or not I  
14 would.  I don't know.

15      Q.    How much time do you spend in Shanghai now compared  
16 to time spent in America?

17      A.    10 to 11 months in Shanghai.

18      Q.    So, you are spending the greater bulk of your time  
19 there?

20      A.    2009, I lived in China, and at the present time I  
21 expect to be spending considerable time in China.

22      Q.    Into the future?

23      A.    Yes.

24      Q.    Are you teaching there?

25      A.    I teach there.  I'm involved in training there and

1 in laboratory diagnostics.

2 Q. We had gone through your manila folder, but I have  
3 not marked everything. What else did you have in the manila  
4 folder?

5 A. I have a summary I made of Mr. Nolen's medical  
6 history that was relevant to my opinions in this case.

7 Q. And I'm going to mark that as Exhibit No. 11,  
8 Dr. Irons.

9 (AT THIS TIME, DOCUMENT WAS MARKED FOR  
10 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 11.)

11 Q. Who provided you with this medical history?

12 A. I did it.

13 Q. You did it yourself?

14 A. Yes.

15 Q. And counsel for Univar told us earlier today that  
16 you were provided the medical records online and you reviewed  
17 those.

18 A. Yes, I did, yeah.

19 Q. Do you know whether or not you have reviewed all of  
20 the medical records, or was it just a portion of medical  
21 records?

22 A. It looks to me like -- well, with the caveat that  
23 it's almost impossible to ever know what all medical records  
24 are, I reviewed a substantial body of records that I believe  
25 provided consistent history for this period of Mr. Nolen's

1 life.

2 MR. SCOTT: We'll be happy to forward what we  
3 sent, either a list or the electronic records of what we  
4 forwarded.

5 MS. PARKS: I think we all have them.

6 Q. How many bone marrows do you recall reviewing?

7 A. Can I take a look at that?

8 MR. SCOTT: You mean pathology reports, I take  
9 it.

10 Q. Yes.

11 A. Two specifically. I believe that some of these  
12 additional follow-up entries also included bone marrow  
13 pathology, but I'm not -- I'm not certain. They weren't  
14 specifically relevant to my opinion with respect to the  
15 disease specificity of his initial disease and those were the  
16 only ones that I have provided some detail.

17 Q. Have summarized in your summary?

18 A. Yeah.

19 Q. All right. Your opinion in this case is that  
20 Mr. Nolen's myelodysplastic syndrome is of the subcategory  
21 that is not known to be related to benzene exposure. Is that  
22 a fair characterization?

23 A. Yes.

24 Q. Do you believe that his 5q minus, can that ever  
25 evolve into AML?

1       A.    Yes, it can.  It has a very low probability.  It  
2 has essentially the lowest probability of the MDS subtypes.

3       Q.    If it evolved into AML, are you able to determine  
4 the subcategory -- your subcategories that you believe exist  
5 of AML that it would evolve into?

6               MR. SCOTT:  Object, form.

7       A.    It could evolve into -- again, it's a function of  
8 clinical sampling and progression, the hypothetical  
9 progression of his disease.  In general, 5q minus syndrome  
10 has a very low likelihood of transformation.  If, in fact, it  
11 did transform, it could transform rapidly which would mean  
12 that hypothetically it could, in fact, be diagnosed directly  
13 as an AML.  It could go through a series of progressive  
14 changes with increasing blast prevalence which would coincide  
15 with if, in fact, clinical analysis was performed during that  
16 period.  It could hypothetically progress to a RAEB 1, RAEB  
17 1, or an RAEB 2.  Those would be the -- the outcomes related  
18 to transformation.

19       Q.    And in any of those transformations -- or if any of  
20 those transformations occur, would you still have the opinion  
21 that it would not be a disease for which benzene would be a  
22 risk factor?

23       A.    Based upon his initial diagnosis which is the  
24 important factor with respect to disease specificity, my  
25 opinion would be the same, that, in fact, 5q minus syndrome,

1 there is no evidence that benzene exposure is associated with  
2 the development of 5q minus syndrome.

3 Q. If he had had myelodysplastic -- oh, I'm sorry. I  
4 apologize.

5 A. Excuse me. 5q minus syndrome in and of itself has  
6 a -- has a risk, albeit small, of transformation to RAEB or  
7 to AML. It's very small. And that's independent of  
8 potential etiology. The 5q minus syndrome itself has a very  
9 low probability of transformation.

10 Q. If Mr. Nolen had a deletion of the 5 chromosome  
11 instead of just the 5q minus, if it was MDS with deletion of  
12 the 5 chromosome, would it change your opinion in any way  
13 that benzene is not a risk factor?

14 A. Previous to now, previous to this point in time, it  
15 was my opinion that it was likely that benzene exposure was  
16 associated with what is described as a specific category by  
17 WHO, therapy-related AML MDS. A characteristic of  
18 therapy-related AML MDS has a very high prevalence of  
19 deletion of Chromosome 5, Chromosome 7 and/or complex  
20 cytogenetic abnormalities involving those two chromosomes.  
21 That particular disease I have presumed based upon the  
22 assumption that benzene exposure is associated with that  
23 classic therapy-related disease would likely be associated  
24 with the development of MDS associated with those  
25 abnormalities. Based upon my recent study, I no longer hold

1 that opinion because there is no evidence for it.

2 Q. And, again, that's based on your study, the  
3 Shanghai study, correct, sir?

4 A. That's correct.

5 Q. Is there any other basis other than your study, the  
6 Shanghai study, on which you base that opinion?

7 A. There are several quantitative epidemiology studies  
8 that are associated with the risk of developing AML  
9 associated with benzene exposure. They do not provide the  
10 resolution with respect to disease category and  
11 characterization of clinical features that our study does.  
12 So, my opinion with respect to the relationship between  
13 benzene exposure and the development of any MDS subtype and  
14 with respect to any AML subtype is predominantly based upon  
15 the Shanghai health study.

16 MS. PARKS: I'm going to object to the  
17 nonresponsive part before you said it's based predominantly  
18 upon the Shanghai health study.

19 Q. I am almost finished, sir. Do you have anything  
20 else in your manila folder that we have not marked as an  
21 exhibit? Your report. Let me get -- I have a copy of your  
22 report, but I'm going to go ahead and put it on there.

23 (AT THIS TIME, DOCUMENT WAS MARKED FOR  
24 IDENTIFICATION PURPOSES AS IRONS EXHIBIT NO. 12.)

25 Q. Sir, I'm going to mark as Exhibit No. 12 a clean

1 copy of your report. Have you made any changes or deletions,  
2 additions to this report?

3 A. No.

4 Q. Are any of your opinions that you have given,  
5 do you intend to do any more work as far as the opinions  
6 you've provided today in Exhibit No. 12?

7 MR. SCOTT: Let me just say this. We have  
8 only recently because we've only taken them provided the  
9 depositions of Dr. Gardner, Dr. Infante, I think Dr. Irons  
10 may have reviewed those, parts of those. I don't think -- I  
11 know just because of the timing he hasn't had a full  
12 opportunity, and I think we don't -- we obviously don't have  
13 all the depositions of all the witnesses and the plaintiff's  
14 witnesses in the case. So, we do anticipate providing those  
15 materials to him and asking him to review them thoroughly,  
16 and with regard to Gardner and Infante, their depositions  
17 more thoroughly than he's had an opportunity to do.

18 Q. In other words, you may have some more criticisms  
19 of plaintiff's experts?

20 MR. SCOTT: I'm sure I will.

21 Q. Just as we may have criticisms of yours. What else  
22 is in your folder there, sir?

23 A. That's it.

24 Q. That's it. All right. I have one more question.  
25 I want to make sure I can form it the way I need to. I did

1 not ask you -- I asked you about smoking. Did you believe  
2 smoking was a risk factor for Mr. Nolen's myelodysplastic  
3 syndrome?

4 A. Yes.

5 Q. Are there any other risk factors that you attribute  
6 to Mr. Nolen's myelodysplastic syndrome?

7 A. No.

8 Q. Have I been cordial to you?

9 A. Yes, ma'am.

10 MS. PARKS: I'm done. Thank you.

11 (12:56)

12 EXAMINATION

13 BY MR. SCOTT:

14 Q. I have just a couple. Dr. Irons, are there any  
15 epidemiology studies in the formal sense of epidemiology  
16 studies which demonstrate that benzene is a cause of -- I'm  
17 going to use the broad category -- of any -- of the  
18 myelodysplastic syndromes?

19 A. Yes, with specific caveats.

20 Q. Okay. Will you explain your answer, then; tell us  
21 which study and what the caveats are?

22 A. There have been several studies that have looked  
23 at -- with varying degrees of exposure specificity to the  
24 epidemiology of AML and MDS. Most of them have  
25 indiscriminately characterized MDS and AML together. A

1 specific example is the NCI China study which looked at MDS  
2 and AML and they combined those -- they combined those two  
3 groups on the presumption that benzene was associated with  
4 the development of a disease very similar to therapy-related  
5 AML MDS which is a very specific category, and they combined  
6 MDS and AML. That makes it extremely difficult to look at  
7 what the specific risk is. If you go back and look at the --  
8 the actual clinical features of those diseases which are  
9 characterized in Travis and in Hayes --

10 Q. Because we are on the record here, if you would be  
11 clear that Travis and Hayes are publications from the NCI  
12 Chinese Academy of Preventative Medicine group of studies,  
13 correct?

14 A. Right, right, and Yin before, Yin '89 which was the  
15 original cohort study. They weren't -- they did not  
16 discriminate therapy-related AML MDS, but rather combined all  
17 cases of AML and MDS. AML and MDS together showed a very  
18 significant -- showed a significant risk associated with  
19 benzene exposure. If you look at -- there are seven MDS  
20 cases included in that analysis. If you go back and look at  
21 their review of the morphology and clinical features, only  
22 five of those cases, five of the seven, were submitted for  
23 histopathologic review, all of them originally diagnosed in  
24 China. Of those five, three no longer meet criteria for MDS  
25 by current diagnostic standards. So, as an example, here is

1 a study that shows a significant risk of benzene -- for  
2 benzene exposure for the development of combination of MDS  
3 and AML, but it does not provide sufficient evidence for a  
4 quantitative relationship with MDS. The strongest study  
5 demonstrating an association between benzene and MDS is my  
6 study in terms of disease specificity and exposure, and  
7 that's because we can discriminate by subtype and distinguish  
8 between MDS and AML and all the other hematopoietic diseases  
9 that are part of the WHO group.

10 Q. Ms. Parks asked you some questions about the bias  
11 associated with this Shanghai health study or claim to be  
12 associated with the Shanghai health study. If one were to --  
13 if I were to ask you what is the strongest scientific  
14 evidence that benzene causes myelodysplastic syndrome,  
15 setting aside the subtype issue right now, what is that?

16 MS. PARKS: Object to form.

17 MR. SCOTT: What is the objection?

18 MS. PARKS: It's leading him, and it's also  
19 vague. What do you mean, strongest?

20 A. Well, the strongest scientific evidence with  
21 respect to disease, specific disease, MDS, I believe is our  
22 study.

23 Q. Now, I think you have opined that Mr. Nolen had a  
24 particular subtype of MDS recognized as 5q minus. Is that  
25 correct?

1       A.    5q minus syndrome, yes.

2       Q.    5q minus syndrome.  How does that differ from --  
3 from deletion of the 5 chromosome?

4       A.    5q minus syndrome is a single clonal chromosome  
5 aberration that along with the clinical features and  
6 presentation that Mr. Nolen had is recognized in the medical  
7 community as being associated with older individuals and  
8 carrying a totally different prognosis than other forms of  
9 MDS.  The absence of a Chromosome 5 or, as I said, complex  
10 cytogenetics involving deletions of 5 and 7 that are found in  
11 therapy-related AML carry -- is associated with different  
12 etiology and carries a much different prognosis.  So, those  
13 are distinguished -- those two are dramatically different.  
14 The diagnosis of 5q minus syndrome is also one that's  
15 associated with specific age in general and carries with it,  
16 as I said, unique features with respect to the morphology and  
17 presentation as well that are distinguished from  
18 therapy-related disease.

19       Q.    What age -- you've said now twice that 5q minus is  
20 associated with age.  Can you describe that for us?  What age  
21 is associated with 5q minus syndrome MDS and how does it  
22 compare to other age groups?

23       A.    It tends to -- it tends to occur in older  
24 individuals, certainly above the age of 50, is more prevalent  
25 in, I believe, the sixth and seventh decades.  So, it tends

1 to be associated with older people. It's not a disease of  
2 young people.

3 Q. There was some discussion with Ms. Parks about  
4 whether, RAEB, R-A-E-B, which is refractory anemia with  
5 excess blasts, is a separate disease entity or not among the  
6 myelodysplastic syndromes. I want to be clear about this.  
7 There is a -- one of the myelodysplastic syndromes is known  
8 as RARS, R-A-R-S, or refractory anemia with ring  
9 sideroblasts, correct?

10 A. Yes.

11 Q. Can RARS cases progress to RAEB?

12 A. Yes.

13 Q. And as I understood it, the criteria for whether a  
14 disease becomes -- or whether an MDS becomes RAEB is the  
15 number of blasts; is that correct, or the percentage of  
16 blasts?

17 A. That essentially is the defining characteristic  
18 that distinguishes RAEB from other subtypes of MDS.

19 Q. You mentioned that between 5 and 9 percent blasts  
20 would be classified as a RAEB 1. Would that be true if you  
21 had a RARS -- a case diagnosed as a RARS case that then when  
22 the docs saw the patient a year later saw excess blasts  
23 between 5 and 9 percent, would that be true of the RARS case,  
24 that it has become -- progressed to a RAEB case?

25 MR. BROWN: Form.

1 A. Yes.

2 Q. Was it still a RARS case to begin with?

3 A. Yes.

4 Q. And if the -- a year later or six months later the  
5 blasts that are observed by the physicians is 10 to 19  
6 percent, what is the disease known as then?

7 A. It would be RAEB 2.

8 Q. Was the diagnosis of RARS still correct when it was  
9 initially made?

10 A. Yes.

11 Q. And if -- we didn't talk about this, but if the  
12 excess blasts become 20 percent or more, what is the disease  
13 then?

14 A. It's acute myeloid leukemia.

15 Q. And was it still a correct diagnosis of RARS way  
16 back when before it progressed through these stages?

17 MR. BROWN: Form.

18 A. Yes.

19 Q. Now, is that true of each of the subtypes of MDS  
20 that it can be, for instance, RCMD, refractory cytopenia with  
21 multilineage dysplasia -- did I get that right?

22 A. Yes.

23 Q. Can that progress through RAEB 1, RAEB 2 and AML?

24 MR. BROWN: Form.

25 A. Yes.

1 Q. Same for MDS unclassified?

2 A. Yes. MDS unclassified -- an MDS unclassified  
3 certainly can progress through RAEB.

4 Q. Are there some instances when the initial diagnosis  
5 is RAEB?

6 A. Yes. It depends on -- depends on the -- the  
7 natural history of the disease and when the patient is  
8 clinically evaluated.

9 Q. Are there different percentages of these various  
10 subtypes of myelodysplastic syndrome that progress to AML?

11 A. Yes.

12 Q. What would be the lowest, as far as progression,  
13 what is the lowest of the subtypes of MDS with regard to  
14 progression to AML?

15 A. 5q minus syndrome.

16 Q. What is the highest?

17 A. The highest would be RAEB 2, and as well the  
18 therapy-related diseases tend to progress very rapidly  
19 independent of what the initial bone marrow morphology looks  
20 like.

21 Q. Are the therapy-related diseases included among the  
22 descriptions of myelodysplastic syndromes in Chapter 5 of the  
23 World Health Organization classification?

24 A. No. They are dealt with independently as a  
25 specific subset because they have features in common and are

1 distinguished from other forms of MDS and AML.

2 Q. Now, several times you've been asked about your own  
3 study being the basis for your opinions. I want to ask a  
4 much broader question. What is the evidence of which you are  
5 aware that benzene exposure has been associated with the  
6 development of MDS 5q minus?

7 A. There are no quantitative epidemiology studies that  
8 provide evidence to indicate that benzene exposure is  
9 associated with the development of 5q minus.

10 Q. If we turn to your study -- would you describe that  
11 as a case series, or how would you describe the -- and I'm  
12 talking about the 2009 paper we've been discussing.

13 A. The 2009 is a case-case comparison superimposed on  
14 a case series. The -- as I said -- as I said before, that  
15 study -- our study does not provide evidence to support  
16 association with 5q minus syndrome. Now, let me say we have  
17 very few cases of 5q minus syndrome in that series, but we  
18 have a very large number of cases that have other chromosome  
19 abnormalities involving other subtypes of MDS. And whether  
20 or not we are talking about 5q minus syndrome or we are  
21 talking about MDS with deletion 5, we have no association  
22 with benzene exposure. As a matter of fact, in our highly  
23 exposed cases we have no deletion 5, and that's similar to  
24 what Vineis reported for organic cases of MDS with organic --

25 Q. Earlier on you mentioned that -- Ms. Parks was

1 asking you about whether there was some independent review of  
2 the findings of the Shanghai health study. With regard to  
3 the diagnosis of each of these cases of myelodysplastic  
4 syndrome, of all of the cases that were diagnosed by the  
5 Shanghai health study group, who did the diagnosis?

6 A. I diagnosed and reviewed every single case. Early  
7 on a Chinese morphologist also reviewed many of the cases.  
8 All of the cases were also independently reviewed by board  
9 certified hematopathologists and then concordance  
10 determined.

11 Q. I'm sorry. Go ahead.

12 A. At periodic intervals we also submitted cases by  
13 request and also election to a third independent reviewer.

14 Q. Who was the hematopathologist that did the  
15 review?

16 A. Dr. John Rider.

17 Q. And then you say periodically these cases were  
18 submitted or some part of the cases were submitted for some  
19 separate review. Who were those people that did the separate  
20 reviews?

21 A. Dr. John Bennett.

22 Q. Is John Bennett the same John Bennett whose name  
23 appears on the World Health Organization classification of  
24 lymphohematopoietic diseases just one right after another?

25 A. That's the guy.

1 Q. I'd have to get through them, but is that the same  
2 John Bennett?

3 A. Yes.

4 Q. Is John Bennett the same John Bennett that in 1982  
5 published the report regarding the classification system then  
6 known as the French American British classification system?

7 A. Yes.

8 Q. Has he been around awhile?

9 A. He certainly has.

10 Q. Is he a well-respected hematologist among the  
11 hematology professionals of the world?

12 MS. PARKS: Form.

13 A. Yes.

14 MR. SCOTT: I think that's all I have.  
15 Thanks.

16 MS. PARKS: Let's change real quick.

17 1:12

18 (WHEREUPON, THERE WAS A BREAK IN THE PROCEEDINGS,  
19 AFTER WHICH THE TESTIMONY RESUMED AS FOLLOWS:)

20 1:13

21 EXAMINATION

22 BY MS. PARKS:

23 Q. Dr. Irons, I just have a couple of questions for  
24 you. Mr. Scott asked you about the fact that there are no  
25 epidemiological studies that show benzene has association

1 with the development of the 5q minus. Do you recall that  
2 syndrome?

3 A. Yes.

4 Q. The reason for that, sir, is because there is no  
5 epidemiological studies that categorize myelodysplastic  
6 syndromes into these WHO categories; is that true?

7 A. It's true that studies that have looked at and  
8 evaluated the association between benzene and MDS have not  
9 provided resolution of the subtypes.

10 Q. Have you recommended that such an epidemiological  
11 study be conducted?

12 A. That's what we did. So, yes.

13 Q. Other than your study?

14 A. Other than my study?

15 Q. Yes.

16 A. The only study I've had any influence or  
17 participation in of this magnitude was mine.

18 Q. Have you spoken with any other scientists such as  
19 yourself on conducting an independent study not paid for by  
20 the API or the oil companies to confirm your findings?

21 MR. SCOTT: Object to the form of the  
22 question.

23 A. No.

24 Q. Dr. Bennett, let me ask you about the diagnosis he  
25 did as a third party. You said you did all the diagnoses to

1 begin with.

2 A. Yes.

3 Q. And then you had some confirmed through an outside  
4 source, correct?

5 A. All of them were independently reviewed.

6 Q. Independently reviewed by either Dr. John Rider or  
7 Dr. John Bennett?

8 A. No, Dr. John Rider reviewed everyone. Dr. Bennett  
9 reviewed specific cases and selected cases. Those were there  
10 were either issues or in the case of the benzene -- the  
11 benzene dysplasia cases, he reviewed those.

12 Q. Were they specifically requested to confirm the  
13 diagnosis pursuant to the WHO classification?

14 A. That was -- that's the basis -- that is the basis  
15 upon which the clinical diagnoses were made, and that's the  
16 basis -- and that's the assumed basis under which they are  
17 reviewed.

18 Q. So, the answer is yes?

19 A. Yes.

20 Q. And who paid Dr. Bennett and Dr. Rider to review  
21 the diagnosis that you had made previously?

22 A. They were both -- they were both subcontracted from  
23 the University of Colorado as part of the Shanghai health  
24 study.

25 Q. And the University of Colorado is the same

1 institute that you work for as well, correct, or did at the  
2 time of your studies?

3 A. Yes.

4 Q. Do you still work for the University of Colorado?

5 A. I'm professor emeritus which means I get an office  
6 and a telephone forever, but I no longer am paid by the  
7 University of Colorado.

8 Q. At what point did you stop being paid by the  
9 University of Colorado?

10 A. In 2007.

11 Q. And have you taught any classes there since 2007?

12 A. Yes.

13 Q. What classes have you taught at the University of  
14 Colorado?

15 A. I've -- I've given seminars and expert sessions to  
16 pathology residents and hematopathology fellows.

17 MS. PARKS: I don't have any more.

18 A. I believe I've also given a lecture or two in  
19 toxicology.

20 MS. PARKS: That's all I have, Dr. Irons.

21 1:16

22 EXAMINATION

23 BY MR. SCOTT:

24 Q. Dr. Irons, do you have the Travis paper -- travis  
25 1994 paper among your references here?

1       A.    I would be surprised if I don't.

2       Q.    If you have it there, did Travis -- there has been  
3 some discussion about whether subtypes of MDS were evaluated  
4 in the NCI papers. Were subtypes of MDS evaluated as early  
5 as 1994 in the Travis paper?

6       A.    Yes, to the degree that was possible at the time  
7 and based upon the material that they had.

8       Q.    Just looking down Tables 2 and 3, I see RAEB-T,  
9 R-A-E-B-T. What is that?

10      A.    That is the older FAB classification, and it's  
11 refractory anemia with excess blasts and transformation  
12 which -- which basically means that it wasn't quite a  
13 leukemia. But that's using the older classification. It  
14 would not be classified as that today.

15               MR. SCOTT: I think that's all I have.  
16 Thanks.

17                               1:18

18                               EXAMINATION

19 BY MS. PARKS:

20      Q.    Doctor, in the Vineis study did they find a strong  
21 association between solvent exposure and myelodysplastic  
22 disorders?

23      A.    They did, but they -- specifically they found no  
24 cytogenetic abnormality involving minus 5 in solvent-exposed  
25 individuals.

1 Q. And speaking of which, do you recall how many cases  
2 of deletion 5q abnormalities were in that study?

3 A. I think they found one or two.

4 Q. So, there were no cases out of one or two cases  
5 there --

6 A. That's correct, for the total that had cytogenetic  
7 abnormalities.

8 Q. So, you would agree that's very small?

9 A. It is a small group, yeah.

10 Q. And in addition to that, in your report one thing  
11 that you stated was, and I quote, because MDS and AML are  
12 distinct diagnostic and biological entities it is  
13 inappropriate to arbitrarily combine these two disease in an  
14 epidemiologic study.

15 Can you show me an article or a study or a  
16 commentary that states that combining MDS and AML is  
17 inappropriate?

18 A. I can show you -- there are several. I can show  
19 you an explicit statement that they are, in fact,  
20 biologically different diseases with different causes.

21 Q. That's actually not my question, Dr. Irons. My  
22 question is, can you show me a study, an article or  
23 commentary that says it is inappropriate to arbitrarily  
24 combine MDS and AML?

25 MR. SCOTT: Object to the form.

1       A.    As I said, I can show you -- there are many --  
2 there are several -- several pieces -- there are several  
3 references and pieces of information to support the  
4 biological basis for discriminating those diseases. With  
5 respect to the opinion as to whether or not it's appropriate  
6 to combine those for purposes of causal inference, the  
7 opinion is mine.

8       Q.    How long have they been combining, and by they, I  
9 mean epidemiological studies, how long have they combined MDS  
10 and AML, to your knowledge?

11       A.    Well, the number that have actually done it is  
12 relatively small. The Hayes study was one of the first based  
13 in epidemiologic point of view. MDS and AML have been  
14 combined in therapeutic studies, studies of  
15 therapeutic-induced disease, for a long time, but there you  
16 are talking about as outlined in WHO a very specific subtype.  
17 The combination of all MDS nonspecific and MDS nonspecific is  
18 not commonly done but has been done in cases such as the  
19 Hayes study.

20       Q.    When you saw that a study inappropriately, in your  
21 words, combined the two diseases, did you write any  
22 commentary, did you write to the authors, did you try to  
23 express your thoughts that that was an inappropriate method  
24 for any of the epidemiological studies like this, such as  
25 Hayes?

1       A.   Specifically, no.

2                   MS. PARKS:  That's all I have.  Thank you.

3                                   1:22

4                                   EXAMINATION

5 BY MR. SCOTT:

6       Q.   One last question.  Do you have the Strom article  
7 handy?

8       A.   Yeah.

9       Q.   I have a question I think we can answer from the  
10 abstract.  I just want you to confirm that the Strom author,  
11 this is M. D. Anderson group, found that drinking wine  
12 reduced the risk for all FAB types of MDS by almost 50  
13 percent.

14      A.   That's correct.

15                   MR. SCOTT:  Love it.  That's it.

16                                   1:22

17                                   EXAMINATION

18 BY MS. PARKS:

19      Q.   I was going to ask you another question, but I'm  
20 okay now.

21                   Did the Strom article also show significant dose  
22 response with myelodysplastic syndromes combined?

23                   MR. SCOTT:  Object to the form.

24      A.   Yes.

25                   MS. PARKS:  That's all I have.  Thank you,

1 sir.

2 MR. SCOTT: No more.

3 1:24

4

5 (CONCLUSION OF DEPOSITION)

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1 NO. B-176,114  
 2 RICHARD E. NOLEN \* IN THE DISTRICT COURT OF  
 AND NITA NOLEN, \*  
 3 \*  
 VS. \* JEFFERSON COUNTY, TEXAS  
 4 \*  
 E.I. DU PONT DE NEMOURS & \*  
 5 COMPANY, ET AL \* 60TH JUDICIAL DISTRICT

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6  
 7 REPORTER'S CERTIFICATION  
 8 DEPOSITION OF DR. RICHARD IRONS  
 9 FEBRUARY 4, 2010  
 10

11 I, STACY AMY BAKLIK, Certified Shorthand Reporter  
 12 in and for the State of Texas, hereby certify to the  
 13 following:

14 That the witness, DR. RICHARD IRONS, was duly sworn  
 15 by the officer and that the transcript of the oral deposition  
 16 is a true record of the testimony given by the witness;

17 That the deposition transcript was submitted on  
 18 2/10/10 to the witness or the attorney for the witness for  
 19 examination, signature and return to me within 20 days;

20 That the amount of time used by each party at the  
 21 deposition is as follows:

22 Ms. Parks - 2 hours, 43 minutes

23 Mr. Scott - 19 minutes

24 That pursuant to information given to the  
 25 deposition officer at the time said testimony was taken, the

1 following includes counsel for all parties of record:

2 MS. D'JUANA PARKS and, Attorney for Plaintiff;

3 MR. ROBERT SCOTT, Attorney for Defendant;

4 MR. MIKE BAKER, Attorney for Defendant.

5 I further certify that I am neither counsel for,  
6 related to, nor employed by any of the parties or attorneys  
7 in the action in which this proceeding was taken, and further  
8 that I am not financially or otherwise interested in the  
9 outcome of the action.

10 Further certification requirements pursuant to Rule  
11 203 of TRCP will be certified to after they have occurred.

12 Certified to by me this 10th day of February, 2010.

13

14

15



STACY AMY BAKLIK, CSR

16

Texas CSR No. 2680

Firm Registration No. 30

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Expiration Date: 12/31/2010

P. O. Box 566

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Nederland, Texas 77627

(409)729-3838

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FURTHER CERTIFICATION UNDER RULE 203 TRCP

21

22 The original deposition was/was not returned to the  
deposition officer on \_\_\_\_\_;

23

24 If returned, the attached Changes and Signature  
page contains any changes and the reasons therefor;

25

If returned, the original deposition was delivered

1 to Ms. D'Juana Parks, the Custodial Attorney;

2 That \$ \_\_\_\_\_ is the deposition officer's  
3 charges to the Plaintiff for preparing the original  
4 deposition transcript and any copies of exhibits;

5 That the deposition was delivered in accordance  
6 with Rule 203.3, and that a copy of the certificate was  
7 served on all parties shown herein on and filed with the  
8 Clerk.

9 Certified to by me this \_\_\_\_\_ day of  
10 \_\_\_\_\_, \_\_\_\_\_.  
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\_\_\_\_\_  
STACY AMY BAKLIK, CSR

Texas CSR No. 2680

Firm Registration No. 30

Expiration Date: 12/31/2010

P. O. Box 566

Nederland, Texas 77627

(409) 729-3838

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1 CHANGES AND SIGNATURE

2 WITNESS NAME: DR. RICHARD IRONS

3 DATE OF DEPOSITION: FEBRUARY 4, 2010

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| 5 PAGE LINE | CHANGE | REASON |
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1 I, DR. RICHARD IRONS, have read the foregoing  
2 deposition and hereby affix my signature that same is true  
3 and correct, except as noted above.

4

5

6

DR. RICHARD IRONS

7

8 THE STATE OF \_\_\_\_\_:

9 COUNTY OF \_\_\_\_\_:

10 Before me, \_\_\_\_\_, on this day  
11 personally appeared DR. RICHARD IRONS, known to me or proved  
12 to me under oath or through \_\_\_\_\_ (description  
13 of identity card or other document) to be the person whose  
14 name is subscribed to the foregoing instrument and  
15 acknowledged to me that they executed the same for the  
16 purposes and consideration therein expressed.

17 Given under my hand and seal of office this  
18 \_\_\_\_\_ day of \_\_\_\_\_, \_\_\_\_\_.

19

20

21

NOTARY PUBLIC IN AND FOR

22

THE STATE OF \_\_\_\_\_

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25

**Richard D. Irons  
4800 Baseline Road  
E104 PMB253  
Boulder, CO 80303**

January 5, 2010

Robert Scott  
Abrams, Scott & Bickley, LLP  
700 Louisiana, Suite 4000  
Houston, TX 77002-2727

Dear Mr. Scott:

You have asked me whether Mr. Richard Nolen's disease, myelodysplastic syndrome (MDS) associated with del(5q), could have been caused or contributed to by his alleged exposure to benzene.

Herewith is a brief summary of my qualifications. I am Professor Emeritus of Toxicology and Pathology at the University of Colorado Denver where I served as a member of the faculty for 20 years. During this period, I was Director of the Toxicology and Environmental Health Sciences Program at the University of Colorado, and leader of the Cancer Causation Program of the University of Colorado Comprehensive Cancer Center. I also am Professor of Pathology and Director of the Fudan-Cinpathogen Clinical and Molecular Research Center (CMRC) Institutes of Biomedical Sciences, Fudan University in Shanghai, China. The CMRC conducts research on the pathogenesis of hematopoietic and lymphoid diseases and provides diagnostic services in hematopathology for 40 hospitals in Shanghai, China. Since 2003, the CMRC has diagnosed over 2000 individual cases of blood disease including 650 cases of myelodysplastic syndromes (MDS) and 750 cases of acute myeloid leukemia (AML). I received a B.A. degree from Raymond College, University of the Pacific, postgraduate training in medical technology at San Joaquin General Hospital and the University of California, San Francisco, and a Ph.D. in Toxicology from the University of Rochester. From 1974 to 1977 I was a Pathology Fellow in Pathology and Immunopathology at Strong Memorial Hospital, University of Rochester. From 1977 to 1988, I was Senior Scientist at the Chemical Industry Institute of Toxicology, Research Triangle Park, North Carolina. I am a Diplomate of the American Board of Toxicology and licensed as a Clinical Laboratory Scientist by the State of California. At various times from 1977 to the present I have taught pathology, toxicology, immunology, hematology, occupational medicine and epidemiology at the university level. I have given more than 100 invited scientific presentations before meetings sponsored by the American Society of

Pathologists, the Brookings Institution, the United States Environmental Protection Agency, the United States Food and Drug Administration, the Royal Society of Medicine, the National Aeronautics and Space Administration, the Society of Toxicology and the Environmental Mutagen Society among others. I am a member of a number of scientific and professional societies including the Society of Toxicology, the International Society of Experimental Hematology, the American Association of Investigative Pathology and the American Society of Hematology, each of which requires nomination and election to membership based on scientific expertise in their respective fields. At various times I have been an editor or member of the editorial boards of 10 peer-reviewed scientific journals including: Toxicology and Applied Pharmacology, Toxicology, Journal of Biochemical Toxicology, Methods in Toxicology, Journal of Cell Biology and Toxicology, and the Journal of Experimental and Molecular Pathology. I am a former member of the United States Environmental Protection Agency Health Effects Review Panel and have served as a consultant to that agency on risk assessment issues pertaining to benzene and 1,3-butadiene. I am a former member of the Board of Directors of the American Board of Toxicology. I have previously served on the National Academy of Sciences Toxicology Information Program Committee and was Chairman of the National Institutes of Health Toxicology Study Section. I have also served as a consultant or advisor to the governments of Canada, Great Britain, the People's Republic of China, the North Atlantic Treaty Organization, and the states of California and Colorado. I am author of the book Toxicology of the Blood and Bone Marrow (Raven Press, 1985) and have written some 19 book chapters including "Benzene and Other Hematopoietic Toxicants," in Hazardous Materials Toxicology (Williams and Wilkins, 1991), and "Histology of the Immune System: Structure and Function," in Toxicology and the Immune System (Raven Press, 1985). I have over 30 years research experience in the fields of toxicology, hematology, pathology and carcinogenesis and am the author of more than 150 books, book chapters, peer reviewed articles and abstracts in scientific journals, over 100 of which have dealt with the mechanisms of bone marrow toxicity, chemical leukemogenesis and clinical and molecular pathology. Several of these have dealt with mechanisms of bone marrow toxicity, the clinical laboratory diagnosis of hematopoietic diseases, mechanisms of bone marrow toxicity, chemical leukemogenesis, clinical and molecular pathology and hematopathology. My qualifications are set forth in greater detail in my curriculum vitae attached hereto as an Attachment.

The statements and opinions made herein below by me are based on: (i) personal knowledge of the scientific literature pertaining to the hazards and toxicity of chemicals and solvents; (ii) facts or data reasonably relied upon by persons in my field, (i.e. toxicology); (iii) my scientific expertise and experience in the conduct of research on the toxicity of benzene, substituted benzenes, including xylenes, toluene and ethyl benzene, and other chemicals; (iv) my scientific expertise and experience in the conduct of research on toxicity of and the mechanisms of the blood, bone marrow, and immune system; (v) my specific experience and expertise in the characterization of the pathogenesis of hematopoietic disease occurring in individuals previously exposed to benzene; (vi) my scientific expertise and experience in the conduct of research on the laboratory diagnosis of hematopoietic and lymphoid diseases, specifically MDS and AML, and (vii) my review of the documents and materials made available to me in this case including: medical records of Mr. Richard Nolen from: Memorial Hermann Hospital, St Luke's Episcopal Hospital, Houston TX, Texas Oncology, PA, Southeast Texas Cardiology Associates, Dr. John Humble, the expert reports of Dr.'s Frank Gardner, Peter Infante, Thomas L. Kurt, John M.

Dement, Nark Nicas, Mr. Frank Parker, the affidavits of Clifton J Barbo and Don Ray, and the oral depositions of Mr. Richard Nolen taken on 1-24-08 and 6-15-09.

Mr. Richard Nolen was diagnosed with MDS 5q- syndrome in November, 2003 at the age of 73. The clinical features, laboratory data and course of Mr. Nolen's disease are consistent with this diagnosis. His previous medical history is significant for a macrocytic anemia since at least 1999, a 50 pack-yr smoking history, hypertension, emphysema and cardiovascular disease. Mr. Nolen was employed in the oil drilling and service industry from approximately 1953-1977.

The public as well as the medical and scientific communities encounter a variety of types of sources of information and documents relating to the potential causes of diseases, including epidemiological (quantitative human) studies, anecdotal case reports, arbitrary collections of cases, published opinions, regulatory documents, review articles, as well as the popular press. For purposes of expressing opinions on causation or the specificity disease, however, it is appropriate that the medical and scientific communities rely on only some of these sources and documents. Relevant epidemiology studies, properly designed, conducted and interpreted, are the most compelling evidence regarding human health effects. Large case series are also useful in resolving specific disease entities and their prevalence in a population provided they utilize standardized criteria for diagnosis and classification that comport with the state of the art in science and medicine. Another important consideration in evaluating the validity of epidemiology studies is the degree of objectivity and precision employed in the selection of "exposed" versus "unexposed" populations. The most reliable studies utilize at least to some degree direct quantitative exposure analyses based on actual measured values of the substance being studied and compare objectively defined cohorts of individuals that differ as little as possible in other parameters such as environment, behavior, age, gender etc. These quantitative studies must be contrasted with "anecdotal case reports" or collections of case reports, studies in which the degree of exposure is unknown or vague, there is no immediate connection between the alleged exposure and the alleged ill effect, and there is little or no ability to control for the possibility of other causative factors. In addition, personal letters, editorial opinions, pamphlets, abstracts, meeting notes, regulatory or court testimony, as well as published opinions are not peer reviewed with respect to scientific content and are subject to numerous types of bias. The formulation of opinions regarding medical causation based on documents such as these is therefore unscientific and speculative. Although textbooks can be useful for background or general information they are not peer-reviewed science and may also be subject to error and bias. Criteria documents and risk assessments promulgated by regulatory governmental or non-governmental agencies are not primary reviewed literature but secondary sources that review information for purposes of supporting regulatory standard setting or risk analysis and are not scientific evidence appropriate for rendering opinions concerning disease specificity and causation.

The accepted methodology in the scientific and medical communities for rendering an opinion on causation of disease consists of the application of uniform criteria for assessing the validity and quality of scientific and medical data. These criteria have been described and discussed in a number of scientific treatises and are variously referred to as the Bradford-Hill criteria, the Henle-Koch postulates or evidence based medicine [1-7]. Under these criteria a series of questions must be answered before reaching a conclusion of causal inference: (1) How strong is the evidence of an association in the quantitative epidemiological literature?; (2) Is the

association reproducible and consistently observed by different investigators in different quantitative epidemiology studies?; (3) How specific is the association with respect to a given chemical or risk factor and specific disease?; (4) What is the temporal relationship between the exposure and the risk of developing the disease?; (5) What is the dose-response relationship between exposure to the chemical and the risk of developing the disease?; (6) Is there a plausible biological mechanism to explain how the chemical or risk factor causes the disease?; (7) Does the hypothesis make sense in terms of what is known about the history and biology of the disease?; (8) Are there alternative mechanisms or known risk factors that potentially could have caused the disease or confound interpretation of the results?

The first 4 of these criteria are essential for reaching a conclusion that a causal association exists between a specific agent or behavior and a disease. Although other criteria, such as the demonstration of dose response, biological plausibility, experimental evidence and evaluation of other potential causes or confounders, are important and necessary in reaching a conclusion that a causal association exists between a given chemical exposure and a specific disease, these criteria by themselves they are not adequate substitutes for specific quantitative epidemiological evidence as outlined in the first 4 criteria. When quantitative epidemiological studies attempting to find a correlation between a particular chemical and adverse human health effects do not reveal a consistent pattern associating a specific disease with exposure to a specific agent, one cannot opine consistent with generally accepted medical or scientific practice that exposure to that particular chemical caused or substantially contributed to the development of that disease.

The first criteria requires that the prevalence of the disease should be significantly higher in those exposed to the hypothesized cause than in controls not so exposed, and that incidence of the disease should be significantly higher in those exposed to the cause than in those not so exposed. The standard adopted and required by the scientific community in evaluating the strength of a statistical association is that the 95% confidence interval not include a relative risk (RR) of 1.0 (i.e. that the range of possible outcomes does not include the null or control value). Relative risk refers to the risk of developing a specific disease in a population exposed to given levels of an agent compared to the risk of developing the same disease in a control population not so exposed. In practice, for the majority of epidemiology studies, this typically requires that a given hypothetical exposure confer a relative risk of greater than 2.0 (i.e. twice the frequency of a specific disease that is encountered in the general population).

The second criteria in establishing causation is that the available independent quantitative epidemiology studies meeting the criteria outlined above establish a consistent pattern of positive results, thus meeting the important scientific requirement for reproducibility. Many ongoing studies of cohort populations result in the publication of multiple updates and follow up analyses on the same group. For purposes of determining causation, these should be considered as a single study with individual reports not regarded as independent evidence, and the results of successive analyses should provide a consistent pattern of results. If the various results forthcoming from such studies are weak or inconsistent, then they do not meet the accepted standard for reproducibility.

The third criteria requires that the quantitative association be demonstrated between a specific chemical or risk factor and a specific disease. It is an established consensus of the medical and scientific communities that cancer is not one but many different diseases that arise

in different cells, involve different genetic or biological events, have different causes and respond to different treatments [8-9]. For example, hematopoietic neoplasms are diseases of the blood that can be distinguished according to specific diagnostic criteria, causation, cell of origin, pattern of genetic involvement, predominant cell types involved, prognosis and treatment. The myelodysplastic syndromes (MDS) and acute myeloid leukemias (AML) are two separate, broad categories of hematopoietic disease that each include a number of specifically defined diseases or subtypes of disease [10-11].

Myelodysplastic syndromes (MDS) are a recognized group of hematologic neoplasms that are characterized by bone marrow failure, *i.e.* a decrease in one or more circulating blood types, accompanied by specific morphologic abnormalities in the bone marrow (dysplasia). The criteria for diagnosis and classification of these diseases in the modern era are outlined in the World Health Organization Classification of Tumours of Hematopoietic and Lymphoid tissues (WHO2001 and WHO2008) [10-11]. The WHO2001 and WHO2008 represent a major departure from previous disease classification schemes (*e.g.* FAB, ICD 7,8,9 etc) in that they provide both the *diagnostic criteria* as well as the terminology for the classification of hematopoietic diseases and utilize all available information, (*i.e.* morphology, immunophenotype, genetic and molecular abnormalities as well as clinical features) to define these diseases [10-12]. WHO2001/WHO2008 have replaced the first attempt by the French-American-British (FAB) Co-operative Group to classify the “dysmyelopoietic syndromes” entirely on morphologic grounds in 1976 [13]. This earlier classification was formalized in a proposal for the morphologic classification of MDS in 1982 [14]. Since then additional major advances in biology, diagnosis and terminology of MDS have resulted in the widespread adoption of the WHO classification.

In the past, recognition of MDS as a specific disease was hampered by the use of uneven, vague and imprecise terminology such as “preleukemia,” “subacute leukemia,” “atypical leukemia” etc. that did not distinguish MDS from other disease entities [15-18]. The older epidemiologic classification schemes, including the ICD-9 classification (1998), often intermingled cases of MDS with different proliferative diseases or leukemias, including leukemias (some AML) and primary myelofibrosis (MF), among others, all of which are now excluded from classification as MDS [19]. These advances in diagnosis and classification of MDS underscore the importance of understanding the classification criteria employed in different studies when interpreting or comparing diagnostic or epidemiologic data. For example, we have described significant differences in the observed prevalence of MDS and AML, as well as their individual subtypes, in a single population occurring as a consequence of using FAB versus WHO classification schemes [20]

Theories on mechanisms of disease causation are not surrogates for reliable quantitative epidemiologic evidence of a causal relationship between a specific agent and a specific disease. However, theories may be informative in evaluating the context of results obtained using current versus older scientific and clinical methodologies. Historical theories regarding the cell of origin and pathogenesis of MDS have presumed a role for the “pluripotential” or hematopoietic stem cell in the evolution of MDS. Nevertheless, the definition of “stem cell,” as variously used in this context is antiquated, inconsistent and ambiguous, and more recent studies have called this terminology into question [21-23]. Some cases of MDS undergo transformation to acute myeloid leukemia (AML), at a rate of about 10-30% that varies with individual subtype [11, 24].

In our own series the overall rate of progression is about 10% [25]. This fact notwithstanding, it is generally accepted in the scientific and medical communities that MDS and AML are distinct and separate diseases [11, 21]. MDS 5q- syndrome is a recognized distinct subtype of MDS with a relatively good prognosis and a transformation rate to AML of typically less than 10% [11, 26]. Medical and scientific authorities do not confuse MDS 5q- syndrome with therapy-related MDS or AML (tAML/tMDS).

The subtype of AML and MDS known to develop in some individuals following therapy with alkylating chemotherapeutic drugs or radiation is tAML/tMDS [27-30]. tAML/tMDS is regarded as a distinct and separate disease from either AML or MDS developing *de novo* and is classified as a separate entity [11, 27, 29-34]. This syndrome presents with distinct clinical, genetic and morphologic features, is formally classified as a separate entity by WHO and should not be confused with the arbitrary co-mingling or combination of other forms of MDS and AML for statistical convenience.

At present there are no epidemiologic cohort or case-control studies that meet sufficient criteria for disease specificity or exposure to quantify the risk of MDS associated with benzene. A series of articles have described and analyzed a retrospective study of benzene exposed workers in China (1972-1987) carried out by the Chinese Academy of Occupational Medicine and the US National Cancer Institute [35-37]. Because these publications analyze and report on the same cohort it is appropriate for purposes of causal inference to review them together rather than as individual independent studies. A total of 7 cases of MDS were initially reported in a cohort of over 74,000 benzene-exposed workers, of which 5 were subject to independent histological review. Based on the older criteria for the classification of MDS used [14], 3 of these cases would not meet current criteria for classification as MDS, and no case of MDS 5q- syndrome was reported. The authors combined the original 7 cases of MDS together with cases of AML to arrive at an estimate of overall MDS/AML risk. Because MDS and AML are distinct diagnostic and biological entities, it is inappropriate to arbitrarily combine these two diseases in epidemiologic studies. As previously noted, epidemiologic or statistical analyses employing arbitrary combinations of AML and MDS cases should not be interpreted as providing evidence relevant to the distinct biological entity, tMDS/ tAML, and does not provide a specific estimate of the risk of MDS occurring in a benzene-exposed population.

In an update analysis of a retrospective mortality study among workers in a petroleum manufacturing plant, Honda et al did not demonstrate any specific quantitative association benzene exposure and the development of AML, the type of leukemia previously demonstrated to be causally associated with chronic exposure to high concentrations of benzene [38]. Further, MDS and other myeloproliferative diseases were indistinguishably grouped together based on a variety of diagnostic criteria over the period from 1940-1989. These authors in fact conclude that if MDS and AML are considered as a single disease category, the combined observed number of deaths is approximately equal to the expected number. Therefore, this study provides no basis for concluding that benzene is associated with the results presented, nor does it reliably establish a significant risk of MDS in this cohort of petroleum workers. Another article by Nisse et al is a retrospective case-control study of occupational and environmental factors and MDS. This study does not find an increase in MDS associated with general solvent exposure and provides no data with respect to benzene exposure and the incidence of MDS. Moreover, MDS was diagnosed according to FAB criteria, which, if evaluated using WHO criteria would result in

significantly smaller number of cases reported [39]. Strom et al evaluated risk factors for MDS in a hospital based case-control study that examined general risk factors, such alcohol use, smoking, exposure to agricultural chemicals, or solvents [40]. These authors did not measure benzene and did not demonstrate a specific association between benzene exposure and RAEB/RAEBT. Further, the authors state that cases were not diagnosed using WHO (2001) criteria because the criteria were not completely implemented at their center before the start of their study. Because cases meeting criteria for diagnosis of RAEBT under FAB are now classified as AML this would have effectively reduced the size of this category by a further 33% in their combined analysis. Vineis et al compared MDS, together with cytogenetic abnormalities, with solvent exposure using FAB criteria and a questionnaire-based assessment strategy [41]. These authors combined MDS subtypes reported into a single category (RA-RAEB) for analysis, which provides a somewhat more accurate comparison of MDS- FAB with WHO criteria. However, their methodology for assessment of solvent exposure did not provide specific information on exposure to benzene. For purposes of discussion, it should be noted that Vineis et al found no excess of cytogenetic abnormalities among subjects exposed to organic solvents in general, and specifically no del(5q) abnormalities in exposed cases.

Despite the lack of appropriate studies to quantify the risk of MDS following benzene exposure, there are studies utilizing state-of-the-art diagnostics that have directly evaluated the clinical, genetic and morphologic features of MDS developing in individuals unequivocally exposed to high concentrations of benzene. We recently reported on a large hospital-based study of 640 individuals diagnosed in Shanghai, China using WHO2008 criteria [23]. A total of about 13% were determined to have some BZ exposure. The frequency of clonal cytogenetic abnormalities was less in this exposed group than for all MDS cases. We also compared characteristics of MDS between a group of individuals who were exposed to very high concentrations of benzene ( $>67 \text{ mg/m}^3$  for at least 6 months with a mean exposure duration of 144 months) to matched cases with no demonstrated benzene exposure. Analysis of the prevalence of MDS subtypes revealed a high odds ratio (OR) for the WHO subtype MDS-U (OR = 11.1) in cases with high benzene exposure. The prevalence of clonal cytogenetic abnormalities was lower in highly exposed cases compared to matched unexposed cases. Cytogenetic aberrations involving del(5q) alone were not found in individuals with a history of high benzene exposure, and no cases of MDS 5q- syndrome were observed in benzene exposed subjects. Further, the pattern of clinical features observed in benzene highly exposed MDS cases are not characteristic of those typically found in tMDS/tAML secondary to treatment with alkylating chemotherapeutic agents. The pattern of MDS subtype observed in our study is similar to those previously described by Vineis et al in a hospital based study of general solvent exposure and MDS in Torino [41]. These results indicate a pattern of clinical and morphologic features in MDS cases associated with benzene exposure that are distinct from either *de novo* or therapy-related MDS. In addition, the morphology and clinical features described above are essentially identical to those previously reported in Brazilian workers heavily exposed to benzene [42].

If there is consistent quantitative evidence of a relationship between exposure to a given agent and development of a specific disease, evaluation of the dose of a chemical that an individual may have received is important in reaching a conclusion of a causal association. Dose-response applies to virtually all man-made or naturally occurring chemicals or drugs. Therefore, in order to evaluate the potential risks of adverse health effects associated with exposure to a drug or chemical, one has to know the actual dose of the substance that is absorbed

and compare that dose to those shown to cause adverse health effects as well as to doses that have not been shown to result in adverse health effects. The dose is the actual amount of a chemical absorbed by the body and is distinguished from "exposure" or "concentration." Exposure is the opportunity to absorb a dose of a substance, but does not automatically imply that absorption has taken place. Concentration refers to the relative amount of a drug or chemical in a mixture, such as food, air or water. In order to determine dose, a toxicologist must know the concentration of the chemical in food, air or water, the total amount of food, air or water taken in by the body, the route and duration of exposure and the rate of absorption of the chemical of interest via that route. Sometimes toxicologists use a type of shorthand terminology to compare very low concentrations (*i.e.* "parts per million" or "parts per billion"). These terms are only useful in directly comparing relative concentrations of the same substance in similar volumes or masses. For example, 1 ppm benzene in air equals about 3.2 mg benzene in a cubic meter ( $m^3$ ) of air. For purposes of determining the opportunity for exposure to benzene it is important to distinguish between the concentration of benzene in air and the concentration of benzene in another solvent.

The vast majority of occupational exposures to benzene are, in fact, not continuous but are sporadic or intermittent. Because the accuracy of exposure assessments in retrospective epidemiological studies is inherently limited, cumulative exposure (ppm.yr) is the generally accepted convention used to estimate dose. Predictably, the majority of quantitative epidemiology studies that have compared different metrics of exposure for evaluating the risk of AML associated with benzene and have confirmed that cumulative exposure remains the most reliable and sensitive metric for evaluating the risk of AML associated with benzene [43-46]. Cumulative exposure metrics include the spectrum of exposure experiences, such as "intermittent," "sporadic," "peak" or "average," and cumulative exposure analyses are consistent with repeated transient or periodic exposure to high airborne concentrations of benzene. In a single study of chemical plant workers, Collins et al failed to observe a strong correlation with cumulative exposure and all leukemias (non-specific). Nevertheless, even using peak benzene exposure as a metric in this particular study, the relative risks reported were not robust, and the significance with respect to specific disease subtypes cannot be determined [47].

In virtually all occupational settings involving potential exposure to benzene, workers experience combined inhalation and dermal exposures. With the possible exception of exposure to very low levels of benzene [50], inhalation is widely accepted as the major route of benzene absorption [48-49]. In this regard, the metrics used to refer to benzene uptake via the skin, *i.e.* "disappearance, absorption, uptake, flux" etc., via are highly variable and critically dependent on the conditions employed in study design. Reliable quantitative data on the percutaneous absorption of benzene is limited with very few studies employing direct measures of benzene dermal uptake *in vivo* [51-52]. These studies indicate that rates of dermal absorption of benzene are relatively low. The majority of studies have either utilized *in vitro* methods, experimental animal models or employed indirect estimates of benzene absorption and are less reliable [53-54]. Even so, it is well established that benzene is poorly absorbed via the skin relative to other solvents, and numerous authorities have observed, a concentration-dependent linear relationship between direct skin contact in solvent for prolonged periods of time, (*i.e.* immersion), and dermal absorption that is preceded by a lag phase ranging variously between 20-90 min [55-59]. It is important to note that, although rarely documented, dermal exposures to saturated benzene vapor or emersion of hands or forearms in pure benzene solvent for periods of time ranging between 10

- 30 minutes are associated with severe irritation of the skin and 2<sup>nd</sup> degree burns [60-61]. Therefore, it is highly unlikely that Mr. Nolen experienced repeated exposure to pure benzene via immersion for 20-40 min per day, and the assumptions made by Dr. Nicas in his estimates of dermal exposure are inconsistent with the absence of dermatopathology in Mr. Nolen's medical history.

In my review of plaintiff's expert reports, several articles and reports are relied upon that do not deal with MDS and are not relevant to questions at issue in this case. However, for purposes of discussion, I will address some of these reports. Dr. Gardner relies on a mouse study that measured aneuploidy in mouse bone marrow cells following dermal exposure to benzene or trichloroethylene. The relevance of this murine model or aneuploidy to the development of MDS in humans associated with benzene exposure has not been established, and the authors state that "the level of aneuploid HSC induced by relatively high doses of benzene and trichloroethylene applied topically in mice cannot be used to estimate genomic damage to human HSC in exposed individuals [62]." Dr. Infante refers to depressed WBC, RBC and neutrophils reported in subjects exposed to benzene at or below 0.25 ppm [63], when, in fact, these results are not found in the publication cited. Further, peripheral blood values reported in both Qu and Lan [64] papers cited by Dr. Infante are within the normal range for clinical laboratory values in China. Moreover, minor fluctuations in peripheral blood CFU have not been validated as sensitive or reliable biomarkers of bone marrow toxicity [65-69].

Dr. Infante cites Kirkeleit et al (2008) as reporting a "significantly elevated risk" of leukemia (non-specific) associated with an average benzene exposure level of 0.037 ppm. The analysis of risk of "leukemia" does not provide evidence of an association with a specific disease and therefore is inappropriate for use in determining causal inference. Further, the authors did not directly measure benzene in this study but estimated exposures for 4 broad categories of upstream petroleum workers based on previous published reports. These authors acknowledged that specific tasks, which have reported real time exposures as high as 16.8 ppm, were major determinants that may contributed significantly to benzene exposure [70]. Moreover, Kerkeleit et al state, "at present it is unclear at which level of exposure benzene poses an increased risk of developing hematopoietic neoplasms. Previous studies that assessed the association between benzene exposure and hematologic neoplasms in cohorts of petroleum workers were limited by the lack of good exposure estimates including information on the variability of benzene exposure. This is also a major limitation of our study." Dr. Infante also refers to a case-control study by Guenel et al (2002) as demonstrating a "significantly elevated OR for leukemia (all types combined)." In this study, no benzene measurements were taken, benzene concentration was not determined in any solvent, the "opportunity for exposure" was determined by company employees rather than an independent party, and the values for cumulative exposure were based on guesses of the benzene content in other materials. Again, the lack of disease specificity as well as the absence of quantitative exposure analysis of benzene renders this study is inappropriate for evaluation of disease causation or dose [71]. Dr. Infante states that Rushton and Romaniuk reported an increased risk of AML and "myeloid leukemia" in a case control study of workers employed in the petroleum industry. Yet, these authors reach the conclusion that "doubt remains whether there is a risk of acute myeloid or monocytic leukemia below 45 ppm.yr [43]." Reference is also repeatedly made to several publications that represent ongoing and follow up analyses of what is commonly referred to the Australian Health Watch Study. Among others, these reports include an updated cohort study of the incidence of cancer in

approximately 18,000 Australian petroleum workers [72] as well as a nested case control analysis of leukemia risk within a much smaller subset (i.e. 79) of workers [73]. These authors variously report an excess risk of benzene exposure in the small subset [73], and no significant increase in risk of [AML] in the entire cohort [72]. The most recent update (not peer reviewed) reports a deficit of "leukemia"(non-specific) [74]. As previously noted, for purposes of causal inference, it is appropriate to consider these as a single study with alternatively weak, insignificant and negative results with respect to the risk of "leukemia" associated with benzene exposure. Finally, as previously cited, several analyses of different epidemiology studies of workers chronically exposed to benzene have reported statistically significant elevations in AML at cumulative exposures between 40-200 ppm.years based on estimates of airborne exposure to benzene [37, 43, 45-46, 75-77]. For reasons previously discussed, none of these studies provide evidence to support a quantitative relationship between chronic benzene exposure and the development of MDS in general or specifically, MDS 5q- syndrome.

In conclusion, it is my opinion based upon a reasonable scientific probability that there is no basis in the scientific literature upon which to conclude that exposure to benzene can result in the development of Mr. Nolen's disease, MDS 5q- syndrome. Further, the assumption of plaintiff's experts that dermal uptake constitutes a major source of Mr. Nolen's alleged occupational exposure to benzene is not supported by the scientific literature, neither is it consistent with Mr. Nolen's medical history. It is my intention to offer these opinions at trial, reserving the right to modify or amend my testimony, pending review of additional records, should they be made available, and to respond to any additional issues or opinions raised by the plaintiffs' experts.

Sincerely,



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Toxicology Training Program, University of Rochester (1970-1974)  
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San Joaquin General Hospital: University of California  
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Raymond College, University of the Pacific (1965-1968)  
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**POSTGRADUATE TRAINING**

Department of Pathology, Strong Memorial Hospital, University of Rochester (1974-1976)  
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National Fellow, National Institute of Arthritis, Metabolism and Digestive Diseases (1974-1976)

**BOARD CERTIFICATIONS AND LICENSES**

State of California: Clinical Laboratory Scientist  
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**PROFESSIONAL EXPERIENCE**

2007-Present, Professor Emeritus of Toxicology and Pathology, University of Colorado Denver

2007-Present, Director, Fudan-Cinpathogen Clinical and Molecular Research Center, Institutes of Biomedical Sciences, Fudan University, Shanghai, China

2005-Present, Professor of Pathology, Fudan University, Shanghai, China.

2005-Present, Professor, Institutes of Biomedical Sciences, Fudan University, Shanghai, China

2002-2007, Professor and Director, Sino-US Joint Clinical and Molecular Laboratory, Fudan University, Shanghai, China

1993-2003, Leader, Carcinogenesis and Prevention Program, University of Colorado Comprehensive Cancer Center

1989-2007, Professor and Director, Molecular Toxicology and Environmental Health Sciences, School of Pharmacy, University of Colorado Health Sciences Center

1989-2007, Professor, Department of Pathology, University of Colorado School of Medicine

1989-2007, Member, University of Colorado Comprehensive Cancer Center

1989-1997, Director, Toxicology Training Program, University of Colorado Health Sciences Center

1987-1990, Adjunct Faculty, Toxicology Program, Duke University

1977-1988, Chemical Industry Institute of Toxicology, 6 Davis Drive, Research Triangle Park, NC 27709.  
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### **UNIVERSITY COMMITTEE ACTIVITIES**

2005- Member, Advisory Committee, Fudan University Centenary Anniversary Celebration

1998-2007, Member, Chancellor's Search Committee, Health Sciences Center

1998-2007, Chairman, Seed Grant Review Committee, Dept Pharmaceutical Sciences

1995-2007, Vice Chancellor's Search Committee, Health Sciences Center

1993-2002, Member, Chancellor's Indirect Cost Recovery Waiver Committee

1993-2001, Management Committee, University of Colorado Comprehensive Cancer Center

1998-2007, Chairman, Chancellor's Environmental Health & Safety Committee, Health Sciences Center

1998-2004, Member, Chancellor's Faculty Advisory Committee, Health Sciences Center

1998- Member, Chancellor's Blue Ribbon Advisory Committee on COMIRB oversight

1999-2001, Chairman, Chancellor's Faculty Advisory Committee, Health Sciences Center

1990-2007, Member, Chancellor's Environmental Health & Safety Committee, Health Sciences Center

1990-1992, Chairman, Chancellor's Environmental Health & Safety Committee, Health Sciences Center

1990-2001, Member, University of Colorado Occupational and Environmental Medicine Residency Advisory Committee

1990-1994, Member, University of Colorado Biotechnology Faculty Advisory Board

1989-1996, University of Colorado Comprehensive Cancer Center Board of Directors

### **ORGANIZATIONAL EXPERIENCE**

#### **Government and Professional Advisory Activities**

Continuing Education Committee, Society of Toxicology (1996-1999)

Health Effects Institute (1993)

Consultant, Health and Welfare, Canada (1991, 1998)

Member, NIH/EPA Superfund Study Section (1991)

Member, Board of Directors, American Board of Toxicology (1990-1994)

Member, Health Professionals Environmental Education Advisory Board, Colorado State Department of Health (1989)

Consultant, State of California Department of Health Services, Air and Water Quality Standards (1988)

Consultant, Occupational Medicine, People's Republic of China (1988)

Member, EPA Health Effects Review Panel (1987-1993)

Chairman, NIH Toxicology Study Section (1986-1987)

Permanent Member, Toxicology Study Section (1983-1987)

Member, National Academy of Sciences Toxicology Information Program Committee (1986-1990)

Consultant, Health Effects Institute, Cambridge, MA (1987)

Consultant, National Toxicology Program, NIEHS (1984-1987)

Consultant, Permanent Commission on Occupational Health, U.K. (1983)

Ad Hoc Member, NIH Special Study Section, Cell Biology (1982)

Ad Hoc Member, NIH Special Study Section, Immunotoxicology (1981)

Consultant, Drug Disposition, Food and Drug Administration (1980)

Ad Hoc Member, NIH Study Section, Toxicology (1979)

### **ORGANIZATION OF SYMPOSIA AND CONFERENCES**

Organization Committee, NIH Symposium on Calcium Homeostasis in Toxicology (1988)

Organization Committee, NIH Symposium on Benzene Toxicity (1988)

Session Chairman, Annual Oncology Conference, University of North Carolina (1984)

Organization Committee, NIH Symposium on Immunotoxicity (1983)

Conference Chairman, Immunotoxicology Symposium, Society of Toxicology, San Diego, CA (March 4, 1981)

Organizer/Chair, Target Organ Toxicity Conference on the Blood, NIEHS, Arlington, VA (Feb. 28-29, 1980)

### **EDITORIAL EXPERIENCE**

Editorial Board, Methods in Toxicology (1990-present)

Associate Editor, Toxicology and Applied Pharmacology (1987-1992)

Editor, Journal of Cell Biology and Toxicology (1985-1995)

Editorial Board, Experimental and Molecular Pathology (1984-present)

Consulting Editor, Journal of Leukocyte Biology (1984-85)

Editorial Board, Toxicology (1984-1994)

Editorial Board, Journal of Biochemical Toxicology (1985-93)

Consulting Editor, Journal of the Reticuloendothelial Society (1982-83)

Editorial Board, Fundamental and Applied Toxicology (1981-83)

Contributing Editor, Environmental Health Perspectives (1980)

## **SOCIETY MEMBERSHIPS**

Society of Toxicology

American Association for the Advancement of Science

International Society of Immunopharmacology

International Society for Experimental Hematology

American Society of Hematology

American Society for Investigative Pathology

Federation of American Societies for Experimental Biology

American Association for Cancer Research

## **TEACHING**

### University of Colorado Health Sciences Center

General and Systemic Pathology

Toxicologic Pathology I

Toxicologic Pathology II

Introduction to Occupational and Environmental Health

Principles of Immunology, Immunopathology and Immunopharmacology

Graduate Immunology

Cellular Pathology

Pathophysiology III (Rheumatology)

Advanced Topics in Toxicology

Introduction to the Practice of Toxicology

Principles of Toxicology: Molecular and Biochemical Mechanisms

Toxicology in the Courtroom

Epidemiology

### Duke University

Mammalian Toxicology (1987-1989)

Occupational Medicine, Hematology (1983-1988)

### North Carolina State University

Immunotoxicology (1982)

School of Veterinary Medicine, Hematology and Toxicology (1984)

Toxicology (1979-1981)

### University of Rochester

Toxicology (1982)

Environmental Pathology/Pathobiology (1974)  
Biochemistry (1973)

NATO Advanced Study Institute, Immunotoxicology (1982)

### **RESEARCH INTERESTS**

Mechanisms of leukemogenesis and lymphomagenesis.

Chemical-viral interactions in leukemogenesis and disease.

Differential diagnosis of hematopoietic and lymphoid neoplasms

Mechanisms and pathogenesis of hematopoietic and lymphoid injury

### **SELECTED INVITED PRESENTATIONS**

"The Shanghai Health Study: Fudan University and Participating Shanghai Hospitals." Health Consequences of Exposure to Benzene, Georgetown University Washington, DC. November 4, 2005.

"Disease Progression, Early Findings of the Shanghai Health Study." Health Consequences of Exposure to Benzene, Georgetown Univ. Washington, DC. November 4, 2005.

"Benzene Poisoning in Shanghai, China: Preliminary Findings." Recent Advances in Benzene Toxicity Meeting, Munich, Germany. October 11, 2004.

"Chronic lymphocytic leukemia in Shanghai." Fudan University, Shanghai, China. October 9, 2003.

"Prospective studies on the pathogenesis of leukemia and non-Hodgkin's lymphoma in Shanghai, China." University of Colorado Health Sciences Center, SOP, May 16, 2003.

"Leukemia & Lymphoma in Shanghai, China." University of Colorado Health Sciences Center, Chancellors Society Luncheon, February 4, 2003.

"Introduction to the Shanghai Health Study." Shanghai Hematology Society, Shanghai, China. October 9, 2002.

"Future role of molecular toxicology and epidemiology studies." Fudan University, Shanghai, China. July 5, 2002.

"Etiology and pathogenesis of lymphoid and hematopoietic diseases." Shanghai, China. May 15, 2002.

"Studies on secondary myeloid disorders and non-Hodgkin's lymphoma." Shanghai Hematology Society, Shanghai, China. August 18, 2001.

~~"Do drugs & chemicals influence the development of EBV-associated NHL?" Shanghai Medical University, Shanghai, China. September 21, 2000.~~

"Hematopoietic stem and progenitor cells as targets for biological reactive intermediates." Sixth International Symposium on Biological Reactive Intermediates, University of Paris, Paris, France. July 19, 2000.

"Cancer Etiology and Chemoprevention Program-Progress," University of Colorado Comprehensive Cancer Center, August 16, 1999.

"Studies on the pathogenesis and mechanisms of bone marrow toxicity, aplastic anemia and leukemia in humans." Dept. of Hematology, Hua Shan Hospital, Shanghai Medical University I, Shanghai, China. August 12, 1999.

"New approaches to the study of bone marrow toxicity and leukemogenesis in humans." Dept. of Hematology, CDC, Shanghai, China. August 9, 1999.

"Chemical-viral interactions in EBV-dependent transformation of human B lymphocytes." Medical Oncology, Univ. Colorado Health Sciences Center, June 22, 1999.

"1st International symposium of mechanisms, models, and predictions of idiosyncratic drug toxicity." Atlantic City, NJ, June 17, 1999.

"Biologic and Genetic Markers," Defense Research Institute, San Diego, CA, May 21, 1999.

"Future Directions in Immunopharmacology and Immunotoxicology." Rho Chi Honor Society, Denver, CO, February 18, 1999.

"Current Progress on Mechanisms of Chemical Induced Leukemogenesis." Exxon Biomedical Sciences, East Millstone, NJ, January 27, 1998.

"Dithiocarbamates as Potential Confounders in Butadiene Epidemiology." University of North Carolina, Chapel Hill, NC, July 18, 1997.

"Butadiene Toxicology and Leukemogenesis." The Toxicology Forum, Aspen, CO, July 10, 1997.

"Characterisation of the Effects of Hematotoxic Agents on Differentiating CD34+ Human Bone Marrow Cells in Liquid Culture." First International Symposium on Hematotoxicology in New Drug Development, Lugano, Switzerland, June 17, 1997.

"Effects of the Benzene Metabolite, Hydroquinone, on Regulation of Differentiation and Proliferation of Human Hematopoietic Stem and Progenitor Cells in Vitro." Society of Toxicology, Cincinnati, OH, March 10, 1997.

"Butadiene Toxicology and Leukemogenesis." The Toxicology Forum, Washington DC, February 26, 1997.

"Studies on the Biologic Plausibility of Butadiene Leukemogenesis-The use of epidemiology as a hypothesis generating tool." Butadiene Research meeting, Chemical Manufacturer's Association, Santa Fe, NM, October 16, 1996.

"Studies on the Effects of Butadiene Metabolites on Human Lymphocyte Activation." Mountain West Society of Toxicology, Snowbird, UT, October 3, 1996.

"Early Events in Chemically-induced Leukemogenesis. A Proposed Model for the Pathogenesis of t-AML." Pathology Grand Rounds, UCHSC, May 16, 1996.

"Overview of chemical leukemogenesis" Expert Leukemia Workshop, Univ. of California, Berkeley, California EPA, NIEHS, Yountville, CA, February 11-13, 1996.

"Effects of Benzene and Other Leukemogenic Agents on Hematopoietic Stem and Progenitor Cell Differentiation." Drug Related Blood Dyscrasias, Saltsjobaden, Sweden, October 12-14, 1995.

"Impact of Benzene Metabolites on Differentiation in Hematopoietic Progenitor Cells." Swedish Toxicology Society, Karolinska Institute, Stockholm, Sweden, October 12, 1995.

"Species Difference in Bone Marrow Effects of Butadiene and Metabolites." Evaluation of Butadiene & Isoprene Health Risks International Symposium, Seattle, WA, June 27-29, 1995.

"The Process of Leukemogenesis." Benzene 95. International workshop on benzene toxicity. Rutgers University, Piscataway, NJ. June 17-21. 1995.

"Impact of Benzene Metabolites on Differentiation in Hematopoietic Progenitor Cells." Benzene 95. International workshop on benzene toxicity. Rutgers University, Piscataway, NJ. June 17-21. 1995.

"Effects of Benzene Metabolites on Human and Murine Bone Marrow Cells." Western States Petroleum Association (WSPA) Benzene Symposium, San Francisco, CA, November 29-30, 1994.

"Hematopoietic Stem Cell Proliferation and Differentiation in Secondary Leukemogenesis." The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, N.T., Hong Kong, July 20, 1994.

"Of Mice and Men: Studies on the Mechanisms of Chemical Leukemogenesis." University of Cincinnati Medical Center, Department of Environmental Health, Center for Environmental Genetics, Cincinnati, Ohio, January 5, 1994.

"Role of bone marrow stem cell populations in development of T cell leukemia." Symposium on Molecular Mechanisms of Cytotoxicity, American College of Toxicology, New Orleans, October 4, 1993.

"Studies on the mechanisms of 1,3-Butadiene induced T cell lymphoma: Relevance of the mouse leukemia model for assessment of risk in humans." Medical Research Council of Britain, Carshalton, Surrey, April 23, 1993.

"Molecular mechanisms of chemical leukemogenesis in humans. Update on health risks associated with benzene exposure." Medical Research Council of Britain, Carshalton, Surrey, April 22, 1993.

"1,3-Butadiene bone marrow toxicity mimics the hematopoietic defects observed in mice bearing Steel or White Spotted mutations." International Symposium on Health Hazards of Butadiene and Styrene, Helsinki, Finland, April 18-21, 1993.

"Mechanism and Relevance of Benzene Toxicity in Humans." Symposium on Toxicology: From Basic Science to Clinical Practice, UK Medical Research Council, Centre for Mechanisms of Human Toxicity, University of Leicester, March 23-24, 1993.

"Stem cell regulation in chemical leukemogenesis." Symposium on Cell Injury, American Association of Pathologists, F. A.S.E.B., Anaheim, April 9, 1992.

"Mechanisms of chemical leukemogenesis: Revisiting the biological basis for assessing risk in humans." The Brookings Institution, International Life Sciences Institute, Washington DC, February 28, 1992.

"Current approaches to understanding the mechanisms of benzene leukemogenesis." Toxic Air Pollutants from Mobile Sources: Emissions and Health Effects. Co-sponsored by Air and Waste Management Association and EPA Environmental Criteria and Assessment Office. Detroit, MI, October 15-18, 1991.

"Risk characterization and the extended spaceflight environment," Man in Space Conference, International Academy of Astronautics, Cologne, Germany, June 20, 1991.

"Current approaches to the assessment of hematotoxicity and immunotoxicity," Johnson Space Center, N.A.S.A., Houston, May 20, 1991.

"A mechanistic approach to the evaluation of benzene toxicity." 8th Annual Conf., Health Effects Institute, Colorado Springs, CO, April 22, 1991.

"Mechanisms of chemical leukemogenesis." Robert Wood Johnson School of Medicine, Piscataway, NJ, April 4, 1990.

"Current approaches to the study of benzene-induced bone marrow toxicity and leukemogenesis." Johns Hopkins University, Baltimore, MD, April 3, 1990.

"Chemical and viral interactions in leukemogenesis." University of Nebraska Medical Center, Omaha, NE, April 24, 1990.

"Butadiene leukemogenesis in the mouse: Potential of chemical-viral interactions." Institute for Toxicology, University of Southern California, Los Angeles, April 14, 1989.

"Comparative morphology of pulmonary immune systems." Symposium on Interspecies Comparisons of Lung Immunotoxicology, Society of Toxicology, Atlanta, GA, March 2, 1989.

"Comparing and contrasting potential mechanisms of chemical leukemogenesis in man." Carolina Occupational Medicine Association, Charleston, NC, Dec 2, 1988.

"Butadiene-induced leukemogenesis." Department of Morbid Anatomy, Chinese University Medical School, Shatin, New Territories, Hong Kong, October 24, 1988.

"Mechanisms of chemically-induced leukemogenesis: potential relevance of mouse models to man." University of Arizona, Tucson, September 21, 1988.

"Butadiene-induced leukemogenesis in the mouse: potential chemical-viral interactions." Exxon Biomedical Sciences, E. Millstone, NJ, July 7, 1988.

"Butadiene-induced leukemogenesis in the mouse." Battelle, N.W. Laboratories, Hanford, WA, June 9, 1988.

"Potential mechanisms of benzene leukemogenesis." Oakridge National Laboratory, Oakridge, TN, May 27, 1988.

"Commentary on benzene and butadiene risk assessment." Workshop on Biological Data for Pharmacokinetic Modeling and Risk Assessment, International Life Sciences Institute & Environmental Protection Agency, Ashville, NC, May 24, 1988.

"Studies on the mechanisms of butadiene-induced leukemogenesis: The potential role of endogenous murine leukemia virus." Workshop on the Toxicity and Carcinogenicity of Butadiene, NIEHS, Res. Tri. Park, NC, April 13, 1988.

"Potential influences of dose and regimen on benzene-induced MDS and leukemia in C57BL/6 mice." Workshop on the Toxicity and Carcinogenicity of Benzene, NIEHS, Res. Tri. Park, NC, March 15, 1988.

"Bone marrow toxicity with special emphasis on the mechanism of butadiene leukemogenesis," Gordon Research Conference on Mechanisms of Toxicity, Meriden, NH, July 27, 1987.

"Progress in understanding mouse leukemia and viral models." IISRP Annual Meeting, Edinburgh, Scotland, June 11, 1987.

"Mechanisms of butadiene-induced leukemogenesis." Haskell Laboratories, E.I. du Pont de Nemours and Co., Wilmington, DE, May 8, 1987.

"Selective activation of endogenous ecotropic retroviruses in the mouse." Environmental Mutagen Society, San Francisco, CA, April 9, 1987.

"Butadiene-induced leukemogenesis in the mouse: Potential chemical-viral interactions." University of California at San Francisco, April 10, 1987.

"Mechanisms of butadiene-induced lymphoma/leukemia: Potential role of chemical-viral interaction." Syntex Distinguished Lectureship in Toxicology, University of Colorado, Boulder, CO, March 13, 1987.

"Studies on the mechanism of 1,3-butadiene-induced lymphoma/leukemia in the B6C3F1 Mouse: Chemically-induced activation of endogenous retroviruses." University of Arizona, Tucson, March 11, 1987.

"Toxicology of the blood and bone marrow." Duke University School of Medicine, Durham, NC, Feb 16, 1987.

"Mechanisms of 1,3-butadiene-induced murine lymphoma." Fall meeting of the Genetic and Environmental Toxicology Association, Stanford Research Institute, Palo Alto, CA, Dec. 4, 1986.

"Immunology as a tool in toxicology research." Annual Conf. on Occupational Health, Modern Toxicology: Research & Testing, American Academy of Occupational Medicine, Washington, DC, Nov. 11, 1986.

"Structure and function of the normal immune system: Laboratory animals." Workshop on the relationship between environmental chemical exposures and the integrity of the immune system, Georgetown University, May 1, 1986.

"Importance of dosing regimen in bone marrow toxicity." Environmental Mutagen Society, Baltimore, MD, April 9, 1986.

"Mechanisms of butadiene-induced leukemogenesis." Duke University Program in Toxicology, Durham, NC, April 7, 1986.

"Mechanisms of 1,3-butadiene-induced carcinogenicity." School of Public Health, the University of California at Berkeley, Oct. 2, 1985.

"Risk assessment issues presented by butadiene." CMA Workshop on Risk Assessment in the Chemical Industry, Washington, DC, Sept. 23, 1985.

"The role of reactive intermediates in sulfhydryl-dependent immunotoxicity." Biological Reactive Intermediates III, College Park, MD, June 8, 1985.

"Toxicology of the blood and bone marrow." School of Veterinary Medicine, North Carolina State University, Raleigh, NC, March 12, 1984.

"Quinones as toxic metabolites of benzene." Second Annual Symposium on Recent Advances in Occupational Cancer, San Francisco, CA, Dec. 7, 1984.

"Mechanisms of benzene-induced bone marrow and immune suppression." Brookhaven Natl. Laboratories, Upton, LI, NY, Feb. 1, 1984.

"Cell biology: Its critical role in toxicology and biotechnology." 3rd Annual Meeting, NC, Soc. Toxicol., Research Triangle Park, NC, Feb. 5, 1983.

"Clinical aspects of benzene exposure," Occupational and Community Medicine, Duke Univ. School of Medicine, Durham, NC, April 18, 1983.

"Benzene-induced immunotoxicity." Univ. of Rochester School Medicine and Dentistry, Rochester, NY, April 23, 1983.

"Bioactivation of benzene and proposed mechanisms of toxicity." Dept. Health and Human Services, Subcommittee on Environmental Mutagenesis, Washington, DC, May 6, 1983.

"Bioactivation of benzene and mechanisms of cellular injury." Royal Society of Medicine, Permanent Commission on Occupational Health, London, UK, Aug. 31, 1983.

"New approaches for the detection of aneuploidy." National Academy of Sciences, Washington, DC, Oct. 5, 1983.

"Critical role of immunology and cell biology in toxicology." N.I.H., Immunotoxicology Workshop, Research Triangle Park, NC, Oct 18, 1983.

"Mechanisms of benzene-induced myelotoxicity." Collegium Ramazzini International Conference on Benzene, New York, NY, Nov. 3, 1983.

## PUBLICATIONS

### BOOKS AND BOOK CHAPTERS

Irons RD and Gross S. (2002) Leukemia and Benzene. Clinics in Occupational & Environmental Medicine. (Whysner J. ed.) 2: 841-843.

Irons RD. (2001) Benzene and Other Hematotoxins, in Clinical Environmental Health and Toxic Exposures. Second edition. Chapter 59, pp. 750-762. (Sullivan J. and Krieger G. eds.). Lippencott.

Irons RD. (1998) Blood and Bone Marrow, in Fundamentals of Toxicologic Pathology, Chapter 9 (Haschek-Hock WM and Rousseaux CG. eds). Academic Press.

Irons RD. (1997) Leukemogenesis as a Toxic Response, in Comprehensive Toxicology. Volume 4: pp.175-199. (Sipes IG, McQueen CA, Gandolfi AJ and Bloom JC. eds.) Elsevier Science, Ltd.

Irons RD, Eberhardt R and Schulz J. (1991) Risk Characterization and the Extended Spaceflight Environment, in Proceedings of 9th International Academy of Astronautics Man in Space Symposium.

Irons RD. (1991) Current Approaches to the Understanding of Mechanisms of Benzene Leukemogenesis, in Proceedings of Toxic Air Pollutants from Mobile Sources: Emissions and Health Effects. Cosponsored by Air and Waste Management Association and EPA Environmental Criteria and Assessment Office.

Irons RD. (1991) Benzene and other Hematotoxins, in Hazardous Materials Toxicology, Chapter 63, pp. 718-731. (Sullivan JB and Krieger GR. eds). Williams and Wilkins.

Krieger GR and Irons RD. (1991) Nonionizing Electromagnetic Radiation, in Hazardous Materials Toxicology, Chapter 116 (Sullivan JB and Krieger GR. eds). Williams and Wilkins.

Irons RD. (1991) The Blood and Blood Forming Organs, in Fundamentals of Toxicologic Pathology, Chapter 16 (Haschek-Hock WM and Rousseaux CG. eds). Academic Press.

Irons RD. (1989) Benzene Case Study, in Biological Data for Pharmacokinetic Modeling and Risk Assessment. Report of a Workshop Convened by the U.S. Environmental Protection Agency and ILSI Risk Science Institute. EPA Publication/600/3-90/019. pp. 24-28.

Irons RD. (1989) Butadiene Case Study, in Biological Data for Pharmacokinetic Modeling and Risk Assessment. Report of a Workshop Convened by the U.S. Environmental Protection Agency and ILSI Risk Science Institute. EPA Publication/600/3-90/019. pp. 29-31.

Irons RD. (1988) Immunotoxicology. In The Year in Immunology (Cruse JM and Lewis RE. eds.) Karger: Basel.

Irons RD. (1987) The normal immune system components and their operation: laboratory animals. In Environmental Chemical Exposures and Immune System Integrity. (Burger EJ, Tardiff RG and Bellanti JA. eds), Advances in Modern Environmental Toxicology. Princeton Scientific Publishing Co., Vol. 13, pp. 15-28.

Irons RD. (1986) The role of reactive intermediates in sulfhydryl-dependent immunotoxicity: interference with microtubule assembly and microtubule-dependent function. In Biological Reactive Intermediates III. (James J, Kocsis JJ, et al, eds.) Plenum Press, pp.645-655.

Rickert DE, Irons RD, Popp JA and Goldsworthy TL. (1986) The effects of diet on the toxicity of nitroaromatic chemicals in rodents. In New Concepts and Developments in Toxicology (Chambers PL et al, eds.), Elsevier, pp. 107-114

Sussman RM, Thomas FB and Irons RD. (1985) Risk assessment issues raised by 1,3-butadiene. In Risk Analysis in the Chemical Industry. Government Institutes, Inc., Rockville, MD, pp. 177-214.

Irons RD. (1985) Toxicology of the Blood and Bone Marrow. New York: Raven Press.

Irons RD and Sawahata T. (1985) Phenols, catechols and quinones. In Bioactivation of Foreign Compounds. (Anders MW. ed.). San Diego: Academic Press, pp. 259-277.

Irons RD and Stillman WS. (1985) Application of Flow Cytometry for the Evaluation of Chemically Induced Alterations in Cell Proliferation and Differentiation in Bone Marrow. In Toxicology of the Blood and Bone Marrow. (Irons RD. ed). New York: Raven Press, pp. 101-118.

Irons RD. (1985) Histology of the Immune System: Structure and Function. In Toxicology and the Immune System. (Dean J. et al, ed.) New York: Raven Press, pp. 11-22.

Pfeifer RW and Irons RD. (1984) Mechanisms of sulfhydryl-dependent immunotoxicity. In Toxicology of the Immune System. (Dean J, et al, ed). New York: Raven Press, pp 255-262.

Irons RD and Pfeifer RW. (1984) Benzene-induced immunotoxicity: the lymphocyte as a tool for studying subcellular mechanisms of toxicity. In Proceedings of the NATO Advanced Studies Institute on Immunotoxicology. Vol G2: 30-35. Berlin: Springer Verlag.

Irons RD, Wierda D and Pfeifer RW. (1983) The immunotoxicity of benzene and its metabolites. In Carcinogenicity and Toxicity of Benzene. (Mehlman MA, ed.), Advances in Modern Environmental Toxicology, Princeton Scientific Publishing Co., Vol. 4, pp. 37-49.

Irons RD, Greenlee WF, Wierda D and Bus JS. (1982) Relationship between benzene metabolism and toxicity: a proposed mechanism for the formation of reactive intermediates from polyphenol metabolites. In Biological Reactive Intermediates II. (Snyder R, Parke DV, Kocsis JJ, Jollow DJ, Gibson GG and Witmer CM, eds). Plenum Press, pp. 299-243.

Irons RD and Pfeifer RW. (1982) Benzene metabolites: evidence for an epigenetic mechanism of toxicity. In The Genetic Effects of Airborne Agents. (Tice RR, Costa DL, Schaich KM, eds). Plenum Press, pp. 241-256.

### **PUBLISHED ARTICLES**

Gross SA, Zhu XZ, Bao L, Ryder J, Le A, Chen Y, Wang XQ and Irons RD. (2008) "A Prospective Study of 728 Cases of Non-Hodgkin Lymphoma from a Single Laboratory in Shanghai, China." International Journal of Hematology, Accepted for publication.

Irons RD and Le AT. (2008) "Dithiocarbamates and Viral IL-10 Collaborate in the Immortalization and Evasion of Immune Response in EBV-infected Human B Lymphocytes." Chemico-Biological Interactions, 172: 81-92.

Lv L, Kerzic P, Lin G, Schnatter AR, Bao L, Yang Y, Zou H, Fu H, Ye X, Gross SA, Armstrong TW and Irons RD. (2007) "TNF- $\alpha$  238A polymorphism confers susceptibility to persistent bone marrow dysplasia following chronic exposure to benzene." Leukemia Research, 31: 1479-1485.

Ryder J, Wang X, Bao L, Gross SA, Hua F and Irons RD. (2007) "Aggressive NK Cell Leukemia: Report of a Chinese Series and Review of the Literature." International Journal of Hematology, 85(1):18-25.

Hu X, Wang X, Bao L, Shui R, Zhu X, Irons RD, Fu H, Chen Y, Chen H, Guo H, Zhao X, Yang X, Li J. (2007) "Cytogenetic and interphase FISH studies in the diagnosis of malignant lymphomas." Chinese Journal of Oncology, (Zhonghua Zhong Liu Za Zhi) 29(1):45-8.

Wang L, Zhou Y, Liang Y, Wong O, Armstrong T, Schnatter AR, Wu Q, Fang J, Ye X, Fu H and Irons RD. (2006) "Benzene exposure in the shoemaking industry in China, a literature survey, 1978-2004." Regulatory Toxicology and Pharmacology, Nov; 46(2): 149-56.

Bao L, Wang X, Ryder J, Ji M, Chen Y, Chen H, Sun H, Yang Y, Du X, Kerzic P, Gross SA, Yao L, Lv L, Fu H, Lin G and Irons RD. (2006) "Prospective study of 174 de novo acute myelogenous leukemias

according to the WHO classification: subtypes, cytogenetic features and FLT3 mutations." *European Journal of Haematology*, 77: 35-45.

Irons RD, Wang X-Q, Gross SA, Bao L, Ryder J, Chen Y, Chen H, Sun H, Zhou J, Ji M, Du X, Fu H and Lin G. (2006) "Prevalence of MDS subtypes in Shanghai, China: A comparison of the World Health Organization and French American British Classifications." *Leukemia Research*, 30: 769-775.

Gross SA, Zheng JH, Le AT, Kerzic PJ and Irons RD. (2006) "PU.1 phosphorylation correlates with hydroquinone-induced alterations in myeloid differentiation and cytokine-dependent clonogenic response in human CD34+ hematopoietic progenitor cells." *Cell Biology and Toxicology*, 22(4): 229-241.

Irons RD, Lv L, Gross SA, Ye X, Bao L, Wang X-Q, Ryder J, Armstrong TW, Zhou Y, Miao L, Le AT, Kerzic PJ, Ni W and Fu H. (2005) "Chronic exposure to benzene results in a unique form of dysplasia." *Leukemia Research*, 29(12): 1371-1380.

Zheng JH, Pyatt DW, Gross SA, Le A, Kerzic PJ and Irons RD. (2004) "Hydroquinone modulates the GM-CSF signaling pathway in TF-1 cells." *Leukemia*, 18: 1296-1304.

Kerzic PJ, Pyatt DW, Zheng J-H, Gross SA, Le A and Irons RD. (2003) "Inhibition of NF- $\kappa$ B by Hydroquinone Sensitizes Human Bone Marrow Progenitor Cells to TNF- $\alpha$ -Induced Apoptosis." *Toxicology*, 187: 127-137.

Irons RD, Pyatt DW, Gross SA and Stillman WS. (2001) "Hematopoietic stem and progenitor cells as targets for biological reactive intermediates." In *Biological Reactive Intermediates VI*, Dansette et al, eds., 441-449.

Baker RK, Kurz EU, Pyatt DW, Irons RD and Kroll DJ. (2001) "Benzene metabolites antagonize etoposide-stabilized cleavable complexes of DNA topoisomerase II $\alpha$ ." *Blood*, 98: 830-833.

Irons RD, Stillman WS, Pyatt DW, Yang Y, Le A, Gustafson DL and Zheng J-H. (2001) "Comparative toxicity of dithiocarbamates and butadiene metabolites in human lymphoid and bone marrow cells." *Chemico-Biological Interactions*, 135-136: pp. 615 - 625.

Irons RD. (2000) "Molecular Models of Benzene Leukemogenesis." *J. Toxicology & Environmental Health, Part A*, 61: 391-397.

Irons RD, Pyatt DW, Stillman WS, Soma DB, Claffey DJ and Ruth JA. (2000) "Comparative toxicity of known and putative metabolites of 1,3-butadiene in human CD34+ bone marrow cells." *Toxicology*, 150: 99-106.

Pyatt DW, Yang Y, Stillman WS and Irons RD. (2000) "Hydroquinone inhibits PMA-induced activation of NF- $\kappa$ B in primary human CD19+ B lymphocytes." *Cell Biology and Toxicology*, 16: 41-51.

Pyatt DW, Yang Y, Le A, Stillman WS and Irons RD. (2000) "Dithiocarbamates inhibit hematopoiesis via a copper dependent mechanism." *Biochemical and Biophysical Research Communications*, 274: 513-518.

Pyatt DW, Yang Y, Mehos B, Le A, Stillman W and Irons RD. (2000) "Hematotoxicity of the Chinese Herbal Medicine, Tripterygium Wilfordii Hook f on CD34+ Human Bone Marrow Cells." *Molecular Pharmacology*, 57: 512-518.

Stillman WS, Varella-Garcia M and Irons RD. (2000) "The Benzene Metabolite, Hydroquinone, Selectively Induces 5q31- and -7 in Human CD34+CD19- bone Marrow Cells." *Experimental Hematology*, 28: 169-176.

Stillman WS, Varella-Garcia M and Irons RD. (1999) "The benzene metabolites hydroquinone and catechol act in synergy to induce dose-dependent hypoploidy and -5q31 in a human cell line." *Leukemia & Lymphoma*, 35: 269-281.

Pyatt DW, Stillman WS, Yang Y, Gross S, Zheng J-H and Irons RD. (1999) "An essential role for NF-Kappa B in human CD34+ bone marrow cell survival." *Blood*, 93: 3302-3308.

Pyatt DW, Gruntmeir J, Stillman WS and Irons RD. (1998) "Dimethyldithiocarbamate inhibits in vitro activation of primary human CD4+ T lymphocytes." *Toxicology*, 128: 83-90.

Irons RD and Pyatt DW. (1998) "Dithiocarbamates as potential confounders in butadiene epidemiology." *Carcinogenesis*, 19: 539-542.

Pyatt DW, Stillman WS and Irons RD. (1998) "Hydroquinone, a reactive metabolite of benzene, inhibits NF- $\kappa$ B in primary human CD4+ T lymphocytes." *Toxicology and Applied Pharmacology*, 149: 178-184.

Gross S, Helm K, Gruntmeir JJ, Stillman WS, Pyatt DW and Irons RD. (1997) "Characterization and phenotypic analysis of differentiating CD34+ human bone marrow cells in liquid culture." *European Journal of Haematology*, 59: 318-326.

Stillman WS, Varella-Garcia M, Gruntmeir JJ and Irons RD. (1997) "The benzene metabolite, hydroquinone, induces dose-dependent hypoploidy in a human cell line." *Leukemia*, 11: 1540-1545.

Pyatt DW, Zheng J-H, Stillman WS and Irons RD. (1996) "Inorganic lead activates NF- $\kappa$ B in primary human CD4+ T lymphocytes." *Biochem. Biophys. Res. Comm.* 227: 380-385.

Irons RD and Stillman WS. (1996) "The effects of benzene and other leukemogenic agents on hematopoietic stem and progenitor cell differentiation." *European J. Haematol.*, 57 (S60): 119-124.

Rothman N, Smith MT, Hayes RB, Li G-L, Irons RD, Dosemeci M, Haas R, Stillman WS, Linet M, Xi L-Q, Bechtold WE, Wiemels J, Campleman S, Zhang L, Quintana PJE, Titenko-Holland N, Wang Y-Z, Lu W, Kolachana P, Meyer KB and Yin S. (1996) "An Epidemiologic Study of Benzene's Early Biologic Effects in Heavily Exposed Workers in Shanghai, China." *Environmental Health Perspectives*, 104 (6): 1365-1370.

Irons RD and Stillman WS. (1996) "The process of leukemogenesis." *Environmental Health Perspectives*, 104 (6): 1239-1246.

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## ABSTRACTS

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