

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF WASHINGTON
AT SPOKANE

NEIL HENRICKSEN AND)
MAURITA HENRICKSEN,)
Plaintiffs,)
VS.) NO.: CV-07-224-JLQ
CHEVRON PHILLIPS CHEMICAL)
COMPANY, LP; ET AL,)
Defendants.)

ORAL DEPOSITION OF
ETHAN A. NATELSON, M.D.
APRIL 11, 2008
VOLUME 1

ORAL DEPOSITION OF ETHAN A. NATELSON, M.D.,
produced as a witness at the instance of the PLAINTIFFS,
and duly sworn, was taken in the above-styled and
numbered cause on April 11, 2008, from 10:58 a.m. to
4:03 p.m., before Jeanne C. Pearl, CSR in and for the
State of Texas, reported by machine shorthand, at the
offices of Fulbright & Jaworski, 1301 McKinney, Suite
5100, Houston, Texas, pursuant to the Federal Rules of
Civil Procedure.

1613-86709

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1 ETHAN A. NATELSON, M.D.,
2 having been first duly sworn, testified as follows:

3 (The time is 10:58 a.m.).

4 EXAMINATION

5 BY MR. SCHMIDT:

6 Q. Hi, Dr. Natelson. Would you please state your
7 name for the record?

8 A. Ethan Natelson.

9 Q. And your business address?

10 A. 6550 Fannin Street, Suite 1001, Houston, Texas,
11 77030.

12 Q. Good morning, Dr. Natelson. My name is Jackson
13 Schmidt. I represent the plaintiffs in this action. I
14 know you have had your deposition taken numerous times
15 so I'm not going to go over the ground rules but for
16 one. And I always do this. It's as much for me as it
17 is for you. We can't both talk at the same time. It's
18 very difficult on the court reporter. So, please wait
19 until I get the entire question out. You're going to
20 know what the question is well before it gets all the
21 way out of my mouth. But if you could wait and pause,
22 that way we have a nice clean record and a happy court
23 reporter.

24 A. I agree.

25 Q. Good. Dr. Natelson, have you seen the

1 disclosure that was filed in this action about the
2 nature and scope of your testimony?

3 A. Are you speaking of this thing?

4 Q. No. Let me show you this. You can ignore the
5 highlighting.

6 A. If I have, I don't recall seeing this.

7 (Exhibit 61 marked.)

8 Q. (BY MR. SCHMIDT) Okay. I'll go over it with
9 you, see if it accurately captures what we're doing.
10 You're right, let's do this thing first. I'm handing
11 you what I've marked as Plaintiff's Exhibit Number 61.
12 Is that a copy of the deposition notice and subpoena?

13 A. Looks to be a copy, correct.

14 Q. And you gathered your files pursuant to that
15 and brought them with you today?

16 A. Yes.

17 Q. Great. We can put that away. I'm going to
18 talk about that later. You're a hematologist-
19 oncologist?

20 A. A hematologist.

21 Q. Okay. The disclosure says hematologist-
22 oncologist. Is that incorrect?

23 A. No. Hematology, the specialty of hematology
24 predated the specialty of oncology. So, all
25 hematologists are oncologists, but in today's speak

1 there are separate pathways in training and separate
2 boards.

3 Q. Hematologist refers to blood; oncologist refers
4 to cancer?

5 A. Yes and no. Hematology refers to diseases of
6 the blood of which some of them may be cancer. And an
7 oncologist is purely dealing with cancer.

8 Q. It says you are expected to testify regarding
9 the medical specialties of hematology; is that true?

10 A. Yes.

11 Q. Oncology?

12 A. Yes.

13 Q. The question of medical causation in this case?

14 A. Yes.

15 Q. The medical and scientific literature regarding
16 gasoline?

17 A. Yes.

18 Q. And that you may address opinions offered by
19 plaintiffs' experts. Does that reasonably describe the
20 scope of the work that you were assigned to undertake in
21 this matter?

22 A. Yes.

23 Q. Have you reviewed everything you need to review
24 in order to form your final opinion in this matter?

25 A. Yes.

1 Q. And is that opinion encompassed in the report
2 that you submitted in this matter?

3 A. Yes.

4 Q. Is there anything else you plan to do or need
5 to do before testifying at trial in this matter in
6 August?

7 A. Not that I'm aware of at this time.

8 Q. Other than probably look over the file and
9 refresh yourself but no additional work?

10 A. No, no additional work.

11 Q. I want to spend a little time talking generally
12 about, since you're going to testify about causation,
13 about carcinogenesis. Cancer is a disease that arises
14 from a single cell; is that true?

15 A. Well, in general that would be a true
16 statement. Certain cancers appear to be multicentric in
17 origin. They arise at the same time in multiple cells.
18 Hodgkin's disease would be an example of that that may
19 arise in two places or non-Hodgkin's lymphoma. So,
20 whether that really came from a single cell or two
21 cells, I don't know would be known.

22 Q. How about AML, is it a considered a clonal
23 disease?

24 A. AML is considered a clonal disease, yes.

25 Q. That means it arises from a single cell?

1 A. Yes.

2 Q. The cell is the basic unit of life for all
3 animals and plants?

4 A. Yes.

5 Q. The human body is a huge cell condominium with
6 trillions of cells?

7 A. Yes.

8 Q. Or trillions of condominium units?

9 A. Yes.

10 Q. For the most part each of those trillions of
11 cells has a form and a function and it performs its
12 assigned role for the good of the whole without causing
13 problems?

14 A. Yes.

15 Q. In order to do this, cells in fact communicate
16 with at a chemical level neighboring cells and the
17 immune system in order to perform their functions?

18 A. As a general statement, that's true.

19 Q. Normal cell cooperation and cell communication
20 is how humans keep healthy and grow as they're supposed
21 to?

22 A. Yes.

23 Q. And cancer is a disease that starts when a
24 single cell instead of cooperating with its neighbors
25 and remaining devoted to the good of the whole sets up

1 shop on its own, acts independently of other cells by
2 ignoring their signals to stop growing and begins
3 dividing and keeps dividing on its own?

4 A. Yes.

5 Q. And if that process is not stopped, the
6 unchecked cell grows into a tumor that invades the
7 surrounding tissue?

8 A. Yes.

9 Q. And it can even send cells out through the
10 blood and lymph systems to travel to distant points in
11 the body and begin growing and turning into tumors
12 there?

13 A. Yes.

14 Q. That's called metastasis?

15 A. Yes.

16 Q. And a tumor, either at the original, called the
17 primary site, or at the remote metastatic site can harm
18 the person in which it is growing?

19 A. Yes.

20 Q. And these tumors, both original and metastatic,
21 are clonal, that is, they arise from a single cell
22 except in the case of non-Hodgkin's and perhaps a few
23 others?

24 A. Yes, they arise from a single cell. They, of
25 course, can mutate and change, but they do arise from a

1 single cell.

2 Q. Now, an organ tumor, say, a lung cancer kills
3 people by setting up metastases usually in bones and in
4 the brain which become tissue growths where they are not
5 supposed to be?

6 A. Well, they can kill people by virtue of
7 obstructing just the lung and causing bad infections.
8 They don't have to metastasize to kill somebody.

9 Q. A disease like AML starts with a single cell in
10 the marrow, but once it becomes cancerous, it makes bad
11 white cells that don't work properly and it also divides
12 sending a copy of itself which also makes ineffective
13 white cells?

14 A. Well, in general that's true. Sometimes the
15 abnormal cells work fairly well in terms of what their
16 function is but they are malignant cells and they grow.

17 Q. Eventually a tumor forms in the marrow and
18 metastatic tumors spread throughout the marrow? This is
19 AML?

20 A. Yes, in AML the spread is more or less
21 confluent in the bone marrow. It's not spotty as it
22 often is in metastatic lung cancer, for example, in the
23 example you gave.

24 Q. And the bad cells overwhelm and crowd out
25 healthy ones and eventually the person has a compromised

1 white cell system?

2 A. Yes.

3 Q. This is bad and often fatal because without an
4 effective white cell system, you can't fend off viruses,
5 bacteria and foreign bodies?

6 A. Yes.

7 Q. And what we're describing is all applicable to
8 what happened to Mr. Henricksen's -- Henricksen when he
9 developed AML?

10 MR. YOUNG: Objection, lack of foundation.

11 A. Well, he developed acute leukemia. So, he
12 presumably has a clonal disease that spread to various
13 sites of his bone marrow.

14 Q. (BY MR. SCHMIDT) Now, back to the individual
15 cell where the AML starts. All of our cells except for
16 circulating red blood cells have a nucleus containing
17 DNA?

18 A. Yes.

19 Q. Each cell's DNA is a chemical blueprint
20 containing information on how the entire human is
21 constructed?

22 A. Yes.

23 Q. Each cell's DNA also controls the individual
24 cell's form and function?

25 A. Yes.

1 Q. Among the many instructions contained in the
2 DNA is the instruction whether a cell should normally
3 divide?

4 A. Yes.

5 Q. For example, you and I routinely slough off
6 dead and dying skin and somehow new skin cells are
7 growing right along underneath in the right place, in
8 the right amount to replace those that have died?

9 A. Yes.

10 Q. And they know to do that because the DNA
11 directs it?

12 A. Yes. There may be other things than the DNA.
13 In other words, a mature cell may have the same DNA as
14 an immature cell, but there are other signals that are
15 telling it to divide.

16 Q. That's right where I'm going next. The kind of
17 DNA instruction telling a cell to grow and replace other
18 cells is called a proto-oncogene?

19 A. It could be. I'm not a proto-oncogene expert.

20 Q. Do you know what a proto-oncogene is?

21 A. I know the term.

22 Q. Cells grow. One way they grow is by dividing
23 and sending out replicas of themselves?

24 A. Yes.

25 Q. If there's a mechanism that directs this

1 process, it's called the proto-oncogene?

2 A. In general terms, yes.

3 Q. The instructions in the DNA telling cells when
4 to stop dividing or not divide are called tumor
5 suppressor genes?

6 A. Such things do exist, yes. Genes that promote
7 growth and genes that retard growth.

8 Q. Is P-53 one of those?

9 A. P-53 is an important gene, yes.

10 Q. It's a tumor suppressor gene?

11 A. Yes.

12 Q. In addition to instructions to divide or not to
13 divide, there are limits called telomeres to the number
14 of times our cells can divide in a lifetime; is that
15 true?

16 A. I don't know the answer to that.

17 Q. Do you know what a telomere is?

18 A. A telomere is a structure in a, in a dividing
19 cell. Beyond that you've exhausted my knowledge of
20 telomeres.

21 Q. If I told you that telomeres define a cell's
22 life span by determining that after a certain number of
23 divisions, a cell just simply can't divide any more,
24 would you know whether that's true or not?

25 A. I would have no knowledge of that.

1 Q. Do you know the number of telomeres that they
2 believe are contained in our DNA?

3 A. No.

4 Q. If I told you the current thinking is that we
5 have about 56, any given cell can divide about 56 times,
6 do you know whether that's true or not?

7 A. I don't know that.

8 Q. Now, there's another mechanism in cells that
9 limit their life spans and that is an emergency
10 mechanism called apoptosis or cell suicide; is that
11 true?

12 A. Yes.

13 Q. Apoptosis is an instruction in the DNA that
14 tells a cell to self-destruct if the cell starts
15 malfunctioning?

16 A. Yes.

17 Q. Cells can also receive instructions from
18 surrounding cells in the immune system telling them
19 whether to divide or to stop dividing?

20 A. Yes.

21 Q. This is accomplished through a receptor on the
22 cell membrane that can receive chemical signals from the
23 cell's immediate micro environment?

24 A. There are many receptors on cell membranes.
25 But in general that would be true.

1 Q. I didn't mean -- I think my question implied
2 there was one, but there are many?

3 A. Yes.

4 Q. And that's so the cell can interact with the
5 surrounding environment?

6 A. Yes.

7 Q. And if neighboring cells or cells from the
8 immune system detect that a cell is malfunctioning, they
9 can send a chemical signal to the cell receptor which is
10 kind of a door bell that sends a cascade of chemical
11 reactions through the cell down to the DNA in the
12 nucleus to tell the cell to divide or not to divide or
13 to destroy itself?

14 MR. YOUNG: Object, compound. Lack of
15 foundation.

16 A. In general, that's true.

17 Q. (BY MR. SCHMIDT) The immune system has cells
18 including macrophages that circulate and if they detect
19 a problem or cell malfunction, they will either try to
20 send such a message as we just discussed or they will
21 actually attack and kill the malfunctioning cell?

22 A. That can be so.

23 Q. We also have a mechanism called a DNA repair
24 mechanism that can fix some defects?

25 A. Yes.

1 Q. In fact, there's the nucleotide excision
2 repair, basic excision repair and DNA mismatch repair
3 that are what we call the DNA repair mechanism?

4 A. I can't argue with you. I'm not a cell
5 biologist. I'm a clinical hematologist, but I accept
6 that.

7 Q. Now, for a cell to become cancerous, to go from
8 a healthy state, say a cell in the bone marrow, there
9 are a great number of defects that have to occur before
10 the cell can move from being healthy to becoming
11 cancerous; isn't that correct?

12 A. Well, I don't know that there are a great
13 number, but there are a number that have to occur.

14 Q. Okay. It's not just one stage, one switch
15 where a cell is healthy one day and one thing happens
16 and it becomes a cancer cell?

17 A. No. With respect to leukemia, there are
18 thought to be at least two hits or something -- multiple
19 hits to make a cell become abnormal.

20 Q. Well --

21 A. A cell, I'd say malignant.

22 Q. One of the things that has to happen, one of
23 the hits, is that the proto-oncogene has to be
24 activated. In other words, the cell has to be -- if you
25 think of the proto-oncogene as a gas pedal, the gas has

1 to be pushed down and the cell has to be told to divide
2 repeatedly; isn't that true?

3 A. Yes, one of those is the FTL-3 gene that can
4 duplicate and stimulate cell division. And certain
5 leukemias will have excess of those.

6 Q. Is an FTL-3 a proto-oncogene?

7 A. I don't know. I don't know how it would be
8 classified.

9 Q. Another thing that has to happen for a cell to
10 become cancerous is that the tumor suppressor gene, one
11 of the tumor suppressor genes, maybe all of them, has to
12 fail?

13 A. I don't know the answer to that.

14 Q. If the gas pedal is depressed and the tumor
15 suppressor gene is the brakes, that instruction in the
16 DNA to prevent an unchecked dividing has to somehow fail
17 for a cell to become cancer; isn't that right?

18 A. I don't know the answer to all of that. You're
19 asking me questions that are not in the realm of
20 clinical hematology. They're in the realm of cell
21 biology or DNA metabolism and that's not my field.

22 Q. Okay. Do you know whether the cell membrane
23 receptor must fail?

24 A. I don't know.

25 Q. If the cell membrane receptor has the function

1 that we described, to receive signals from the micro
2 environment and do things like activate the apoptosis or
3 tell the cell to quit dividing, doesn't that make sense
4 that that has to fail in order for a cell to become
5 cancerous?

6 MR. YOUNG: Objection, calls for
7 speculation.

8 A. I don't know the answer to that.

9 Q. (BY MR. SCHMIDT) Do you know whether the
10 telomeres need to be overridden in order for a cell to
11 become cancerous?

12 A. I don't know that, either.

13 Q. You do know that one of the ironies of cancer
14 is that a cancer cell, unlike other cells, doesn't have
15 a defined lifetime? It will go on forever if it can?

16 A. It can be immortal, yes.

17 Q. Yes. And the irony is that the mortal cell
18 kills the larger organism?

19 A. Frequently.

20 Q. Yeah. And in order for a cell to become
21 cancerous, certainly the apoptosis mechanism has to be
22 overridden somehow? That's the cell suicide function?

23 A. Yes.

24 Q. And, finally, well, not finally, another
25 genetic defect that has to occur is for the DNA repair

1 mechanisms have to fail?

2 A. Yes.

3 Q. So, these are the sorts of genetic defects that
4 must occur for a healthy cell to become cancerous and
5 those include proto-oncogene failure, tumor suppressor
6 gene failure, cell membrane receptor failure, telomeres
7 overridden, apoptosis thwarted and DNA repair mechanism?

8 MR. YOUNG: Object to compound question.
9 Lack of foundation. You can answer.

10 A. I can only answer in general terms because that
11 type of discussion is not my field. I'm not a cell
12 biologist.

13 Q. (BY MR. SCHMIDT) Now, just because some of
14 these kinds of injuries occur at the genetic level, that
15 does not mean that a cell will go on to become cancer,
16 does it?

17 A. You mean if a single defect occurs, will a cell
18 become cancerous?

19 Q. Right.

20 A. I don't know the answer to that, either.

21 Q. Let me pose this hypothetical to see if you
22 understand what I'm saying. Say that a cell receives a
23 hit from something that damages its genetic material.
24 Say it damages the apoptosis mechanism?

25 A. Right.

1 Q. If the DNA repair mechanism remains intact, the
2 cell may be able to fix itself and go on and continue to
3 lead a healthy life?

4 A. Or if the cell mechanism is overwhelmed. In
5 other words, if there are enough simultaneously
6 occurring hits to overwhelm whatever repair mechanism is
7 in force and effect or if the repair mechanism might
8 weaken with age, there could be a lot of things, again
9 speaking theoretically about this.

10 Q. But just because some damage occurs does not
11 mean that a cell will eventually go on to become a
12 cancer cell?

13 A. Probably not.

14 Q. Our cells are getting hit all the time and
15 they're repairing themselves, aren't they?

16 A. Yes.

17 Q. Here I've lived to be 56, you know, and this
18 has been going on since childhood. I'm blessed I don't
19 have cancer. And that's because these mechanisms, the
20 ability of the cell to repair itself and that's true for
21 all of us who don't have cancer?

22 MR. YOUNG: Objection, lack of foundation.
23 Calls for speculation.

24 A. It would be speculating, but I'm glad that you
25 don't have cancer.

1 Q. (BY MR. SCHMIDT) In fact, isn't it true that
2 the system of cell repair usually works so well that
3 it's generally a question of odds in terms of the number
4 of hits? If you get enough damage to your cells,
5 eventually the odds are that one single cell will make
6 it through the stages of genetic injury and become
7 cancer?

8 A. Well, it's a question of how you define hit.
9 In other words, our cells are all -- in the case of
10 white blood cells, for example, we have to reproduce --
11 we have to reproduce these cells and totally replace
12 them about three times a day which requires millions of
13 cell divisions. And we have mechanisms for breaking our
14 DNA and then repairing the DNA. And a break can occur
15 spontaneously without an external hit. Just a break
16 occurs because when you break up a lot of DNA, sometimes
17 the break might be wrong. So, the hit as you're talking
18 about can be endogenous or it can be exogenous from
19 outside the organism.

20 Q. You raise a good point. Let's define hit if
21 we're going to use that term today. Can we have an
22 understanding that when you and I say hit, we mean some
23 sort of injury at a genetic level to the DNA in the
24 cell?

25 A. Yes.

1 Q. And I understand and agree with you that the
2 hit can be external or it can be just an internal
3 malfunction?

4 A. Yes.

5 Q. And some people actually have sort of
6 programmed internal malfunctions and that's what we
7 consider a genetic defect?

8 A. That's true.

9 Q. Something they're born with?

10 A. Yes.

11 Q. One of the reasons cancer is a disease of older
12 people is that in accumulating the hits that you need
13 for a cell to become cancerous, it just -- usually the
14 odds require that it takes a long time?

15 A. I'm sorry, you'll have to run that one by me
16 again.

17 Q. The reason cancer is more prevalent in old
18 people is that they are simply exposed to more hits?

19 A. Well, I don't know the answer to that. They
20 may be exposed to more hits or they are unable to
21 repair -- less able to repair the hits they're exposed
22 to.

23 Q. Okay. So, let's flip it. Young people also
24 get cancer?

25 A. Yes.

1 Q. And that could just simply be a question of bad
2 luck like rolling double 6's six times in a row. They
3 get the required hits in far fewer exposures than other
4 people. That's one theory?

5 MR. YOUNG: Objection, lack of foundation.
6 Compound question.

7 A. Yes.

8 Q. (BY MR. SCHMIDT) The other may be that a young
9 person is born with one of those genetic
10 susceptibilities that leads to cancer earlier than other
11 people have?

12 A. That would be speculation because the ones we
13 identify are quite rare.

14 Q. But genetic susceptibility does mean that some
15 people have a defect or defects in their DNA that simply
16 predispose them to cancer?

17 A. Yes, some of these are known, yes.

18 Q. We know from the epidemiology where you have
19 groups of workers with essentially the same exposures to
20 benzene, for example, some will get the disease but many
21 will not?

22 A. That would be true.

23 Q. And the explanation for this is that some
24 people have a genetic susceptibility that other people
25 don't have?

1 MR. YOUNG: Objection, lack of foundation.

2 A. That would be speculation.

3 Q. (BY MR. SCHMIDT) Do you have any other theory
4 as to why that might be?

5 A. Well, from having worked in a laboratory, my
6 father's laboratory in my younger years, I know full
7 well that two people in the same room and you might
8 measure the ambient level of a particular compound in
9 that room, one person's working close to a hood, a fume
10 hood, the other one is not, one is near a window. So,
11 the amount that individuals in the same room get of that
12 compound can be vastly different. And, so, in other
13 words, if I have an occupation where someone says the
14 average worker has X exposure, it doesn't mean they all
15 have X exposure.

16 Q. Right. But my question pre-supposed that we
17 have groups of workers with essentially the same
18 exposures. And we know that's true. For example, the
19 shipyard studies for asbestos exposure, are you familiar
20 with any of those?

21 A. No.

22 Q. Let me ask it hypothetically. Assume you have
23 a group of workers that are essentially exposed to the
24 same carcinogen over a sufficient period of time, a few
25 of them will develop cancer and the vast majority will

1 not. You'd agree with that?

2 A. Yes.

3 Q. And the thing that would account for it in that
4 scenario is genetic susceptibility?

5 A. That might be one factor.

6 (Exhibit 62 marked.)

7 Q. (BY MR. SCHMIDT) Let me hand you Plaintiff's
8 Exhibit 62. If you would turn to the page I've
9 attached, 618, and read the paragraph labeled chemicals.
10 You don't have to read it out loud.

11 A. Okay. I've read this paragraph.

12 Q. Are you familiar with Harrison's Principles of
13 Internal Medicine?

14 A. Yes.

15 Q. Is this an authoritative text?

16 A. Well, I don't look at any text as
17 authoritative. They're useful references. I have a
18 Harrison's. I have other ones in internal medicine.
19 But a textbook is a textbook.

20 Q. This is a textbook that you learned internal
21 medicine from, one of them, in medical school, correct?
22 Not this edition?

23 A. Correct.

24 Q. Is there anything in that paragraph labeled --
25 headed chemicals that you disagree with?

1 A. Well, this is a speculation. In the paragraph
2 it says but susceptibility must also be important.
3 That's a speculation as only a minority of even heavily
4 exposed workers develop benzene myelotoxicity.

5 Q. Isn't that something we just discussed and you
6 agreed that in my scenario that was the case, that
7 genetic susceptibility explained why some did and some
8 did not develop cancer?

9 A. It could be an explanation.

10 MR. YOUNG: Objection, misstates the
11 witness's testimony.

12 A. Yeah, I think I said that is speculation, it
13 could be.

14 Q. (BY MR. SCHMIDT) The record will reflect what
15 you did say. Would you agree with the statement that
16 polymorphisms in genes metabolizing carcinogens is a
17 type of genetic defect that makes one person more
18 susceptible than another to developing AML?

19 A. I don't know.

20 Q. Would you turn to acute myeloid leukemia,
21 epidemiology and etiology which is I think your
22 reference number 4?

23 A. Yes, I have it.

24 Q. Okay. And turn to page 2103. Now, you
25 consider this article authoritative and one that you

1 have relied on in forming your opinion in this case?

2 A. Well, I don't consider it authoritative. I
3 don't consider any particular source as authoritative.
4 They're all useful. They are references and I have
5 referenced it for certain purposes in this report.

6 Q. I direct your attention in the far right-hand
7 column on 2103, the paragraph beginning right up above
8 physical and chemical factors. I'm going to read the
9 first sentence. Data have been published recently
10 showing that individuals with certain polymorphisms in
11 genes metabolizing carcinogens have an increased risk of
12 developing AML. Do you agree with that statement?

13 A. I don't know. It references a specific paper
14 that I've not read.

15 Q. A polymorphism in gene is a genetic defect; is
16 that true?

17 A. I don't know. I'm not a DNA geneticist.

18 Q. You do hold yourself out to be an oncologist?

19 A. Hematologists treat cancer.

20 Q. Would a polymorphism in gene that gave someone
21 an increased risk of developing AML be a genetic defect
22 that pre-disposed a person to AML? Is that what you
23 understand this sentence to mean?

24 MR. YOUNG: Objection, lack of foundation.

25 A. That's what that -- yes, that's what this

1 comment refers to.

2 Q. (BY MR. SCHMIDT) Do you agree that there may
3 be genetic variability in terms of how people respond to
4 what we just described as hits?

5 A. I think that may be so.

6 Q. That would include how people -- that we find
7 some people are much more sensitive to chemotherapy than
8 others?

9 A. It is true that people -- there is a variation
10 in sensitivity to chemotherapy. It isn't vast, but some
11 people do get cytopenic easier than others.

12 Q. Isn't it true that in some patients the dose
13 that wouldn't bother the next fellow makes their blood
14 counts disappear?

15 A. That would be very unusual. Maybe so, but it's
16 unusual.

17 Q. Dr. Natelson, I'm quoting from testimony you
18 gave in the case of -- do you remember giving a
19 deposition in Jesus Valentine Frias versus Shell Oil
20 Company?

21 A. Yes.

22 Q. I'll show you. Begins down there and then
23 continues on the next page.

24 A. Yes, that's what I said at that time.

25 Q. Has your knowledge of medicine or about

1 susceptibility to these things changed since the date of
2 this deposition?

3 A. No. I've said that there is a variation in
4 what people get with these drugs.

5 Q. And here you said there's a lot of variability?

6 A. There's variability.

7 Q. You said there was a lot of variability, did
8 you not?

9 A. If you like "lot", that's fine. I did say
10 that, I can agree with that.

11 Q. That was my question. And you also agreed that
12 the principle of variability is as true of chemical
13 exposure as it is to chemotherapy exposure?

14 MR. YOUNG: Objection, lack of foundation.

15 A. Yes, I said that.

16 Q. (BY MR. SCHMIDT) In fact, chemotherapy
17 exposure is chemical exposure?

18 A. Yes.

19 Q. Do you agree that AML disease, that is
20 associated with or caused by benzene exposure?

21 A. Can be, yes.

22 Q. I want to now talk about what you and I
23 described as hits and how benzene -- benzene's role in
24 carcinogenesis. Benzene damages myeloid chromosomes; is
25 that correct?

1 A. Yes.

2 Q. Is that one of the things it does?

3 A. Yes.

4 Q. There are other genetic damages that it can
5 cause?

6 A. Such as? I'm not sure what you're talking
7 about.

8 Q. Is that the only kind of genetic damage that
9 benzene can cause is damage to the myeloid chromosomes?

10 A. Well, it can damage lymphoid chromosomes, too.
11 I mean, it damages chromosomes.

12 Q. And persistent damage to the myeloid
13 chromosomes can lead to leukemia?

14 A. Yes, if that damage can't be repaired.

15 Q. Is one of the things that benzene can damage
16 include the DNA repair mechanism?

17 A. Yes, that is thought to be so.

18 Q. And the more hits one has the more damage
19 accumulates and becomes persistent?

20 A. Yes.

21 Q. And each of these hits and the resulting damage
22 in sufficient quantity can become a factor contributing
23 to the development of leukemia?

24 A. Yes.

25 Q. And one of the reasons the risk of leukemia

1 increases with age is that the older one gets the
2 greater the opportunity to accumulate damages -- damage
3 to the DNA of any particular cell that might lead to
4 cancer?

5 A. Well, there's a greater likelihood. The
6 mechanism is not known with certainty. It could be
7 failure of repair.

8 Q. I agree, but it's a greater likelihood
9 question?

10 A. Yes.

11 Q. Now, I'm going to ask you a hypothetical. For
12 a particular cell that eventually goes on to become AML,
13 assume that all of the hits that damage the DNA includes
14 damage to the proto-oncogenes, tumor suppressor, et
15 cetera, were caused by benzene, every single one of
16 them, you would say that AML was certainly medically and
17 scientifically the cause of the development of the AML?

18 MR. YOUNG: Objection, incomplete
19 hypothetical. Calls for speculation. Compound. Lack
20 of foundation. Go ahead.

21 A. I'm not certain that I understand your
22 question.

23 Q. (BY MR. SCHMIDT) I'll be happy to --

24 A. Tell me again.

25 Q. -- restate it. And, Dr. Natelson, if I ask

1 confusing questions through the course of the day,
2 please do that. Say I don't understand and I'd like you
3 to rephrase and I'll be happy to. Okay?

4 I want you to assume that a particular cell
5 in the bone marrow goes on to become AML. It's that
6 first cell that goes through all the stages we
7 previously discussed. Got that?

8 A. All right.

9 Q. And assume that all of the hits that lead to
10 that final stage where it is an independent cell working
11 against the good of the whole were caused by benzene
12 exposure. You understand that?

13 A. All right.

14 Q. In that case you would say that the development
15 of the AML was medically and scientifically caused by
16 benzene exposure, would you not?

17 A. Yes.

18 Q. But in any particular case there's no way we
19 can actually know this, can we?

20 A. That's true.

21 Q. We can't look in, find the cell or look at one
22 of the clones and somehow read its history and see what
23 the exposures came from, can we?

24 A. Correct.

25 Q. And I think you've already said, but I just

1 want to make sure, leukemia is a cumulative disease;
2 that is, it is caused by a number of genetic defects
3 accumulated over time?

4 A. How large that number is is unknown, but it is
5 likely more than one.

6 Q. And each and every exposure to benzene
7 contributes to the development of the disease, leukemia?

8 A. Well, that would be true of a cumulative dose
9 of any chemical, whether it's benzene or anything else.

10 Q. And that would also be true of a particular
11 kind of leukemia which would be AML, each and every
12 exposure contributes to the development of the disease?

13 MR. YOUNG: Objection, asked and answered.

14 A. Well, the development of acute myeloid leukemia
15 and benzene exposure is thought to be a cumulative dose
16 effect so that the more doses you have, the more the
17 possibility increases.

18 Q. (BY MR. SCHMIDT) And I should ask it a
19 different way because you and I talked about hits, being
20 a hit was defined as genetic injury?

21 A. Yes.

22 Q. So, it's actually more accurate to say each and
23 every hit as you and I have understood that term today
24 contributes to the development of the disease AML?

25 A. Yes.

1 Q. So, to the extent that a person is exposed to
2 benzene over a 20 or 30-year period, if you believe that
3 a person's AML was caused by benzene exposure, each and
4 every exposure is deemed by medical science to have
5 contributed to the development of the AML?

6 MR. YOUNG: Objection, lack of foundation.
7 Calls for speculation.

8 A. Well, it would depend on when the exposure was
9 relative to the occurrence of the leukemia.

10 Q. (BY MR. SCHMIDT) But explain that.

11 A. Well, in other words, if I give somebody
12 chemotherapy, for example, I give them lots of hits.
13 All right? And they have a particular risk of catching
14 acute myeloid leukemia but that risk occurs within a
15 fairly defined period of time. If 30 years pass and I
16 don't give them any more of that chemotherapy drug and
17 they haven't caught leukemia, they're not likely to get
18 it from the hits I gave them 30 years earlier.

19 Q. Okay. Then you and I have been
20 miscommunicating. I'm going to ask the question again.
21 To the extent a person is exposed to benzene over a 20
22 or 30-year period and that person develops AML, okay, so
23 I left that out the first time. That's my problem.

24 A. Okay.

25 Q. So, imagine it's a 30-year exposure to various

1 degrees of benzene, but we'll call them hits, that they
2 were enough to cause genetic damage. And if you form
3 the opinion as a medical doctor that the AML was
4 causally related to the benzene exposure, you would also
5 believe that each of the hits contributed to the
6 development of the AML?

7 MR. YOUNG: Objection, asked and answered.

8 A. In general, that's true, yes.

9 Q. (BY MR. SCHMIDT) Now, benzene clears the body,
10 correct?

11 A. Benzene clears the body?

12 Q. An exposure to benzene, a hit 30 years ago
13 isn't going to be there even next week?

14 A. No. The metabolites are short-lived.

15 Q. And the reason these early hits are deemed to
16 contribute to the causation, it's not because of benzene
17 toxicity or the presence of benzene, it's the presence
18 of the resulting genetic defect, correct?

19 A. Yes.

20 Q. And in the course of, say, a 30-year period of
21 exposure to benzene, while there may be a number of
22 hits, a number of the hits may actually go away. They
23 may actually be repaired by the DNA repair mechanism;
24 isn't that true?

25 A. Yes.

1 Q. It's only when enough damage accumulates that
2 all the stages have been passed that are required, and
3 you've said you don't know how many those are
4 particularly but there is a number, only once that's
5 been achieved can an AML tumor arise?

6 MR. YOUNG: Objection, asked and answered.

7 A. I think I have answered that, but yes.

8 Q. (BY MR. SCHMIDT) Here I want to come at it a
9 different way. This accumulation of damage that we're
10 talking about is what you mean when you say that every
11 exposure contributes to the development of the AML?

12 A. Yes.

13 Q. Another hypothetical. I want you to go back
14 and imagine that same healthy cell in the marrow that
15 becomes AML and makes it through all the stages. And in
16 this hypothetical somewhere between one and four --
17 strike that. Some of the hits that are required are
18 caused by benzene and some others are caused by either
19 genetic susceptibility, some other defect or some other
20 chemical insult. Do you understand that?

21 A. Yes.

22 Q. Okay. And in that case the benzene-caused hits
23 would be factors contributing to the causation. Would
24 you agree to that?

25 MR. YOUNG: Objection as an incomplete

1 hypothetical with undefined terms. Go ahead, Doctor.

2 A. I think if what you're suggesting is that if I
3 gave two mutagenic drugs simultaneously, I would
4 increase the potential for damage and the risk of
5 leukemia. I think that's what you're saying. I'm not
6 certain.

7 Q. (BY MR. SCHMIDT) The hypothetical is the
8 leukemia has arisen and let's say for the purpose of the
9 hypothetical, let's say there are eight genetic defects
10 that have to occur. Imagine four of them are caused by
11 benzene, four of them are caused by smoking.

12 A. Okay.

13 Q. Okay? In that case, the resulting AML, you
14 would say that the benzene is a factor contributing to
15 the causation, correct?

16 A. Yes.

17 Q. And you would also say the smoking is a factor
18 contributing to the causation?

19 A. Yes. I don't know how benzene -- it's not
20 known how benzene contributes, but we're assuming that
21 it does in the way you're defining it. So, I would say,
22 yes, they're both contributory.

23 Q. And in this hypothetical if the cancer could
24 not and would not arise but for the genetic damage
25 caused by the benzene, you would have to say that it was

1 a substantial contributing factor, would you not?

2 MR. YOUNG: Objection, speculation. Calls
3 for a legal conclusion now without defining the terms.
4 Go ahead.

5 A. Run that one by me again. I'm not certain
6 exactly what you're asking.

7 Q. (BY MR. SCHMIDT) You've got the hypothetical
8 in mind?

9 A. Yes.

10 Q. Smoking and benzene, causation of an AML, in
11 that hypothetical if the cancer could not and would not
12 have arisen but for the benzene exposure, you would
13 consider that a substantial contributing factor?

14 MR. YOUNG: Same objections as previously
15 stated.

16 A. Yes.

17 Q. (BY MR. SCHMIDT) And the same for the smoking,
18 you would consider that in that hypothetical a
19 substantial contributing factor, would you not?

20 MR. YOUNG: Same objection.

21 A. Yes.

22 Q. (BY MR. SCHMIDT) In terms of the amount of
23 benzene that it takes to -- and by amount I mean the
24 dose, either cumulative or through an intense short
25 period exposure -- the amount that it takes to cause

1 injury can vary widely person to person because of
2 genetic susceptibility?

3 MR. YOUNG: Objection, lack of foundation.

4 A. I don't know that that's so.

5 Q. (BY MR. SCHMIDT) I'm going to read you a
6 question and answer you previously testified to in that
7 same Frias. It's your opinion that a high dose of
8 benzene doesn't necessarily mean it damaged the bone
9 marrow is the question. Answer: Well, there are
10 different susceptibilities people have, probably on a
11 genetic basis. So, a single dose that didn't affect the
12 blood count might well not affect the bone marrow,
13 either?

14 MR. YOUNG: Doctor, before you answer,
15 Counsel, could you just show it to him?

16 MR. SCHMIDT: I'll be glad to.

17 MR. YOUNG: Thanks.

18 A. Well, I think what you're saying is taken out
19 of context. What I was asked is that and what I said is
20 that I said in terms of damage to the bone marrow, I
21 said I would say that it would have to be enough to
22 damage the bone marrow and the way you would assess that
23 damage would be reductions in the white blood cell count
24 that were substantial and measurable. So, in other
25 words, what I said is that if a person was getting

1 enough drug to damage the bone marrow, I would expect to
2 see that reflected in falls in the peripheral blood
3 count. But it's your opinion that a high dose of
4 benzene doesn't necessarily mean it damaged the bone
5 marrow. Well, there are different susceptibilities
6 people have, so a single dose that didn't affect the
7 blood count might not affect the bone marrow, either.
8 In other words, all I said is you gave somebody a low
9 dose of something, it wouldn't drop the white count, it
10 wouldn't bother the bone marrow.

11 Q. (BY MR. SCHMIDT) You also said different
12 susceptibilities. In other words, different people will
13 react differently to the same dose of benzene?

14 A. I think we already covered that with
15 chemotherapy. It's a matter of degree.

16 Q. Right. Do you have your -- it's going to be
17 here. It's your article, Critical Reviews in
18 Toxicology, Zhang. I can tell you which cite it is.

19 A. Yes, I have it here only because I have it in
20 blue.

21 Q. It's your reference 47 in your report; is that
22 correct?

23 A. Yes.

24 (Exhibit 63 marked.)

25 Q. (BY MR. SCHMIDT) Doctor, I've handed you

1 what's been marked Plaintiff's Exhibit 63. Would you
2 identify that for the record?

3 A. Yes, this is my report in this case.

4 Q. Okay. And, so, when we talk today about your
5 report, we're referencing Exhibit 63?

6 A. Yes.

7 Q. That will be our understanding. And that's
8 your only report in this case?

9 A. Yes.

10 Q. Doctor, I want to direct your attention to
11 table 4. You might want to familiarize yourself with
12 that portion.

13 A. Let me see where that's referenced in the text.

14 Q. It's on page 13 under Roman numeral V, first
15 sentence.

16 A. Yes, I understand that.

17 Q. Table 4 is a summary of studies showing
18 positive results of benzene exposure on and then it has
19 and initial CA but that means chromosomal abnormalities?

20 A. Yes.

21 Q. And a chromosomal abnormality is a genetic
22 defect or a hit?

23 A. Could be, yes.

24 Q. What else could it be?

25 A. Well, this is chromosomal abnormalities, but as

1 we'll probably get into it's not defined as myeloid
2 cells. And I'm guessing that most of these are lymphoid
3 cells.

4 Q. That's fine. But what this is is studies of
5 chromosomal abnormalities resulting from benzene hits,
6 is it not?

7 A. No. What happens is these are studies of T-
8 lymphocytes generally. And when you actually look at
9 the papers, you will see that both control populations
10 and patient populations have aberrations, controls having
11 no benzene at all. And we know many every-day compounds
12 can produce these kinds of aberrations in lymphocytes.
13 So, that we have what we have. In other words, I can't
14 dispute what the text says, but I don't, I don't find
15 any pertinence to this in acute myeloid leukemia.

16 Q. But it does sound like you dispute what the
17 text says?

18 A. No.

19 Q. The text says this is a review of studies
20 showing chromosomal abnormalities associated with
21 benzene exposure?

22 MR. YOUNG: Objection, argumentative.

23 A. That's the title of the study.

24 Q. (BY MR. SCHMIDT) And the text that references
25 this starts with the statement that since the 1960s

1 approximately 50 cytogenic studies in benzene-exposed
2 individuals have been conducted. Most studies have
3 shown a positive association between benzene exposure
4 and increased chromosomal abnormalities. Did I read
5 that correctly?

6 A. Yes.

7 Q. And cytogenic, what does that mean?

8 A. Cytogenetic, it means --

9 Q. I'm sorry.

10 A. -- the DNA in the cell, you might say. Cell
11 DNA.

12 Q. Let's go on a diversion here for a minute. In
13 your report you talk about karyotyping?

14 A. Yes.

15 Q. And that's a study of chromosomes, is it not?

16 A. Yes.

17 Q. And there was a karyotyping test done on Mr.
18 Henricksen that you saw?

19 A. Yes.

20 Q. And it showed no dislocation of chromosomes 5
21 and 7?

22 A. Correct.

23 Q. Is karyotyping the same thing as cytogenetic --
24 a cytogenetic study?

25 A. They're quite similar. Karyotype is the

1 analysis of the 46 chromosomes in a normal person's
2 cell.

3 Q. And what's inside a chromosome?

4 A. You mean what's it composed of?

5 Q. Uh-huh.

6 A. Various base pairs, adenine, guanine, cytosine.
7 It's got linkages between these nucleic acids.

8 Q. Genes?

9 A. And there are genes in there, yeah, less micro
10 molecular, yes.

11 Q. And, so, the karyotyping study is of these
12 relative terms of the DNA, these large clumps which are
13 the 46 chromosomes, correct?

14 MR. YOUNG: Objection to the term. Object,
15 lack of foundation. Speculation. Go ahead, Doctor.

16 A. Usually when we're talking about a person's
17 karyotype, we're talking about the 46 chromosomes in
18 that person's cells.

19 Q. (BY MR. SCHMIDT) And it's not a study or
20 analysis of anything inside the chromosomes; is that
21 correct?

22 A. That's correct.

23 Q. Okay. There are genetic studies that can be
24 done to look inside for other defects in the genes or in
25 the DNA itself inside the chromosome, correct?

1 A. Yes, some of those are called point mutations
2 or small defects, yes.

3 Q. And as far as you know, no such study was done
4 on Mr. Henricksen, such study?

5 A. I'm not aware of any such study.

6 Q. You haven't seen one?

7 A. No.

8 Q. One could have been done?

9 A. Yes.

10 Q. The kinds of studies that Zhang is looking at
11 on table 4 are not the karyotyping, looking at
12 chromosomes, but it's the kinds of studies where they're
13 looking inside for other kinds of genetic damage; is
14 that true?

15 A. I don't know the answer to that and I doubt
16 that. In other words, here what they're talking about
17 is hyper and poly. They're talking about numbers of
18 chromosomes. And the studies you're talking about on
19 point mutations wouldn't have been available in many of
20 these years. So, I think this is simply looking at the
21 chromosomes, counting their numbers and looking at their
22 shape and size.

23 Q. And looking for all sorts of abnormalities, in
24 particular?

25 A. Yes.

1 Q. I want to see if I'm understanding this table
2 correctly. If I look down starting at the beginning of
3 table 4, you see the middle column, benzene exposure?

4 A. Yes.

5 Q. And then you come down to Fredga, a 1979 study?

6 A. Yes.

7 Q. To the right they're looking at mean part per
8 million benzene exposure of ten?

9 A. Yes.

10 Q. Is that what I understand that to mean? And at
11 that level they're finding certain genetic
12 abnormalities?

13 A. Well, it gives ranges here. In other words, it
14 could be a ten part per million year and it could be up
15 to 43 years.

16 Q. Right. But at the level of benzene that
17 they're looking at here, they did detect certain
18 chromosomal abnormalities, correct? Far right-hand
19 column?

20 A. Yes.

21 Q. Similarly, Picciano, and here we have the
22 benzene exposure described as less than ten with a mean
23 of 2.1?

24 A. Yes.

25 Q. That's parts per million?

1 A. Yes.

2 Q. And they're detecting genetic abnormalities at
3 that level in this study?

4 A. It says -- let's see what the SCA stands for.

5 Q. The key is on the next page. See if I see it.

6 A. See if we can find what an SCA means.

7 Q. I don't see where you see -- oh.

8 A. What they looked at, in other words, it says
9 their end point. Now, in some of these columns, looking
10 at the numbers of chromosomes, it says hypo meaning less
11 than 46 or poly meaning more than 46. There's a blank
12 after that particular one. So, they don't tell us that
13 they notice any change in the number of chromosomes.
14 And then under this one it says under SCA, it says B and
15 m-a-r and I don't know what that means.

16 Q. B is break?

17 A. Okay.

18 Q. The arrow pointing up means increase?

19 A. Increase in B and an increase in mar, whatever
20 that is.

21 Q. Markers?

22 A. Markers. Yeah, markers. Okay. That's what
23 they say.

24 Q. So, they say that at a mean part per million
25 exposure of 2.1, they're detecting an increase in breaks

1 and in markers?

2 A. Yes.

3 Q. That means that they're detecting what you and
4 I have described as hits?

5 A. Could be.

6 Q. It is, isn't it?

7 A. I don't know. These studies, as I said, often
8 produce abnormalities in normal individuals. And I
9 don't know the relevance of any of this. But we have
10 what we have. In other words, as you've described,
11 these people have a study that was published years ago
12 and they claim that they looked at 200 cells, I assume
13 lymphocytes, and they found some structural
14 abnormalities, breaks in the chromosomes.

15 Q. Which you and I have described as hits,
16 correct?

17 A. Could be.

18 Q. We have described those as hits. Breaks in
19 chromosomes are hits, aren't they?

20 A. They could be, yes. This is a study -- you're
21 going from one situation, breaks in a person's bone
22 marrow chromosomes and then here you're going to
23 something that's more macro. In other words, it's a
24 dented fender. It's not the substructure of the
25 chromosome. I don't know what they looked at and the

1 relevance of it. But they say they saw an abnormality.
2 I can't argue with that.

3 Q. That's all I'm trying to establish here. If we
4 go down to Sarto, at benzene exposures of .2 to 12.4,
5 they're finding genetic abnormalities, correct?

6 A. Yes.

7 Q. That was a 1984 study?

8 A. Yes.

9 Q. Damrau, 1986, exposures of 1.6 to 3.1, they're
10 finding genetic abnormalities in this 1986 study,
11 correct?

12 A. Yes.

13 Q. Jablonick and A with a back slash, I mean a
14 forward slash over it, a 1987 study shows exposures to
15 benzene at the level of .5 to 1.2 part per million and
16 they're detecting that that constituted a hit, correct?

17 A. Yes.

18 Q. Continuing down, Yardley Jones, a 1990 study,
19 exposure at the level of -- how do you read that number?
20 It looks like a one to a ten and I don't see -- what
21 does the exponent mean, the G? You see that?

22 A. I see an exponent, but your eyes are better
23 than mine. I can't see the G.

24 Q. It's my glasses.

25 A. I don't know what that is. It's probably an 8,

1 not a G. But I don't know. I don't know what they mean
2 by that.

3 Q. In any event they also detect a hit at whatever
4 level that is, correct?

5 A. Yeah, it says less than a hundred cells. That
6 could be one cell or it could be ten. I don't know how
7 many cells they studied.

8 Q. The 1992 study right below it, Sasiadek, it's
9 exposure at a level below ten and then again I can't
10 read that exponent. But they see a number of genetic
11 abnormalities out there on the right, correct?

12 A. Yes.

13 Q. And here we also have Tompa, a 1994 study, one
14 to 21 part per million exposure, they show a genetic
15 defect, correct?

16 A. They just show an increase in whatever NCA and
17 SCA stand for again.

18 (Exhibit 64 marked.)

19 Q. (BY MR. SCHMIDT) Okay. Let me hand you that.

20 A. Okay.

21 Q. Have you ever seen this study before?

22 A. No.

23 Q. Do you understand it to be -- it's an animal
24 study looking at low level benzene exposure?

25 A. Yes, in mice.

1 Q. And they say in the summary at the very
2 beginning that the concentrations were zero, 40, 100 and
3 1,000 parts per billion that they were exposing the
4 animals to?

5 A. Yes.

6 Q. And they found significant increases in
7 chromosome aberrations in spleen lymphocytes?

8 A. Yes.

9 Q. How much smaller is 40 parts per billion than
10 one part per million?

11 MR. YOUNG: Objection, relevance. Lack of
12 foundation.

13 A. Well, it would be a factor of a thousand.

14 Q. (BY MR. SCHMIDT) It would be 5,000?

15 A. This would be -- this is parts per billion. In
16 other words, I guess you would add three zeroes on to
17 parts per million. In other words, this is a thousand.
18 Is that right? In other words, if I had one part per
19 million, I would have a thousand part per billion; is
20 that correct?

21 Q. I think that's right.

22 A. Okay. So, this is one part per million.

23 Q. Yes. How does 40 parts per billion compare?
24 It's a heck of a lot smaller, correct?

25 A. Yes.

1 Q. Okay. And then you see -- I think the quickest
2 way to see the effect of these exposures is probably
3 figure 1 on page 222? This indicates that they find
4 some chromosomal damage or hits at 40 parts per billion
5 benzene concentration, higher levels at a hundred parts
6 concentration, correct?

7 A. Yes.

8 (Exhibit 65 marked.)

9 Q. (BY MR. SCHMIDT) I think we're done with that.
10 I'm handing you another article entitled Hemotoxicity in
11 Workers Exposed to Low Levels of Benzene. The lead
12 author is Qing Lan, and I'll ask you if you've seen this
13 before?

14 A. I may have, but not in detail. I haven't
15 studied it.

16 Q. What I'm particularly interested in is table 1,
17 but take whatever time you need to familiarize yourself
18 on that.

19 A. Okay. I see what they have here.

20 Q. And does table 1 show that, for example, the
21 exposed population is exposed to or at levels of less
22 than one part per million? And if you go down and
23 compare their peripheral blood cell counts, in each
24 category are lower than those in the control group; is
25 that correct?

1 A. Yes.

2 Q. Does that suggest that exposures of less than
3 one part per million constitute -- to benzene constitute
4 what you and I have been calling hits?

5 MR. YOUNG: Objection, lack of foundation.
6 Calls for speculation.

7 A. No, not necessarily. All of these white counts
8 are within the normal range. They do show a trend. In
9 other words, they run from about 5,000 to 7,000, the
10 normal being 5 to 10,000. And a number of people,
11 normal people are below 5,000. I can't testify as to
12 how they measured their part per million levels of
13 benzene, whether that was accurate. I see the numbers
14 here which is a trend. I don't know that the mechanism
15 is necessarily chromosome damage.

16 Q. (BY MR. SCHMIDT) But the trend is lower white
17 counts?

18 A. The trend is lower white counts, yes.

19 Q. And that's true at the higher levels of
20 exposure to the right?

21 A. Yes.

22 Q. Did you see plaintiffs' expert Dr. William
23 Sawyer's report in this action?

24 A. Yes.

25 Q. Did you see that he testified that he thinks

1 that Mr. Henricksen experienced peak exposures of up to
2 5.2 parts per million?

3 A. I have his report in here. I think what I had
4 is that he thought the cumulative exposure was three
5 parts per million. I don't remember what he said about
6 peak.

7 Q. I'm sorry, that was -- I think you're thinking
8 of --

9 A. Kaltofen.

10 Q. Kaltofen, yes.

11 A. Yes.

12 Q. Did you see Dr. Sawyer's report, the
13 toxicologist?

14 A. Yeah, that's in here, also.

15 Q. You don't need to look it up. I'll just tell
16 you that he found peak exposures of 5.2 parts per
17 million. 5.2 parts per million are certainly a great
18 deal higher than any of the parts per billion cited in
19 the Au study?

20 A. Yes.

21 Q. And higher than a great number of the exposures
22 we saw in the Zhang study?

23 A. Yes.

24 Q. Mr. Kaltofen saw peak exposures of 6.2 to
25 9.2 parts per million. Again, those are significantly

1 higher than we just saw in these previous three studies?

2 A. Yes.

3 Q. There's a Carolyn Phillips' Shell study, have
4 you seen that, of exposures to tanker drivers top
5 loading?

6 A. No.

7 Q. She found that five percent of the time top
8 loaders who were exposed to benzene in excess of 1.5 to
9 2.5 parts per million, do you believe that's sufficient
10 to constitute a hit?

11 A. That she found peak exposures?

12 Q. Five percent of the time top loaders exposed to
13 benzene were exposed in excess of 1.5 to 2.5 parts per
14 million?

15 A. Not to myeloid chromosomes.

16 Q. Same for Mr. Kaltofen's peak exposures of 6.2
17 to 9.2, is that sufficient to constitute a hit? Will it
18 cause chromosomal damage?

19 A. I don't know the answer to that in terms of
20 myeloid chromosomes.

21 Q. How about 5.2 parts per million, is that
22 sufficient to constitute a hit?

23 A. As a peak, probably not.

24 Q. So, you aren't sure whether 6.2 to 9.2
25 constitutes a hit, but 5.2 you think is too low?

1 A. Yes, because I don't know that we have a lot of
2 studies on myeloid chromosomes in benzene-exposed
3 individuals at peak levels and/or the significance of
4 that. So, I would just have to say I don't really know.

5 Q. How about chronic long-term exposure, is 8.3
6 part per million years sufficient to constitute a hit?

7 A. I don't know the answer to that, either, in
8 terms of a hit.

9 Q. So, you can't say one way or the other whether
10 it is or it isn't?

11 A. No.

12 Q. Is that correct?

13 A. That's correct.

14 MR. SCHMIDT: Let's take our break.

15 (Break taken from 12:19 p.m. to 12:27 p.m.)

16 Q. (BY MR. SCHMIDT) Dr. Natelson, you're a
17 clinician?

18 A. Yes.

19 Q. As a clinician when a patient walks in the door
20 with some blood-related complaint, you do a differential
21 diagnosis?

22 A. Yes.

23 Q. And what do you understand that to be or would
24 you explain that to the jury?

25 A. There is some abnormality noted. Let's say

1 it's a high white blood cell count or an abnormal
2 clotting test or an enlarged lymph node. We try to
3 identify what the process is and then what the potential
4 causes for that process might be.

5 Q. And by what that process is, what the disease
6 is, in other words, diagnose the disease? Is that what
7 you mean?

8 A. Well, not exactly.

9 Q. Okay.

10 A. Let's just take a high white blood cell count.
11 The process might be infection. There could be many,
12 many different kinds of infections. Or the high white
13 count could be on the basis of malignancy and there
14 could be many different kinds of malignancies that
15 produce the white count. So, we try to pigeon-hole the
16 specificity of the abnormality and then look at
17 illnesses that might cause that.

18 Q. Oh, I see. If it's a cancer, you're specifying
19 the process, but there's still a number of different
20 cancers that it could be?

21 A. Correct. That's particularly true with
22 elevated lymphocyte counts in the blood.

23 Q. And similarly if it's the result of an
24 infection, that's only the first step. Now you have to
25 figure out what the agent is that is the infection?

1 A. That's correct. And even if it is an
2 infection, in other words, is it simply an inflammation
3 in the system. Let's say someone with rheumatoid
4 arthritis might have a high white count from irritation
5 of the joints, but not infection. But they might have
6 infection. So, you have to look at what the type of
7 cell it is, is it malignant, is it non-malignant and
8 what the various potential causes for that elevation
9 might be in the case of a high white count.

10 Q. And as I understand differential diagnoses,
11 what you then do is identify the suspects and then do
12 what you can to eliminate to see if you can exclude
13 those from being the actual causes?

14 A. Yes.

15 Q. That's the process?

16 A. Yes.

17 Q. And one of the things in that process you have
18 to do is determine if there are any confounding factors
19 or anything in the patient's background that might
20 explain the cause?

21 A. Yes.

22 Q. Are you aware of any chemical apart from
23 benzene that causes AML?

24 A. Certainly a multitude of our chemotherapy drugs
25 do. There are all different chemicals.

1 Q. Apart from chemotherapy agents and benzene, are
2 you familiar with any other chemicals that are medically
3 accepted to cause AML?

4 MR. YOUNG: Objection, lack of foundation.
5 Outside the scope of this witness's designation. Go
6 ahead.

7 A. Well, let me think about that. And you're
8 excluding radiation? I mean, that could be in the form
9 of a chemical.

10 Q. (BY MR. SCHMIDT) Yes.

11 A. Because these days some of our chemotherapy
12 drugs combine a drug with a radioactive source. But in
13 terms of chemicals that cause acute leukemia, many drugs
14 can do it. Some of our immunosuppressant drugs can.
15 And certainly many of the drugs we use in chemotherapy
16 can. Those would come to mind at the moment.

17 Q. Okay. You're not aware that Mr. Henricksen had
18 any chemotherapy treatments prior to the development of
19 his AML, are you?

20 A. No.

21 Q. Or any other drug treatment that you believe
22 leads to AML prior to the development of his AML?

23 A. No.

24 Q. Now, when a patient comes in and you do the
25 differential diagnosis, one of the things you do is take

1 the patient's medical history for risk factors?

2 A. Yes, that would be so.

3 Q. You do a physical exam?

4 A. Yes.

5 Q. You might look at epidemiologic data?

6 A. Depending on what the illness is you're looking
7 at.

8 Q. If you think it might be AML?

9 A. Well, I'm not sure in what way. In other
10 words, if someone comes in and says they're in this case
11 a tanker truck driver, would I normally go and get the
12 epidemiology of that, I might.

13 Q. Certainly one of the things you take in the
14 history is you'd be looking for the drug and chemical
15 exposure history?

16 A. Yes, in a case of leukemia, certainly.

17 Q. And you'd look at laboratory findings?

18 A. Yes.

19 Q. And you'd do your own tests?

20 A. Well, I would look at the blood film under the
21 microscope and the bone marrow and we'd look at
22 chromosome studies and a number of other things we do.

23 Q. In this case, in Mr. Henricksen's case, which
24 of those things did you do?

25 A. Well, I didn't have the access to his

1 peripheral blood and bone marrow to look at, but I
2 certainly had the reports. So, we saw the reports that
3 indicated that he meets criteria for acute myeloid
4 leukemia with large numbers of what we call blast cells
5 in the bone marrow. He had cytogenetic data, a
6 karyotype done and that showed he had what's referred to
7 as diploid chromosomes or normal chromosomes by that
8 analysis. We then saw the history that he worked as a
9 tanker driver. We looked at his family history and he
10 did not have any evidence of acute myeloid leukemia in
11 the family but his mother had breast cancer. And that's
12 been thought in some studies to be a risk factor for AML
13 in children. And his mother did have breast cancer
14 according to the history. And then we looked at his --
15 the treatment that was given and the consequences of the
16 treatment.

17 Q. So, you reviewed his medical records. You also
18 looked at epidemiologic data?

19 A. Yes.

20 Q. When you say that he had the karyotyping and it
21 showed normal chromosomes, I think one of the things
22 we've been talking about here this morning, though, is
23 you know as a fact that he does not have normal DNA or
24 did not when he developed the disease because it's a
25 disease that is by definition one that's caused by

1 abnormal DNA?

2 A. Well, he had no defined abnormality that we
3 saw.

4 Q. Right. But you know as a fact that he had
5 genetic defects that caused the disease because that's
6 what causes the disease, correct?

7 MR. YOUNG: Objection, asked and answered.

8 A. That may be so, but we had none that were
9 identified.

10 Q. (BY MR. SCHMIDT) I understand that. But you
11 understand AML to be a disease that is caused by genetic
12 defects?

13 A. We think that's so.

14 Q. The breast cancer from his mother, if I
15 understand you and understand your report, there is some
16 evidence that if someone's mother develops breast
17 cancer, that person being the child, is at an increased
18 risk for developing AML?

19 A. That's what the literature suggests, yes.

20 Q. Is that a genetic predisposition to the
21 development of AML?

22 A. The mechanism is unknown.

23 Q. It could be genetic?

24 A. It could be genetic.

25 Q. What else could it be?

1 A. It could be environmental. In other words,
2 familial. We see, for example, in Hodgkin's disease
3 there's an increased risk in siblings. And it's
4 siblings of the same sex. In other words, if you're a
5 man with Hodgkin's disease, it's your brother that has
6 it, not your sister. If you're a woman with Hodgkin's
7 disease, it's your sister that has it, not your brother.

8 Q. It being an increased risk?

9 A. The disease, yes, risk of the disease. And,
10 so, it may be environmental, not genetic in that
11 particular case. But we don't know the answer with
12 breast cancer. It's an observation that's been made and
13 but not very well defined.

14 Q. Well, let's go back to your reference number 4
15 which is acute myeloid leukemia epidemiology and
16 etiology we looked at earlier.

17 MR. YOUNG: I'm sorry, Jackson, what
18 reference?

19 MR. SCHMIDT: It's reference 4. It's from
20 the American Cancer Society. And table 2 on page 2102.

21 A. Yes.

22 Q. (BY MR. SCHMIDT) And table 2 is a list of risk
23 factors associated with AML?

24 A. Yes.

25 Q. And the first risk factor is a genetic

1 disorder?

2 A. Yes.

3 Q. And there's a number of them listed between
4 Down's syndrome and I won't even try to pronounce the
5 last one. Have you seen any evidence that Mr.
6 Henricksen had any of those genetic disorders?

7 A. No.

8 Q. Similarly under physical and chemical
9 exposures, benzene is listed and you have seen that he
10 does have a history of benzene exposure?

11 MR. YOUNG: Objection, lack of foundation.

12 A. Well, he has a history of gasoline and fuel
13 exposure. There is benzene in those fuels.

14 Q. (BY MR. SCHMIDT) And you've seen a report, for
15 example, from Mr. Kaltofen which calculates an amount of
16 benzene that he may have been exposed to, correct?

17 MR. YOUNG: Object to the term calculates
18 and lack of foundation. Go ahead.

19 A. Yes, he gives an estimate of benzene exposures.

20 Q. (BY MR. SCHMIDT) So, that's one risk factor
21 that you identified that may have caused Mr.
22 Henricksen's AML?

23 A. No, because there is no -- and as your experts
24 have admitted, there's no evidence that diesel fuels or
25 gasolines are carcinogenic.

1 Q. There is evidence that benzene is carcinogenic?

2 A. Yes.

3 Q. And you've admitted that benzene is in
4 gasoline?

5 A. Yes.

6 Q. Drugs such as Pipobroman, any evidence that Mr.
7 Henricksen was ever exposed to that drug?

8 A. No.

9 Q. Pesticides?

10 A. I don't know that.

11 Q. You don't have any evidence that he was
12 exposed?

13 A. I don't have any evidence of that.

14 Q. Cigarette smoking?

15 A. He did smoke at one time.

16 Q. And that was some 25 years previous?

17 A. Yes.

18 Q. And you conclude in your report that you don't
19 think that that's a risk factor or a cause of his AML?

20 A. Correct.

21 Q. Because it's so remote?

22 A. It's too remote.

23 Q. Similarly embalming fluids are listed here, you
24 don't have any evidence he was exposed to embalming
25 fluids, do you?

1 A. No.

2 Q. Herbicides, any evidence he was exposed?

3 A. No.

4 Q. Then there's a category called radiation
5 exposure. You don't have any evidence that prior to the
6 development of his AML in August of 2003 that he was
7 ever exposed to either non-therapeutic or therapeutic
8 radiation?

9 A. No.

10 Q. And then finally there's a category of
11 chemotherapy I think we've already discussed, you don't
12 have any evidence that prior to the development of his
13 AML in 2003 Mr. Henricksen was ever exposed to
14 chemotherapy?

15 A. No.

16 Q. Did you see any medical records from Mr.
17 Henricksen's treating physicians where they indicated or
18 concluded that Mr. Henricksen's AML was either related
19 to benzene or gasoline?

20 A. I don't recall that. I don't recall that with
21 certainty, let's put it that way.

22 Q. Do you recall one way or the other?

23 A. I just can't for certain recall that.

24 Q. Is there any impact on the therapy or treatment
25 if an AML is considered de novo or secondary? Are they

1 treated exactly the same or may they be treated
2 differently?

3 A. Differently.

4 Q. So, that's one of the reasons it's important as
5 a clinician to try to figure out whether a particular
6 AML is secondary to some sort of exposure or arises de
7 novo because that will have an impact on how you treat
8 the patient?

9 A. Yes.

10 Q. And what is the difference in treatment?

11 A. Well, it's generally been found by many, many
12 observers that secondary leukemias do less well than de
13 novo or primary leukemias. They're more aggressive.
14 They may have a different constellation of chromosome
15 abnormalities, but in general they respond poorly to
16 therapy. And, so, if I have a person, for example, that
17 has a secondary leukemia, the initial treatment is going
18 to be the same as someone with a de novo leukemia. But
19 if I'm able to get that person into remission and I feel
20 they have a secondary leukemia, I'm much more likely to
21 advise a bone marrow transplant while they're in that
22 first remission because a secondary leukemia is more
23 highly likely to relapse. And the success of a marrow
24 transplant is much better when it's done during a first
25 remission than in a second or third remission or when

1 the person is in relapse.

2 Q. Now, there's no single one test that will prove
3 with certainty what the cause of AML is?

4 A. That's correct.

5 Q. In fact, you can never know with certainty what
6 the cause is, can you?

7 A. That is correct.

8 Q. And that's why as a clinician you go through
9 all the things we just talked about to try to get your
10 arms around as much information as you can to make the
11 best educated estimate you can as to what the cause is?

12 A. That's true in all aspects of medicine, whether
13 you're talking about leukemia or just a simple
14 pneumonia. We look in terms of probabilities because we
15 don't in many instances make a certain definition of
16 causation.

17 Q. And in terms of determining probabilities, the
18 more information you have, the more accurate your
19 ultimate analysis can be?

20 A. Yes.

21 Q. So, for example, if Mr. Henricksen had been
22 your patient and had come in, it's important not just to
23 have the epidemiology but to have the family history,
24 exposure history, the blood tests and all those sorts of
25 things in order to make the best estimate possible as to

1 the cause of his disease?

2 A. Yes.

3 Q. And as a clinician you wouldn't just rely on
4 one thing like the epidemiology to make that
5 determination?

6 A. No. You would look at the constellation, in
7 the case of leukemia, the constellation of things.

8 Q. You were taught in medical school that a
9 benzene-related leukemia may present with
10 myelodysplastic syndrome but may also present without
11 myelodysplastic syndrome?

12 A. I'm not sure if I was taught much in medical
13 school about benzene. I was certainly aware that
14 benzene could cause myeloid leukemia by virtue of Dr.
15 Aksoy's studies, but those were primarily in the 1970s.
16 I was already well out of medical school. I really
17 can't recall in detail what I was told about benzene in
18 medical school.

19 Q. Did you have Cecil and Lobe's Textbook of
20 Medicine in medical school?

21 A. Yes, I did.

22 Q. If I told you that the 1953 edition said, and I
23 know that's before your time, said that a benzene-
24 induced leukemia may present with or without
25 myelodysplasia, would you have any reason to dispute

1 that?

2 A. I wouldn't have any reason to dispute that.

3 Q. And would you dispute the truth of the
4 statement?

5 A. It is true we think about two-thirds of
6 secondary leukemias present with a phase of
7 myelodysplasia or one-third does not.

8 Q. Would you agree with the statement that
9 inasmuch as the body develops no tolerance to benzene,
10 it is generally considered that the only absolutely safe
11 concentration for benzene is zero?

12 MR. YOUNG: Objection, lack of foundation.

13 A. Well, you have to say safe from what.

14 Q. (BY MR. SCHMIDT) Safe from let's say genetic
15 damage?

16 A. Safe from developing acute leukemia?

17 Q. Let's start there, safe from developing acute
18 leukemia.

19 A. No, I think there's no evidence that low dose
20 benzene causes acute leukemia.

21 Q. How about safe from developing some level of
22 genetic damage, hits?

23 A. I know of no evidence of that. In other words,
24 such things conceivably could occur on a theoretic
25 basis, but I don't know any evidence of sustained damage

1 from that.

2 Q. How about evidence that damage just is
3 incurred, not whether it's sustained?

4 A. Well, you've pointed out some papers about
5 lymphocyte damage can be incurred, but we're talking
6 myeloid leukemia here and there's less evidence for that
7 there.

8 Q. Are you aware of evidence that myeloid damage
9 can occur at low levels of exposure to benzene?

10 A. At low levels, I know that Dr. Irons has done a
11 series of bone marrows in people that have benzene
12 exposure. In fact, I reference one of those papers. I
13 don't recall what levels those people had, but he did
14 see abnormalities in the bone marrow.

15 Q. Could you get me that cite, please?

16 A. It's Stillman's paper. Let's see if it's in
17 here.

18 MR. YOUNG: I think it's number 60.

19 MR. SCHMIDT: Oh, okay. That's why. I was
20 going to say I didn't see Irons cited.

21 A. Yeah. Stillman -- Irons is the last author on
22 that paper.

23 MR. YOUNG: Could you read the title?

24 A. The title is the Benzene Metabolite
25 Hydroquinone Selectively Induces 5q31 and 7 in Human CD

1 34 Positive CD 19 Negative Bone Marrow Cells. Actually
2 I think I -- he has done studies, but this particular
3 paper doesn't deal with the whole body. In other words,
4 he has done serial chromosomes on people. This
5 particular paper refers to lymphocyte bone studies.

6 Q. (BY MR. SCHMIDT) And I don't see anything in
7 here where he indicates at what exposure levels he's
8 seeing these changes.

9 A. Let me see.

10 Q. He talks about levels of hydroquinone?

11 A. Right. What he's measuring is the metabolite
12 and I don't know how much benzene it takes to get to
13 that metabolite.

14 Q. And I don't think he explains in here.

15 A. He probably doesn't explain.

16 Q. Okay. So, the question was do you believe that
17 it is the only absolutely safe concentration from
18 genetic damages zero and your answer was?

19 MR. YOUNG: Asked and answered.

20 A. No. My answer was that I don't believe that
21 low dose benzene causes sustained genetic damage.

22 Q. (BY MR. SCHMIDT) My question was can a genetic
23 damage be incurred at low levels and that was where I
24 think you said you don't know?

25 A. I said we saw it in lymphoid cells. You showed

1 me the papers. But I said -- and we know it can happen
2 in myeloid cells based on some of this work, but I don't
3 know the levels that would be necessary to cause that.

4 Q. Now, as I understand it, the mechanism by which
5 benzene causes hits is there's topoiso -- please
6 pronounce it for me.

7 A. It's called topoisomerase.

8 Q. Thank you. There's a topoisomerase inhibitor
9 that is a metabolite of the benzene; is that correct?

10 A. That's correct. Hydroquinone which is one of
11 the metabolites of benzene in high concentrations
12 inhibits the topoisomerase II system. There are several
13 topoisomerase enzymes. A particular one is inhibited by
14 benzene metabolite.

15 Q. And that affects the DNA directly and sort of
16 strips it of its ability to recombine when it splits?

17 A. What happens is the DNA is tightly coiled. And
18 as the cell divides, it's got to uncoil. And it can
19 break as it's uncoiling. So, what topoisomerase does is
20 it programs breaks at particular levels so that DNA can
21 fall apart in a programmed way and then be put back
22 together in a programmed way. And, so, if the
23 topoisomerase system is inhibited, then breaks can occur
24 at unwanted sites and might not be able to be repaired
25 is the idea.

1 Q. So, that's one mechanism. There's also
2 something, muric acid or muriatic acid that is a
3 metabolite that is thought to cause damage?

4 A. I don't know that's so. In other words, the
5 damage that's done through the topoisomerase inhibition
6 frequently causes what we call translocations where
7 pieces of one chromosome moves to another. And the
8 situation with benzene is that it's considered a
9 radiomimetic drug because it causes a lot of these 5 and
10 7 abnormalities which are usually not caused by
11 topoisomerase inhibition. So, there may be more than
12 one way benzene might damage DNA. It could be through
13 the topoisomerase system or it could be through another
14 system.

15 Q. I've also seen in the studies here that free
16 radicals are generated and a free radical is essentially
17 an oxygen molecule looking to bond with another oxygen
18 molecule, isn't it?

19 A. Yes.

20 Q. And by doing that it steals an oxygen molecule
21 from a healthy cell and can damage the cell that way?

22 A. Yes.

23 Q. Are you aware that free radicals are associated
24 with benzene causing damage to DNA?

25 A. I don't know that. As with many drugs that

1 damage DNA, we know in general terms the mechanism, but
2 the specifics are not always well-known. And, so, in
3 benzene we don't know the exact mechanism of action as
4 to how it damages DNA. We have a number of speculations
5 and theories about that.

6 Q. Did you see in one of these studies there was
7 an interesting discussion that they think that some
8 people genetically are better able to fend off the
9 metabolites than others? Have you read that?

10 A. I think I may have read that, but that's
11 basically still speculation. In other words, it sounds
12 right, but we don't know that it is right.

13 Q. And that's one of the speculations about
14 genetic susceptibility, why some people can deal with
15 exposure better than others is because they can deal
16 with metabolites better?

17 A. Yes.

18 Q. Does the topoisomerase --

19 A. That's very good.

20 Q. I'm trying -- besides inhibiting the ability of
21 the DNA to come back together, does it leave it exposed,
22 the DNA exposed to injury from other metabolites?

23 A. I think that's probably so. There are many
24 different types of topoisomerase inhibitors, some
25 directly complex with it and some inhibit it in other

1 ways. I'm not a topoisomerase chemist, but I do know
2 that there are more than one type of inhibitor. But one
3 would guess that that makes sense that if the DNA is
4 broken in part, it's easier to be damaged by a second
5 drug.

6 Q. Can you state to the jury the level of exposure
7 below which you think benzene is not capable of causing
8 any of the cellular changes or genetic damages we've
9 been calling hits?

10 MR. YOUNG: I'm going to object to the
11 question. I think we've changed the definition of hits
12 yet again. So, to the extent you understand, you can
13 answer.

14 A. My thinking of hits is there are unsustained
15 hits and sustained hits. In other words, a damage to a
16 lymphocyte chromosome may be repaired very quickly. It
17 doesn't persist. In the case of leukemia we're looking
18 for defects that persist. And I think it's likely, and
19 I don't know the level of that, but I think it's very
20 likely that it's very high doses of benzene that cause,
21 let's say, a perpetuating hit.

22 Q. Is that cumulative doses or peak doses?

23 A. High doses of cumulative. High cumulative
24 doses is the best we know.

25 Q. You've already earlier testified that you

1 couldn't say what the level was for peak exposures?

2 A. That's right.

3 Q. Have you ever reviewed the preamble to the
4 final OSHA rule on occupational exposure to benzene?

5 A. Probably not.

6 Q. I'm just going to read a sentence and see if
7 you agree with it. Animal studies indicate that
8 intermittent exposures, paren, a good model for
9 fluctuating peaks, end paren, cause greater decreases in
10 certain blood counts than continual exposures at the
11 same level.

12 MR. YOUNG: I'm going to object. Lack of
13 foundation. The witness is not a toxicologist nor was
14 he designated to speak on animal studies or toxicology.
15 Go ahead.

16 A. As Mr. Young commented, I mean, these are
17 animal studies we're dealing with. And I certainly am
18 not an expert on animal studies and drugs are handled
19 differently in animals than in humans. So, I really
20 can't comment on that statement.

21 Q. (BY MR. SCHMIDT) And that's fine. So, you
22 can't -- can you comment on the statement that
23 intermittent exposures which they call a model for
24 fluctuating peaks cause greater decreases in blood
25 counts than continual exposures?

1 MR. YOUNG: Same objection.

2 A. I don't know that. I can't comment on it.

3 Q. (BY MR. SCHMIDT) Do you consider hydroquinone
4 a poison?

5 MR. YOUNG: Objection, lack of foundation.
6 Same objections as previously stated.

7 A. Well, it is a poison, but as all poisons it's
8 the dose that makes the poison. So, it depends on how
9 much.

10 Q. (BY MR. SCHMIDT) Same is true for chemotherapy
11 agents, they're poisonous?

12 A. That's correct.

13 Q. Do you believe that there's a single threshold
14 exposure level -- this is different from what I've asked
15 you before -- that applies to everyone or does genetic
16 susceptibility mean that at different levels different
17 people will experience different effects from exposure
18 to benzene?

19 MR. YOUNG: Object to a compound question.

20 A. It's a compound question, but I think this:
21 That if we look at our chemotherapy experience where we
22 have drugs that damage DNA and cause leukemia and we
23 know exactly what the dose was because they didn't smell
24 it, we injected it IV, we have a huge amount of data.
25 And what we find is that the incidence of leukemia

1 begins with cumulative dose. And it is remarkably
2 similar among most people. In other words, if we give
3 the drug Cyclophosphamide or Cytosan, you don't much see
4 any acute leukemia until you get to about 20,000
5 milligrams administered. Then you start seeing
6 leukemia. And, of course, if you give more drug, you
7 will see more instances of leukemia. But the early
8 threshold you don't see people getting it at five
9 milligrams or ten or a hundred or 5,000. You see them
10 at 20,000 milligrams. So, maybe there's a difference,
11 but it doesn't look like it's vast, at least in the case
12 of the good data we have for various chemotherapy drugs.

13 Q. (BY MR. SCHMIDT) Certainly people react to
14 chemotherapy differently?

15 A. Yes.

16 Q. The idea of chemotherapy is actually to depress
17 the blood counts. You want to give the agent to the
18 level of tolerance, don't you?

19 A. Well, you want to give it to the -- that's sort
20 of you might say old speak.

21 Q. Okay.

22 A. In other words, that's what --

23 Q. I learned it from you.

24 A. That's what we've done for many, many years ago
25 is give the drugs to tolerance. Now you want to smart

1 drug. For example, in the case of chronic myeloid
2 leukemia we want to give a pill that inhibits the
3 mechanism of the leukemia and there is no tolerant dose.
4 In other words, we don't have to escalate the dose to
5 get a response. A very small dose works because it's
6 targeted therapy. That's the buzz word today. And, so,
7 you want targeted therapy which doesn't require you
8 causing the most damage you can get. But with many
9 cancers today we still use the theory that you
10 mentioned, that you give the drugs to tolerance.

11 Q. Okay. First I want to establish that the
12 targeted theory, that's -- that application of
13 chemotherapy is not the basis for any of the studies you
14 cite regarding the effects of chemotherapy in your
15 report?

16 A. That is correct.

17 Q. So, the tolerance theory is you hit them with
18 enough and then you have to let the patient rest for
19 three or four weeks before you can give them another
20 dose of chemotherapy because you've got to let the blood
21 count come back; is that correct?

22 A. You don't have to, but you often do.

23 Q. And, so, the therapy is given -- it's a major
24 dose of chemotherapy on day one and then you do another
25 dose in three or four weeks and you continue this for

1 four to six months?

2 A. Well, generally in acute leukemia the most
3 characteristic therapy which is what Mr. Henricksen got
4 is you give one particular drug continuously for about
5 seven days and you give another drug for about three
6 days. It's called seven and three therapy. So, you
7 don't give them all on the first day, but you give them
8 all over the first week, let's put it that way. And
9 then it may take you two or three weeks to recover from
10 that and then you could introduce the drugs again.

11 Q. Have you ever tried to do an equivalence in
12 terms of part per million exposure between the dose that
13 someone like Mr. Henricksen is getting in chemotherapy
14 versus occupational benzene exposure?

15 A. No, I don't know that I've ever seen anybody
16 attempt that.

17 Q. I'm just trying to figure this out
18 conceptually. I would assume that the dose of
19 chemotherapy relative to an occupational benzene
20 exposure would be many factors higher on a per day basis
21 or per application basis?

22 MR. YOUNG: Question calls by its terms for
23 an assumption and for speculation.

24 A. Well, I suppose you could look at it that way,
25 but you have to keep in mind that when we're giving a

1 chemotherapy drug, we're giving it over a very, very
2 short interval. In the case of someone who has a large
3 cumulative dose of benzene, they may have taken some
4 years to accumulate that. And, so, milligram per
5 milligram, it may not be all that much different. We
6 just give a lot of it at one time with chemotherapy.

7 Q. (BY MR. SCHMIDT) And an exposed worker may get
8 it at lower doses over a many-year period?

9 A. Yes.

10 Q. And that way they both arrive at the same
11 cumulative dose?

12 A. Let me put it this way: For example, if I take
13 somebody and I use this drug Cyclophosphamide which is
14 an alkylating agent that gives you 5 and 7 just like
15 benzene does, if we give that drug by mouth over a long
16 period of time or we give it intravenously over a
17 shorter period of time, the time -- the cumulative dose
18 to catch leukemia is quite similar. In other words,
19 whether we give the drug over an extended period by
20 mouth, once you get up to about that 20,000-milligram
21 level, you're at high risk of catching leukemia whether
22 you got it -- whether you took it for three years at a
23 low dose or whether you took it for four months at a
24 higher dose. The cumulative dose is quite similar.

25 Q. You're aware Mr. Henricksen worked as a tanker

1 driver for 29 years?

2 A. Yes.

3 Q. You've never heard of anyone taking
4 chemotherapy for 29 years?

5 A. No. I think that would be extraordinary.

6 Q. I do, too. When you look at epidemiology, do
7 you require a doubling of the risk in order to believe
8 that there's a causal relationship?

9 A. Well, in epidemiology what you like is multiple
10 studies and consistency. And, so, yes, you would like a
11 doubling of the risk, but more than that you would like
12 to see that that's a consistent finding among a number
13 of studies.

14 Q. Are you familiar with any authoritative medical
15 or scientific text that says a doubling of the risk is
16 required in order to make an association?

17 A. I have articles that suggest that. For
18 example, there was an article published in the Journal
19 of Science about perhaps ten years ago about just this
20 subject. And they interviewed the medical editors of
21 the New England Journal and many of the prominent
22 scientific journals asking them just that question. And
23 many people said, you know, I wouldn't even consider a
24 paper unless it had a tripling of the risk. And some
25 people say I'd like a risk by four. And then others

1 said, well, it might be lower if I had multiple studies.
2 And, so, I don't know that there's a uniformity of
3 opinion on that, but certainly there are people who say,
4 yes, you have to have at least a doubling of the risk to
5 find some significance.

6 Q. And there are others who don't require that?

7 A. Well, I'm not an epidemiologist, but I'm
8 answering your question. Yes, I'm aware of at least one
9 paper in a prestigious journal that says that.

10 Q. Are you aware of any actual formal papers that
11 studied the issue and reached a conclusion?

12 A. No.

13 Q. Are you aware of any other sources that address
14 the issue?

15 MR. YOUNG: Asked and answered.

16 A. No.

17 MR. YOUNG: Off the record.

18 (Break taken from 1:10 p.m. to 1:11 p.m.)

19 Q. (BY MR. SCHMIDT) With high dose chemotherapy
20 there's a risk of developing myelodysplasia or leukemia
21 that peaks at three to seven years and is usually gone
22 by years 11 or 12?

23 A. That would be a true general statement, yes.

24 Q. Is that -- and I don't know what the high dose
25 is, that's some testimony you previously gave in a

1 case -- is that high dose chemotherapy a much larger hit
2 than, say, an 8 ppm year cumulative dose to benzene?

3 A. Yes.

4 Q. Isn't chemotherapy treatment much more
5 analogous to benzene poisoning or toxicity than to long-
6 term chronic industrial exposure to benzene?

7 A. Run that question by me again.

8 Q. Isn't chemotherapy treatment much more
9 analogous to benzene poisoning or toxicity than long-
10 term chronic industrial exposure to benzene?

11 A. In general, that would be true. But as I
12 commented on the Cytosan situation, some of these --
13 some of the knowledge about that has to do with long-
14 term therapy, in other words, like a year to two or even
15 three years of continuous oral therapy. But, in
16 general, high dose chemotherapy is very myelosuppressive
17 and that would be what you might expect with very high
18 dose levels of benzene.

19 Q. And that kind of chemotherapy involves an acute
20 insult and injury to the bone marrow?

21 A. Yes.

22 Q. And it would certainly constitute what we've
23 called a hit, it causes genetic damage?

24 A. Yes. And in some people obviously it's
25 sustained because they may catch leukemia.

1 Q. But after the application, whether it be one
2 time or seven days or three days, in the tolerance model
3 that we've been talking about or giving to tolerance,
4 you give the patient a break so that their bone marrow
5 can recover?

6 A. Yes.

7 Q. And chronically exposed industrial workers
8 exposed to low doses don't get that kind of break for
9 recovery?

10 MR. YOUNG: Objection, calls for
11 speculation.

12 A. Probably true.

13 Q. (BY MR. SCHMIDT) Have you ever seen a medical
14 or scientific paper giving data on the average latency
15 period for developing AML for tanker drivers like Mr.
16 Henricksen?

17 A. Not that I'm aware of.

18 Q. How about for refinery workers?

19 A. No.

20 Q. What is the longest latency period you've seen
21 in the published literature for the association between
22 benzene exposure and the development of AML?

23 A. Well, there are anecdotal papers that allege
24 very long latency, but they're not epidemiologic papers.
25 So, if a person has benzene exposure 40 years ago and

1 catches leukemia when he's 80, the author may think it
2 has to do with the benzene. But there's no way to know
3 if that's so.

4 Q. So, for the anecdotal papers what's the longest
5 latency period you've seen for the development of AML?

6 A. I don't really know. I know that there are
7 some out there. I can't quote one as we speak. But
8 it's likely to be very long.

9 Q. More than 40 years?

10 A. I don't know about more than 40 years, but it
11 could be long.

12 Q. And by anecdotal paper, you mean case reports?

13 A. Yes.

14 Q. And for epidemiological study, what is the
15 longest latency period you have seen for the development
16 of AML, secondary AML?

17 A. Secondary AML, I'd have to say -- we're talking
18 specifically to benzene; is that right?

19 Q. Yes.

20 A. I don't know the answer to that in the studies
21 that are commonly looked at, the Aksoy studies, the Hays
22 study. I don't know the answer to that. In general,
23 the statements are that they resemble the chemotherapy
24 experience. But the longest number is very hard to say
25 because you see when someone works for 35 years and then

1 catches benzene, you don't really know when during that
2 35 period they really got the cumulative dose and the
3 latency clock began. And, so, I think many of the
4 benzene studies don't speak very well for accuracy and
5 latency. But, in general, they speak to similarities
6 with the chemotherapy experience.

7 MR. YOUNG: So that the record is clear, I
8 think he meant to say catch AML, not catch benzene in
9 his last answer.

10 A. Did I say catch?

11 MR. YOUNG: I just want to make that clear.

12 Q. (BY MR. SCHMIDT) There's something I didn't
13 understand there where you say where they get the
14 cumulative dose. Does that mean where they acquire the
15 final genetic insult or the initial one?

16 A. Analogous to the chemotherapy experience, I
17 start giving somebody chemotherapy. Well, I stop when
18 they've had a small amount. There isn't any latency
19 because they're never going to catch the leukemia. The
20 latency really begins when I get to a dose that's enough
21 of a dose to cause leukemia. Now, in the case of
22 chemotherapy, most of our drugs are given only, let's
23 say, over perhaps a 4-month period. So, it doesn't make
24 any difference whether I pick the first dose of drug or
25 the last dose. The true latency begins somewhere in the

1 middle, but it doesn't make any difference because
2 they're so close together. When somebody has a
3 cumulative dose of benzene that causes AML and they've
4 worked for 35 years, we don't really know when they
5 accumulated that cumulative dose. So, it's very
6 difficult to have the accuracy that you have with the
7 chemotherapy experience. Nevertheless, what the authors
8 say who studied the major studies of this is that
9 they're quite analogous to the chemotherapy studies,
10 albeit, the data is not very good.

11 Q. So, you would not start the clock running on a
12 latency period for a benzene exposure from the date of
13 the worker's first exposure?

14 A. No. And, in fact, in the Hays study he
15 specifically does not do that. He says that I think
16 it's six months. In other words, he said they had to
17 have worked there a fixed period of time before they
18 started the clock. And I don't remember the number, but
19 I believe it was six months. He took people that had
20 worked with benzene during a 15-year interval and that's
21 what he looked at. But he didn't count someone who had
22 only worked there a day. In other words, they had to
23 have been in there for -- in the atmosphere for a fair
24 amount of time. I believe it was six months, but don't
25 hold me to that. So, that's why I say it's very hard to

1 look at those studies and come up with the accuracy of
2 data that you get from the chemotherapy studies.

3 Q. So, it would also be very difficult to
4 calculate the actual latency period in any particular
5 case because you don't know when the person acquired the
6 cumulative dose necessary to cause the disease?

7 A. In general, that would be true. They're not
8 accurate, but when you look at the totality of the data,
9 the authors suggest they're quite similar to the
10 chemotherapy experience.

11 Q. And since you do not believe that Mr.
12 Henricksen's AML is associated with his benzene
13 exposure, you don't have any opinion as to what his
14 latency period for benzene exposure is since you don't
15 believe he ever acquired the cumulative dose to start
16 the clock running?

17 A. Well, he wasn't exposed to pure benzene. He
18 was exposed to fuels which are not -- and by your own
19 expert's admission thought to be proven to be
20 carcinogens. And, so, the situation with fuels, in
21 addition as we hadn't discussed, is that there's a
22 difference, at least many people believe a difference in
23 getting exposed to benzene in a near pure benzene
24 environment such as let's say Dr. Aksoy's people working
25 with glues or the Pliofilm study and having benzene in

1 the milieu of gasoline or fuels where there can be
2 competitive metabolism. So, in other words, the theory
3 is that let's say a ten part per million exposure with
4 pure benzene isn't necessarily equivalent to that same
5 amount of benzene when you're getting it in the form of
6 gasoline because the metabolism situation is different.
7 You've got competition. And, so, all we can say is
8 that. And as I've said in my letter, I don't think that
9 Mr. Henricksen's AML is likely to be caused by his fuel
10 exposures.

11 Q. Cite every authority that stands for the
12 proposition that there is some unequivalency between
13 pure benzene exposure and benzene delivered through the
14 mechanism of gasoline in terms of what you call it,
15 metabolite competition?

16 A. Yes.

17 MR. YOUNG: To the extent you have a
18 photographic memory to do so, Doctor, you may answer the
19 question.

20 A. Well, you've asked two different questions in a
21 way. One article I reference, the Jamal article
22 discusses both animal studies and studies that have to
23 do with the competing metabolism and I think I reference
24 that in here. In the case of the latency similarities,
25 for example, I probably have an article by Morgan in

1 here. In the Hays study he says something like the
2 latency is analogous to the wave and fall effect that we
3 see with chemotherapy. Dr. Aksoy used the figure around
4 six years in people who had gotten pancytopenic and then
5 recovered and then went on to catch leukemia. He said
6 that was about a 6-year latency. In the Silver and
7 Rinsky article, looking at the Pliofilm study, they
8 comment that the first -- that ten years looks to be, I
9 may have it in this group of papers, that a short
10 latency is what you see with benzene.

11 Q. (BY MR. SCHMIDT) I'm not interested in the
12 latency right now. I'm just interested in the competing
13 metabolism aspect of this. Is the Jamal the only
14 article you can cite for that proposition?

15 A. That I brought with me today, yes.

16 Q. Are you aware of any others out there?

17 A. Well, he's got a huge reference list, so that
18 there are obviously others.

19 Q. Are you aware that Mr. Henricksen worked
20 continuously as a tanker truck driver from 1974 to
21 August of 2003 when he was diagnosed?

22 A. Yes.

23 Q. Isn't it true that in an epidemiological study
24 the longest the latency period can be is the period for
25 which the workers were followed?

1 MR. YOUNG: Objection, lack of foundation.

2 The witness is not an epidemiologist.

3 A. That's true. I suppose it's how you define
4 latency. In other words, as I said, if you have two
5 groups and you want to claim that the fact that somebody
6 got leukemia when they're 80 had to do with the fact
7 that they got benzene exposure when they were 20, you
8 have to have a control group that you followed that
9 length of time to see if there are differences in the
10 incidents.

11 Q. (BY MR. SCHMIDT) Correct. To do that you
12 would have to follow them for 60 years?

13 A. For many years. As in the Pliofilm study where
14 they followed them from birth to death, so to speak,
15 whereas I will assume happened in the Australian benzene
16 study.

17 Q. But if you have a study where you've been
18 following the workers for 12 years, the longest latency
19 period you can have in that study is 12 years?

20 A. Yes, in a benzene situation, that's true.

21 Q. Right. Have you ever done a study of benzene
22 exposure on latency?

23 A. No.

24 Q. Which studies in your report stand for the
25 proposition that chemotherapy is a reliable analog for

1 benzene exposure in the context of latency?

2 A. Well, the Hays study certainly says that. I
3 believe the paper written by Morgan says that. I assume
4 I have that among these references.

5 MR. YOUNG: You can look at your report.
6 It's not a memory contest.

7 A. Let me see if that's in there someplace.

8 Q. (BY MR. SCHMIDT) I don't see either Hays or
9 Morgan, but I may be missing something.

10 A. I probably didn't -- I'll look for Hays in a
11 minute. Let me look at my reference list here. Well, I
12 didn't cite them in here, but I think my own paper cites
13 them. In other words, I guess it's like a secondary
14 leukemia. I've got secondary citations in my paper. I
15 cite a number of them in my paper.

16 Q. You cite in 93, to be exact.

17 A. Well, it's not 93. I cite from page 7,
18 reference 7 to reference 18 all say that.

19 MR. YOUNG: So the record's clear, could
20 you just read the title of your paper, Doctor, so the
21 record reflects what you two were talking about?

22 A. Benzene-Induced Acute Myeloid Leukemia, a
23 Clinician's Perspective.

24 Q. (BY MR. SCHMIDT) I'm sorry, I was looking at
25 the wrong paper.

1 MR. YOUNG: I'm sorry, Jackson, I just
2 wanted to make sure.

3 MR. SCHMIDT: No. I'm glad.

4 Q. (BY MR. SCHMIDT) Which --

5 A. Where I'm looking at that is on the first page.

6 Q. Is it seven?

7 A. It's this last sentence on that bottom
8 paragraph there.

9 Q. What I need is which reference. Is it your
10 number 3?

11 MR. YOUNG: His number 3, right.

12 Q. (BY MR. SCHMIDT) There we go. 79 cites. So,
13 in your reference number 3 which is Benzene-Induced
14 Acute Myeloid Leukemia by yourself, you say cites 7
15 through --

16 A. 18.

17 Q. And, so, reference number 17 is the Hays
18 article that you previously referred me to?

19 A. Yes.

20 Q. And that's Hays 97?

21 A. Yes.

22 Q. And reference 9 is the Morgan article that you
23 previously referred to?

24 A. Yes.

25 Q. It's a 2005 article?

1 A. Yes.

2 Q. Did you perform a study that was the basis of
3 this article?

4 A. No.

5 Q. Did you do any research apart from looking at
6 other articles to do this article?

7 A. No.

8 Q. I take it if I would ask you is the latency
9 period for a long-term chronic low dose benzene exposure
10 in the development of AML different from the latency
11 period for short-term high dose exposures, you'd say you
12 don't believe that the first long-term low dose even
13 causes AML; is that correct?

14 MR. YOUNG: Objection to the undefined
15 terms.

16 A. I would say that the causation is related to
17 the cumulative dose. And if you get that cumulative
18 dose over a relatively short period, two or three years,
19 that might be equivalent to getting that cumulative dose
20 over 20 years.

21 Q. (BY MR. SCHMIDT) And would the latency period
22 be the same?

23 A. Once you achieve that cumulative dose, I would
24 think it would be, yes. Analogous to what we see with
25 oral Cytosan versus intravenous Cytosan.

1 Q. Is latency a bell curve?

2 A. No. At least from the chemotherapy data it
3 seems to be somewhat increasing. In other words, you
4 begin to see cases of leukemia at particular dosage and
5 that number increases up to a point with higher doses
6 than that. In other words, you have more cases.
7 Putting that into perspective, with a standard therapy,
8 let's say for breast cancer or Hodgkin's disease, you
9 might expect to see four to five percent of those
10 patients catching acute leukemia. With high doses of
11 those drugs, you might chase that up to 12 percent
12 catching acute leukemia. But it wouldn't be a hundred
13 percent.

14 Q. Right.

15 A. But it would be higher with increase in the
16 cumulative dose.

17 Q. I'm just going to show you my understanding and
18 you can correct me on this. I thought that the way
19 latency worked is that there's a peak period where
20 you're most likely. So, if you have, say, a 15-year
21 latency period, the peak period would fall somewhere in
22 the middle where you're most likely to develop the
23 disease after which the likelihood falls off. So, it
24 would look like this, this being the peak period?

25 A. Oh, okay. We may be talking about two

1 different things. My understanding is that in one of
2 these articles I reference, it sort of shows that kind
3 of nicely. Let me just see if I can find that off the
4 bat. I think I referenced it in here. Yeah, it's my
5 reference 42.

6 Q. Okay. That's one of your articles that I do
7 not have.

8 MR. YOUNG: We'll get you a copy.

9 A. Let's see if I can find that.

10 MR. YOUNG: Who is the author?

11 THE WITNESS: Praga.

12 MR. YOUNG: Praga. It's actually 43,
13 Jackson, on the one that you and I have.

14 MR. SCHMIDT: And I have that one.

15 A. And I've got it here, also.

16 Q. (BY MR. SCHMIDT) And I don't see a bell curve.

17 A. Here's what I'm talking about. These are
18 people who are getting two different drugs. One is
19 basically a topoisomerase II inhibitor which it's an
20 Adriamycin like drug on the upper axis. On the bottom
21 is Cyclophosphamide and they've got the dose in
22 milligrams per meter squared. And what happens is you
23 see -- at this number, these are people that caught
24 leukemia. And you see nobody caught it until they got
25 up to this cumulative dose. Then as the cumulative dose

1 keeps rising, they get more cases up to a point. But
2 these cases all occurred at different times, but they
3 all occurred within that two- to ten-year interval. In
4 other words, there's a window of catching it; you
5 increase the number of cases that occurred during the
6 window with the higher doses. But these doses are all
7 given over a relatively short period of time so you know
8 the latency and that latency remains two to ten years,
9 you just increase the number of people that you gave the
10 leukemia to with the higher doses.

11 Q. This one, the vertical axis is the probability
12 of developing it and the horizontal axis is the
13 administered cumulative doses?

14 A. Correct.

15 Q. And the bell curve I was showing you, the
16 horizontal axis is time. And, so, again, sort of back
17 to my question, is this bell curve that I have drawn
18 very crudely an accurate representation of I guess this
19 axis would be dose and this would be time?

20 A. Yeah. Let's say here is where cumulative dose
21 has been reached. You're now in the sweepstakes for
22 catching leukemia. And now we're going to measure our
23 time. This peak is generally considered to be about
24 three to seven years. And it could be as short as two
25 years, it could be as long as 10 to 11 years or so. But

1 what happens is the peak is generally reached around
2 three to seven years after you've accumulated the
3 cumulative dose.

4 Q. And then after you get past the peak your risk
5 starts to decline?

6 A. Starts to slowly go down and eventually it gets
7 to indistinguishable from the general population.

8 Q. And if I wrote here sufficient cumulative dose,
9 you'd agree that's what that's supposed to be?

10 A. Yes.

11 (Exhibit 66 marked.)

12 Q. (BY MR. SCHMIDT) Why don't we mark this so if
13 we ever have to talk about it again. Now, I've just
14 marked Exhibit 66 which is the drawing that you and I
15 have both contributed to, correct?

16 A. Yes.

17 Q. Just a couple of more questions, then we can
18 break for lunch. Does that bell curve in Exhibit 66
19 represent the kind of latency period that would be
20 experienced by someone who instead of getting sharp peak
21 doses as a chemotherapy patient would get relatively low
22 level doses until the sufficient cumulative dose is
23 achieved?

24 A. We think that's so. In other words, that there
25 should be -- in general, with chemotherapy, and it seems

1 to be similar with benzene, it's the cumulative dose,
2 not the peak dose that determines the risk. And whereas
3 in the case of the chemotherapy, we know the beginning
4 of latency very closely. We don't know that with the
5 benzene data because there are fewer cases and they've
6 been treated over a long period of time. But, in
7 general, those that have observed these leukemias
8 suggest that the latency is the same.

9 Q. And you cite for that, you gave me Morgan and
10 Hays?

11 A. Morgan and Hays are two and Aksoy would be a
12 third one that suggests that. And then Silver and
13 Rinsky looking at the Pliofilm study. Finklestein,
14 another one looking at the Pliofilm study. All of these
15 references suggest that there's an analogy between the
16 benzene data and the chemotherapy data.

17 Q. At the end of the day there's no hard and fast
18 rule for when you would expect AML to develop as a
19 result of benzene exposure?

20 A. Well, within reason. In other words, if one's
21 exposure ended and now a 30-year interval has elapsed
22 and they catch leukemia, I would say it's highly
23 unlikely to be related to that benzene. Just as I say
24 when a person stopped smoking 25 or 30 years ago and now
25 caught leukemia, it's highly unlikely it would be

1 related to the smoking.

2 Q. Isn't there sometimes in chronic long-term
3 exposures cause changes to the marrow that's not normal
4 but it's not yet leukemia, either, and that can
5 percolate for a number of years before it either
6 resolves back to healthy tissue or becomes leukemia?

7 MR. YOUNG: Objection, incomplete
8 hypothetical. Calls for speculation.

9 A. Well, what you're really talking about is
10 myelodysplasia. And, in general, if you look at people
11 that we diagnose with myelodysplasia, there are not many
12 of them still standing after about three years. And
13 some may go as long as ten years or sometimes a little
14 longer. But in the main myelodysplasia is not a good
15 thing to have.

16 Q. (BY MR. SCHMIDT) Right.

17 A. And it will -- it may convert to acute leukemia
18 or predisposed to infection. And often these are older
19 people with myelodysplasia and they may die of an
20 unrelated cause.

21 Q. How about anemia, doesn't that sometimes show
22 the same where it develops and then doesn't go one way
23 or the other and can just percolate without many
24 clinical symptoms for quite awhile?

25 A. Well, if you looked at -- myelodysplasia

1 generally refers to lowering of the red blood cells
2 which is anemia, lowering of the white cells or
3 leukopenia and lowering of the platelets or
4 thrombocytopenia. And, in general, anemia is the
5 predominant cytopenia in myelodysplasia. So, again, I
6 think you're really referring to myelodysplasia. There
7 are some people who will get a chemical exposure and
8 they get a depressed bone marrow and that might be
9 characterized by anemia. And over many months they may
10 recover from it and not have myelodysplasia. That
11 certainly can occur.

12 Q. And that can affect a latency period?

13 A. Well, not necessarily. It just means that they
14 got enough dose to whack their bone marrow, but they
15 managed to recover it. In other words, that's what
16 Aksoy saw. He saw people who would get a pancytopenia,
17 meaning all three elements would go down, they would
18 recover from that. They'd be fine. But then on an
19 average of six years later they'd have acute leukemia.
20 In other words, they recovered but really didn't
21 recover. In other words, they recovered their blood
22 counts but not their genetics of the bone marrow.

23 Q. I think my question is simpler than that. It
24 just wasn't well phrased. It's just simply that
25 different people who achieve a sufficient dose to

1 develop leukemia, and I think we've agreed that because
2 of genetic susceptibility there can be a variability
3 there, also develop a disease at different times. Some
4 can develop it very quickly; some develop it much later?

5 MR. YOUNG: Objection, compound. And asked
6 and answered.

7 A. Well, as I said, the interval can be 2 to 11
8 years.

9 Q. (BY MR. SCHMIDT) Right.

10 A. And it can be broken down a little further in
11 the sense that most people believe that if the drug is a
12 topoisomerase inhibitor, which some believe benzene is,
13 the latency period is short as opposed to an alkylating
14 agent which some people believe benzene is, it can be
15 longer. But they both come within that two to ten-year
16 window.

17 MR. SCHMIDT: Let's take a break for lunch.

18 (Lunch taken from 1:44 p.m. to 2:01 p.m.)

19 (Exhibit 67 marked.)

20 Q. (BY MR. SCHMIDT) I'm going to do a bit of
21 housekeeping. This is the Zhang article we talked about
22 earlier. Do you agree?

23 A. Yes.

24 Q. And that's been marked as Plaintiff's Exhibit
25 67. Thank you. Are you familiar with Rinsky's follow-

1 up study of 2002?

2 A. In general terms, yes.

3 Q. Do you recall that they saw an average latency
4 of 25.2 years with a range of 2 to 51 for AML's?

5 MR. YOUNG: Please look at the paper.

6 A. Let's look at the paper and see about that. Is
7 that a paper I referenced?

8 Q. (BY MR. SCHMIDT) I don't know that you have.
9 And unfortunately I was just looking for it. I can't
10 put my finger on it. I don't see it, Dr. Natelson, so
11 let me just ask it this way: In preparing your latency
12 opinion in this case, did you take a look at Rinsky and
13 consider whether to use any of the information in that
14 article?

15 A. Well, I looked at an article on this subject by
16 Rinsky. And it has another author. And it's in the
17 2000s and he's got a subtitle in that article that says
18 Benzene, the Disease of Short Latency and in there he
19 uses the ten-year figure. I think it's Silver and
20 Rinsky. But I don't think I have that here. I can't of
21 course anticipate every question you ask, so I can't
22 have all these references at my fingertips.

23 Q. I understand. Can you name for me an article
24 in the peer reviewed literature discussing the
25 methodology for determining causation in AML

1 specifically with respect to benzene exposure that
2 states chromosomal abnormalities are to be used to
3 determining or helping to determine the causation for
4 AML with respect to benzene exposure?

5 A. Well, the Zhang article that we talked about
6 comments about their frequency and uses the figure
7 around 90 percent that we see abnormalities. Now, that
8 article isn't designed to look at causation; it's just a
9 statement of fact in their mind that that is a common
10 phenomenon. There are many other articles that say the
11 same thing, but I don't know that they reference it in
12 the exact way you phrased it.

13 Q. When Zhang says 90 percent of secondary AML's
14 show chromosomal abnormalities, is that correct?

15 A. No. He says 90 percent of people with
16 benzene-induced disease show chromosomal abnormalities.

17 Q. And what are included amongst those chromosomal
18 abnormalities? Is it just 5, 7 location?

19 A. No. It could be any type.

20 Q. Is it true that between 50 and 70 percent of
21 people with benzene-induced AML have the deletion of or
22 abnormalities in chromosome 5 and 7?

23 A. Is it true that 50 percent --

24 Q. 50 to 70 percent?

25 A. That's a general figure that's given for all

1 chemical-induced leukemias including benzene is that
2 some will say as high as 90 percent. But generally
3 about 50 to 75 percent is what people would say.

4 Q. Which means that somewhere between 25 and 30 to
5 50 percent of people with benzene-induced AML's do not
6 show deletions or abnormalities in chromosome 5 and 7?

7 A. Yes.

8 Q. If someone does not have the deletion in 5 or
9 7, that does not exclude benzene in causation, does it?

10 A. No.

11 Q. And, by the way, just for the jury's benefit,
12 there's no way we can draw blood from Mr. Henricksen
13 today and test it for chromosomal abnormalities that
14 caused his leukemia because he doesn't have the same
15 blood system that he had before; isn't that right?

16 A. That's correct, he has all donor's chromosomes.

17 Q. Is aplastic anemia considered a precursor to
18 AML?

19 A. An occasional precursor to AML, yes.

20 Q. Myelodysplasia, is it considered a precursor to
21 AML?

22 A. Yes.

23 Q. Once a person develops AML and presents and can
24 be diagnosed with that disease, can you also see the
25 underlying precursor disease or has it disappeared by

1 that point?

2 A. Well, frequently you can see it in different
3 ways. For example, you may see it by morphology.
4 Certain types of myelodysplasia are associated with what
5 we call ringed sideroblasts. On the iron stain they
6 have rings of iron, red cell precursors, that are very
7 distinctive. When they proceed on to catch leukemia,
8 they retain those cells. And, so, in a sideroblastic
9 anemia, you often can see evidence that it began as a
10 sideroblastic anemia even when it's progressed into
11 acute leukemia. In other instances a person with
12 myelodysplasia may have a 5 or a 7 abnormality or
13 another abnormality. They proceed into leukemia and
14 they continue to have those same chromosome
15 abnormalities. They may acquire even new ones. But
16 often they will have the same ones.

17 Q. Is it possible to have a precursor blood
18 disorder like myelodysplasia or aplastic anemia or
19 another one, AML develops and then clinically it's
20 impossible to detect the previous existence of the
21 precursor blood disease?

22 A. Well, certainly in the sense that you may have
23 someone with acute leukemia and let's say you have no
24 knowledge of their past medical history and no records.
25 And they suddenly come in with 90 percent blasts in

1 their bone marrow, you'd be very hard-pressed to
2 determine anything other than they had 90 percent blasts
3 in their bone marrow and whatever chromosome
4 abnormalities there were in those blast cells.

5 Q. What percentage of blasts in his bone marrow,
6 if any, did Mr. Henricksen have when he presented?

7 A. I think he had something like 62 percent. I
8 might have that in my letter here. Let's see what that
9 said. 75 percent blast forms.

10 Q. And he presented with acute leukemia?

11 A. Yes.

12 Q. Can people have a precursor condition like
13 myelodysplasia, go undiagnosed and then develop AML?

14 A. Yes.

15 Q. When was Mr. Henricksen's last physical
16 previous to his diagnosis?

17 A. I don't know.

18 Q. Have you seen any records from his clinical
19 treatment prior to diagnosis?

20 A. I don't recall that.

21 Q. So, you wouldn't know whether there was any
22 blood work done?

23 A. No.

24 Q. Is it your position that in order to attribute
25 benzene exposure as a cause of AML, there is a

1 requirement of a precursor condition such as aplastic
2 anemia or myelodysplastic syndrome?

3 A. No.

4 Q. When you say that a leukemia is de novo, does
5 this mean that you don't know what the cause is?

6 A. That would be one aspect of de novo.

7 Q. What's the other aspect or other aspects?

8 A. Other aspects? Well, de novo carries with it
9 certain aspects to that diagnosis. It typically refers
10 to a leukemia that in today's world people call de novo
11 or primary or spontaneous or endogenous. Those are all
12 words that have been used to describe de novo leukemia.
13 And it's a leukemia that presents suddenly without a
14 period of myelodysplasia. That as many as 45 to
15 50 percent of the time has normal chromosome studies in
16 the marrow. And when chromosome studies are found to be
17 abnormal, frequently involve characteristic
18 translocations. And it's a type of leukemia that
19 typically responds well to chemotherapy at least
20 initially and remission is usually easy to choose, easy
21 to derive, but only in a limited number of patients can
22 it be cured. So, a typical person with de novo leukemia
23 may have a long period of remission, but in the main
24 except for a few unusual chromosome aberrations typically
25 wants to relapse. And it is a leukemia of which we can

1 find no known etiology and by definition it's a person
2 who has no known exposure to environmental chemicals.
3 So, for example, I have two articles here from 2008 that
4 are not in the group I referenced because they're newer
5 than my letter. And they both discuss what de novo and
6 what secondary leukemia means. And I have these
7 highlighted. You can see what two recent authors say
8 about these terms primary, de novo, secondary and
9 hematotoxins, for example. That's one and here is
10 another.

11 Q. So, when you say that it's a requirement for de
12 novo that a person has no known exposure to
13 environmental chemicals, is benzene considered one of
14 those environmental chemicals?

15 A. Absolutely.

16 Q. So, in order for someone to be diagnosed with a
17 de novo as opposed to a secondary, that person can't
18 have benzene exposure?

19 MR. YOUNG: Objection, misstates his
20 testimony.

21 A. No. In other words, if I say that the person
22 has benzene-induced leukemia, what I am saying is that
23 that is a secondary leukemia and it cannot be a de novo
24 leukemia. And, also, I think I have other references
25 that show just exactly how that works. And, let's see,

1 I'm looking for the article -- I thought I had that.
2 For example, this is an article, again, that's not in my
3 list. It's discussing erythroleukemia. That's also
4 referred to as M6 acute myeloid leukemia and it's a type
5 of leukemia that's thought to be potentially caused by
6 benzene. So, what the person does in this study is they
7 establish the world's largest group of patients with
8 this leukemia and they have 62 such patients.

9 Q. (BY MR. SCHMIDT) So, this is a case controlled
10 study?

11 A. Yes, in a sense. And what they do is they want
12 to know the characteristics of this erythroleukemia and
13 how many are de novo and how many are secondary and to
14 what they're secondary to. So, what they do is they've
15 got 62 patients and they tell us the clinical features
16 of all cases were reviewed with particular attention
17 given to previous medical history including exposure to
18 toxic agents, chemotherapy, radiation and presence of
19 autoimmune disease. And after looking at that, they say
20 of these 62, 55 presented with de novo acute leukemia,
21 parentheses, sudden onset without previous radio-
22 chemotherapy, toxic exposure or neoplastic or autoimmune
23 diseases. In other words, 55 of the 62 were de novo.
24 Of the remaining ones, in three of the remaining
25 patients a myelodysplastic syndrome preceded the AML.

1 In two patients the disease was therapy-related from
2 chemotherapy. One patient had undergone kidney
3 transplantation, so he had immunosuppressive drugs. And
4 one patient had been chronically exposed to solvents
5 which perhaps could be benzene-induced.

6 Q. Do you know whether it's benzene?

7 A. It doesn't say. It just says exposed to
8 solvents. So, this gives you a general idea of a number
9 of things. It shows how de novo is separated from
10 secondary and it gives you what everybody says, that
11 environmental causes of acute leukemia are very unusual.
12 In this particular group they only had one of the 62
13 that might have been caused by benzene. That's in this
14 article. And in the same regard here's another modern
15 article, they want to do the same thing for
16 myelodysplasia. So, they want to study the chromosomes
17 on de novo myelodysplasia. How do they do that? They
18 take all of their cases and they say patients with a
19 diagnosis of chronic myelomonocytic leukemia, which used
20 to be called a type of myelodysplasia, those previously
21 treated with chemo-radiation for other cancers or for
22 non-malignant disorders, for example, autoimmune
23 diseases, and those previously exposed to environmental
24 carcinogens were excluded for the study. And, so, the
25 rest, the 331 are de novo, primary, myelodysplasia. So,

1 whether you're talking about myelodysplasia or acute
2 leukemia, by definition benzene-induced disease is not
3 in the mix. And when you say someone has de novo
4 leukemia, you're talking about certain defined
5 characteristics of the leukemia and you're excluding
6 those people in whom you think chemicals, both
7 environmental or therapeutic, were causative.

8 Q. These are mutually exclusive classes, secondary
9 versus de novo?

10 A. Yes. That's what the modern literature tells
11 us about these.

12 Q. Let me see. I would like to mark these and
13 make them exhibits.

14 MR. SCHMIDT: Can we go off the record for
15 a second?

16 (Break taken from 2:21 p.m. to 2:22 p.m.)

17 Q. (BY MR. SCHMIDT) Back on the record. I want
18 to go back to this acute myeloid leukemia, epidemiology
19 and etiology from the American Cancer Society that was
20 your reference number 4.

21 A. Yes, I have that.

22 Q. And if you'd just turn to the second page, page
23 2100. Right-hand column at the bottom of the first full
24 paragraph, I'm going to read this. I'm just not sure I
25 understand it and I want to hear your thinking on it.

1 It says by contrast AML with genotypes typical of
2 younger patients, true de novo AML, has an approximately
3 flat incidence throughout life. Also, in progressive
4 age groups. Approximately five percent of elderly
5 patients with AML are estimated to belong to the true de
6 novo AML group which is consistent with the incidence in
7 younger patients?

8 A. Well, what he has reference to is that with age
9 the incidence of leukemia goes up steadily and this
10 graph he shows demonstrates that.

11 Q. Right.

12 A. Also, with age the incidence of 5 and 7's goes
13 up because older people get 5 and 7's whether they have
14 chemical exposure or not. But the translocations in de
15 novo leukemia, you especially see a lot of
16 translocations and normal chromosomes. In the case of
17 the translocations, that incidence is flat throughout
18 life. So, unlike the 5 and 7's which increase into the
19 elderly, in the de novo types of leukemia with the
20 translocations, that incidence is steady throughout
21 life. And you can make out of that what you will.
22 There will be several possible explanations for that.

23 Q. The statement that five percent of elderly
24 patients with AML are estimated to belong to the true de
25 novo group, does that mean that on an epidemiologic

1 basis only five percent of elderly patients with AML
2 have those AML's be de novo AML's?

3 A. No. I think what he's talking about are the
4 translocations. In other words, that even though we
5 have a lot of older people with AML, the number with
6 what we call balanced translocations, which is one of
7 the characteristic things about de novo, that incidence
8 is constant throughout life. And, as I say, the
9 pertinence of that could be debated as to why that's the
10 case.

11 Q. Your own article under tab 3 and the summary at
12 the top states although distinction between secondary
13 AML and the far more common de novo AML is difficult to
14 establish with certainty in any given case.

15 A. Where did I say that?

16 Q. Right up here.

17 A. Okay. Yes. That's correct. In any given case
18 of acute myeloid leukemia, we cannot prove the etiology
19 with certainty.

20 Q. As I understand it, there have been at least
21 two instances in which you have attributed AML to
22 benzene exposure in your clinical practice?

23 A. I say two. I can think of one right off the
24 bat which was a case of erythroleukemia, interestingly
25 enough, as I mentioned previously. That man had been

1 exposed in a refinery in Louisiana to benzene, among
2 other chemicals, and had repeated episodes of
3 pancytopenia as Dr. Aksoy described but always would
4 recover. And then he had one and didn't recover and got
5 acute leukemia. And I felt very confident his was
6 chemical-induced.

7 Q. Did you have a dose calculation? Did you know
8 how much he had been exposed to?

9 A. No. But he had worked there for many years in
10 that job. He was probably about 65ish or 66 when I saw
11 him. And maybe a little younger than that. Maybe about
12 60. And he had worked there his entire career.

13 Q. 30 plus years?

14 A. 30 plus years. And he had had repeated,
15 because it was a company, he had like frequent blood
16 counts. So, we had all sorts of history of blood
17 counts. And you can see the dips, the peaks and the
18 valleys. And they would take him out of whatever he was
19 doing and then when his counts got better, they'd take
20 him back. And, so, I didn't have any doubt that his was
21 chemical-induced, but I still couldn't prove it. I
22 mean, even in his case it's just inference based on what
23 we're seeing because there's no way to prove any given
24 case. But I felt fairly confident his was
25 chemical-induced.

1 Q. And as we talked earlier, doctors deal in the
2 world of probabilities rather than certainty?

3 A. That's right.

4 MR. SCHMIDT: Let's go off the record.

5 (Break taken from 2:28 p.m. to 2:28 p.m.)

6 Q. (BY MR. SCHMIDT) Then, Dr. Natelson, in one of
7 your depositions that I read there was another case of a
8 man who drove a tanker truck for 30 years. He had some
9 sort of benzene-containing product which he regularly
10 sampled or inspected. He received significant peak
11 exposures and you determined based on the work history
12 that his disease was induced by benzene exposure. Do
13 you remember that?

14 A. I don't remember. I'm not certain. I don't
15 dispute that, but I'm trying to think of who that would
16 be.

17 Q. Would you like to see the --

18 A. Yeah, what I said.

19 Q. I think it starts on page 44.

20 A. But this man didn't have acute leukemia. He
21 had myelofibrosis.

22 Q. You know what, my note says that. I'm sorry.

23 A. It's a different illness, but it's not acute
24 leukemia.

25 Q. And in this diagnosis of myelofibrosis did you

1 have a dose calculation?

2 A. No.

3 Q. But you were comfortable in these two cases of
4 attributing these diseases to benzene without a dose
5 calculation?

6 A. Well, the first case for certain because I had
7 the history -- I didn't have the dose, but I had the
8 blood counts. The second case I would say that I would
9 consider it. In other words, myelofibrosis is a very
10 peculiar illness and there is no epidemiological data
11 linking it to benzene but there are anecdotal case
12 reports kind of like my patient. And, so, I really
13 don't know whether he did or didn't, but he did have
14 that interesting history.

15 Q. Well, you were asked here about cases where you
16 had attributed them to benzene exposure. This
17 myelofibrosis is one that you testified to?

18 A. I probably did. I don't dispute that he might
19 have had it from that, but it wasn't acute leukemia.

20 Q. And we established it can be important to
21 whether you attribute it to benzene or not because that
22 may affect the ultimate course of treatment?

23 A. Yes. We don't have very good treatment for
24 myelofibrosis aside from marrow transplantation. So, in
25 his case it wouldn't have affected much. But, yes, we'd

1 like to know what the etiology was.

2 (Exhibits 68 through 71 marked.)

3 Q. (BY MR. SCHMIDT) Dr. Natelson, the four
4 articles that you wanted to bring to my attention that
5 were not referenced in your report have now been marked
6 and I just want to see if you -- I'll hand them to you
7 and I'll let you identify them. The first one is
8 Exhibit 68?

9 A. Yes, this is entitled Incidence and Prognostic
10 Significance of Karyotype Abnormalities in De Novo
11 Primary Myelodysplastic Syndromes, a Study on 331
12 Patients From a Single Institution. This one is
13 Battling the Hematological Malignancies, the 200 Years'
14 War.

15 Q. That is 69. And I've just handed you
16 Exhibit 70, would you identify that?

17 A. Treatment and Evaluation of High Risk
18 Myelodysplasia.

19 Q. And finally?

20 A. Acute Erythroid Neoplastic Proliferations, A
21 Biological Study Based on 62 Patients.

22 Q. Thank you. If you could get your report in
23 front of you which is Exhibit 63. I notice on the first
24 page, bottom paragraph, routine laboratory studies
25 disclosed a reduced white blood cell count of 1100 cubic

1 millimeters and then a severe anemia. Was there a
2 particular kind of anemia that he presented with?

3 A. Well, we call this myelophthisic anemia. And
4 that means an anemia due to bone marrow replacement by
5 something bad. And he basically had half the blood he
6 should have. In other words, a normal man's hemoglobin
7 is 14, he was 7. So, he had half a tank. And the
8 normal white cell count is 5,000, his was 1,000. And
9 the normal platelet count is about 200,000 and his was
10 40,000. So, all of his cell lines were reduced because
11 of the production. The factory of the bone marrow was
12 replaced by leukemia cells.

13 Q. Now, I take it you draft these reports on a
14 computer?

15 A. Yes.

16 Q. And in a report like this, a litigation report,
17 do you often start with one that you prepared in a
18 previous case and cut and paste sections out so you
19 don't have to rewrite them from scratch?

20 A. I might. Particularly the opening paragraph
21 that has to have certain disclaimers in there and all
22 that sort of stuff.

23 Q. How about the section on page 2 from the first
24 full paragraph from the top starting in attempting to
25 assign causation, is that paragraph one that you have

1 put in other reports?

2 A. Or something similar, yes.

3 Q. And is that true for the next one, two, three
4 paragraphs? I notice, for example, they have nothing
5 specific to Mr. Henricksen in them.

6 A. Well, they would be different. I'm sure if you
7 looked at other reports, there would be some subtle and
8 some significant differences. But, in general, the
9 context would be similar because, in other words, I'm
10 being asked how do I assign causation and that doesn't
11 change. So that there would be similarities. It
12 changes in the case of what the illness might be or
13 where it was from or what the exposure was.

14 Q. On to page 3, the last sentence in the partial
15 paragraph at the top that says few review articles have
16 attempted to accurately break down the relative
17 frequency among the various causes of secondary AML.
18 But in one large series of individuals with AML, 2,037
19 were considered de novo, 281 on the basis of prior MDS
20 and 184 relating to prior neoplastic therapy. And that
21 is from Bacher?

22 A. Yes.

23 Q. Were any of these individuals with AML
24 evaluated for benzene or gasoline exposure?

25 A. The article does not comment about that.

1 Q. It doesn't have anything to do with benzene or
2 gasoline exposure, does it?

3 A. No.

4 Q. Do you know how these individuals were
5 selected?

6 A. No. Except that the authors selected them
7 based on whatever criteria they chose to use.

8 Q. Which was just basically if you had AML, wasn't
9 it?

10 MR. YOUNG: Objection, the periodical
11 speaks for itself.

12 A. No. They all had AML.

13 Q. (BY MR. SCHMIDT) Right.

14 A. But, in other words, the authors decided based
15 on, for example, as in the papers I've shown you here
16 why they call them de novo and why they call them
17 secondary.

18 Q. But it's not an industrial exposed cohort?

19 A. Certainly not.

20 Q. Down to the third paragraph, in that first
21 sentence in which you state that in the case of benzene
22 or solvent exposures, numerous large, serial
23 epidemiologic studies involving hundreds of thousands of
24 workers with potential for benzene and other hydrocarbon
25 exposures have failed to show any statistically

1 significant increase in the incidence of AML in
2 developed countries for many years. Does this mean to
3 suggest that you do not believe that benzene causes AML
4 in industrially-exposed workers?

5 MR. YOUNG: Objection, report speaks for
6 itself.

7 A. Not at all. In other words, there is no doubt
8 that benzene under certain conditions and dose levels
9 can cause AML and I've said that. It's just that in
10 these particular studies that I've cited where there is
11 potential for exposure, there is no statistically
12 significant increase in the incidence.

13 Q. (BY MR. SCHMIDT) And you agree there's also
14 another body, a large number of studies that have
15 numerous large, serial epidemiologic studies where they
16 do find a significant increase in the incidence of AML
17 as a result of the exposures?

18 MR. YOUNG: Objection, lack of foundation.

19 A. You'll have to show me which ones those are.

20 (Exhibit 72 marked.)

21 Q. (BY MR. SCHMIDT) Doctor, I've marked
22 Plaintiff's Exhibit 72. It's a population-based case
23 control study of childhood leukemia in Shanghai by Shu.
24 Have you seen this study before?

25 A. No.

1 Q. In the summary you see the sentence ANLL was
2 linked to maternal occupational exposure to benzene
3 during pregnancy and this is ANLL developing in the
4 children. Do you understand that?

5 A. I see that.

6 Q. Okay. ANLL is the disease that Mr. Henricksen
7 had falls under that rubric?

8 A. Yes.

9 Q. And if you turn back to page 642, table 7?

10 A. I don't have page 642.

11 Q. Oh, they're double-sided.

12 A. Oh, that's why.

13 Q. See the top line benzene?

14 A. Yes.

15 Q. You have an odds ratio of 2 to 2.3 that is not
16 statistically significant. It's .9 to .43?

17 A. I see that, but it doesn't tell me what kind of
18 leukemia we're talking about here.

19 Q. Right. That's childhood leukemia. I believe
20 we have a -- we'll see. But you agree it shows an
21 increased risk for leukemia related to benzene?

22 MR. YOUNG: Objection, the document speaks
23 for itself.

24 A. Which is not statistically significant.

25 Q. (BY MR. SCHMIDT) I understand, but it shows an

1 increased risk?

2 MR. YOUNG: Same objection.

3 A. It shows an increased risk of what isn't
4 specified as to what type of leukemia.

5 Q. (BY MR. SCHMIDT) Now, look down below in table
6 8. You see the far right-hand column, ANLL?

7 A. Yes.

8 Q. And we have a line for benzene and here the
9 odds ratio is 4 with a 1.8 to 9.3 confidence index.

10 A. That's so, but these are -- it's hard to equate
11 this to what we're talking about here. The mother is
12 exposed to benzene, not the person with the leukemia.
13 These are children and mothers exposed. Now, that's not
14 exactly comparable to Mr. Henricksen's situation.

15 (Exhibit 73 marked.)

16 Q. (BY MR. SCHMIDT) I'm handing you Exhibit 73
17 which is an article by Glass, et al., called Leukemia
18 Risk Associated With Low-Level Benzene Exposure?

19 A. Yes.

20 Q. September of 2003, Epidemiology?

21 A. Yes.

22 Q. Have you seen this article before?

23 A. Yes. What is described here is the cases of
24 acute leukemia in the Australian benzene study. And Dr.
25 Glass now tells us that there is no increased incidence

1 and there's no relationship between any leukemia and
2 dose or duration of employment.

3 Q. In this article?

4 A. In this study.

5 Q. In this article?

6 A. Oh, in this article, yes, this is her case
7 control study where she interviewed her people. Yes, I
8 have seen this article.

9 Q. And in this article she does find an increased
10 risk for leukemia at low level --

11 A. These are the same patients that she's
12 describing in the modern articles that show no increased
13 risk.

14 Q. Well, now, her later articles you're farther
15 away from the stop exposure time, aren't you?

16 A. This article is written in 2003. The study
17 ended -- was closed in 1999.

18 Q. Okay. Nonetheless, in this article does she
19 not find exposures on table 5? Again, this is all
20 leukemia, not AML. You see the intensity, exposure
21 intensity group at the lower, the lower staff of table
22 5? You understand that means peak exposures?

23 MR. YOUNG: Objection, lack of foundation.

24 A. I'm not sure what column you're having me look
25 at.

1 Q. (BY MR. SCHMIDT) Here we go.

2 A. Okay. The bottom lines here. Correct.

3 Q. Where you have peak exposures of greater than
4 3.2 ppm, the odds ratio is 20.4 with a confidence index
5 of 1.6 to 270 which is statistically significant?

6 A. Yes, but these are not AML's. These are
7 combined leukemia cases. And as I commented, they are
8 the same cases that she describes now and suggests
9 there's no increased incidence.

10 Q. If you look down at the -- she does have an
11 ANLL figure in table 6 where you have an odds ratio of
12 7.17 with a confidence index of 1.27 for 40.4?

13 A. Yes, I see it.

14 Q. That shows a statistically increased risk of
15 ANLL, doesn't it?

16 A. Yes.

17 Q. Is the Hays study that you cite in your report
18 the 1997?

19 A. Yes. You're looking at table 2?

20 Q. I'm not sure I am. Here we go, yes, table 2,
21 the far left-hand column, average ppm exposure less than
22 ten. And if you come down on the left, you have for
23 ANLL/MDS, the precursor, when you combine those two, you
24 have a risk ratio of 3.2 with a confidence index that is
25 statistically significant?

1 A. Again, this is not a pure culture of acute
2 myeloid leukemia and, so, it doesn't exactly reflect the
3 illness that Mr. Henricksen has. And there is I believe
4 considerable dispute about what the benzene levels were
5 that these people were exposed to and they weren't
6 tanker truck drivers. These were painters. They were
7 also exposed to solvents, pesticides. So, it's not
8 comparable to what Mr. Henricksen has.

9 MR. SCHMIDT: But that's not the question.
10 I object and move to strike.

11 Q. (BY MR. SCHMIDT) We're talking about your
12 sentence that said about studies of numerous large-scale
13 industrial exposures?

14 A. Okay. See, on that same thing that you're
15 talking about when we restrict it to the leukemia, the
16 one up where he says ANLL, he's got the confidence level
17 as non-statistically significant.

18 Q. Right. But the odds ratio or risk ratio is
19 two?

20 A. Yes.

21 Q. It's a doubling of the risk, correct?

22 A. Yes.

23 (Exhibit 74 marked.)

24 Q. (BY MR. SCHMIDT) Doctor, I'm directing your
25 attention to Exhibit 74 which is an article by Kirkeleit

1 dated 2008, I believe, Increased Risk of Acute
2 Myelogenous Leukemia and Multiple Myeloma in a
3 Historical Cohort of Upstream Petroleum Workers. Have
4 you seen this before?

5 A. I'm not certain. Yes, you're talking about
6 table 4? Which one?

7 Q. Before we get there, I want to talk -- if you
8 go to the page, and unfortunately these pages aren't
9 numbered, so it's the fifth page in that has discussion
10 on the right-hand side?

11 A. Yes.

12 Q. At the very bottom, pooled full shift
13 measurements from processing and drilling areas in the
14 period 1994 to 2003 and then number 367 to show the
15 number of samples show an arithmetic mean benzene
16 exposure of .037 ppm?

17 A. I don't see that. It says crude oil assays,
18 mean and median value of .28 benzene by weight. Is that
19 what you're talking about?

20 Q. Keep going. I'm sorry, you have to flip the
21 page.

22 A. Oh. An arithmetic mean benzene exposure of
23 0.037 part per million.

24 Q. Which you would agree is a very low exposure?

25 A. That would be a very low exposure, yes.

1 Q. If you look up above, table 3, and you find the
2 column acute myelogenous leukemia on the left?

3 A. Uh-huh.

4 Q. You come across, you have a risk ratio of 2.89
5 which is more than a doubling of the risk, correct?

6 A. Yes.

7 Q. And you have a confidence index of 1.25 to 6.67
8 which is statistically significant, isn't it?

9 A. Yes.

10 Q. And if you look back on the front page, Mr.
11 Kirkeleit says the results, it's at the end of his
12 abstract paragraph, the results suggest that benzene
13 exposure which most probably caused the increased risk
14 of acute myelogenous leukemia also resulted in an
15 increased risk of multiple myeloma. You see that that's
16 his conclusion?

17 A. Yes.

18 Q. So, would you now agree with me that while
19 there are some studies that do not find an association
20 between benzene exposure in the context of your sentence
21 that we were referring in your report, there are others
22 that do?

23 A. I would put other, singular. The ones you've
24 shown me, this is the Kirkeleit study is the one that
25 shows the statistics of significant increase. The ones

1 with children whose mothers had exposed, I don't think
2 that's anything comparable to what we're talking about.
3 The last study I think basically shows nothing. And I
4 think the Hays study doesn't show statistical
5 significance when you're talking about leukemia itself.
6 This one does. So, what you've shown me is one study
7 here to support what you suggest. And this study is
8 very aberrant because it also shows an increased risk of
9 multiple myeloma and many, many studies have shown no
10 risk of multiple myeloma including the Glass study that
11 you cited. So, this is an aberrant study. And, as I
12 said, what you're looking for is consistency in
13 epidemiologic studies and I've listed a lot more than
14 one study.

15 Q. Is it your testimony that Dr. Glass has
16 repudiated her 2003 report?

17 MR. YOUNG: Objection, misstates testimony.

18 A. I don't know if she has repudiated it, but we
19 can read what she says about it right now. And she says
20 about that cohort that there is no increased risk of
21 acute leukemia and no relation between increasing dose
22 or duration of employment.

23 Q. (BY MR. SCHMIDT) Is it an identical cohort?

24 A. It's the identical cohort. It's the same 11
25 guys who have acute leukemia.

1 Q. What's your authority for the statement in the
2 next sentence, the paragraph midway down page 3 that you
3 have to have at least 200 part per million years
4 exposure to associate benzene to AML?

5 MR. YOUNG: Objection, the reference is in
6 the report itself.

7 A. The references are in the report. And I didn't
8 say that you had it. I said I just cited some. I said
9 what I typically held is that I don't know what the dose
10 is except it's extremely high and not likely to be
11 achievable in the modern era. And I cited in here
12 Wong's and another article in which they show that you
13 have to have 200 part per million years exposure to have
14 statistical significance. And then two other articles
15 showing that in one case at levels of 40 you don't have
16 an increased incidence and another one which is a small
17 study showing remarkably high levels, also with no
18 increased incidence. But I'm just pointing out what the
19 literature says.

20 Q. (BY MR. SCHMIDT) And the Glass study that we
21 just looked at -- I get confused. Which one is that?

22 A. It's this one right here?

23 Q. At the end of this paragraph, in another small
24 but carefully studied group, it's the Swaen study, with
25 the mean exposure of 159 ppm years, the incidence of AML

1 was not increased?

2 A. Yes.

3 Q. You have to show me where it says AML because
4 what I see is all leukemias. It's table 3 is where I
5 was looking.

6 A. Well, there's only one person with leukemia in
7 this cohort and they expected one. I will grant you I
8 don't think he comments in here about the type of
9 leukemia. Actually I hadn't noticed that.

10 Q. So, your reference at that last sentence of the
11 third paragraph on page 3 to AML is incorrect?

12 A. No. It's still correct because there would be
13 no statistically significance even if that one case was
14 an AML.

15 Q. Do you think that there's an equivalence
16 between looking at all leukemias and all AML's?

17 A. Oh, excuse me, I'm sorry, I want to go back, he
18 does tell us.

19 Q. Okay.

20 A. If you read this sentence in here, he says the
21 single leukemia was not AML. So, there were no AML's in
22 that entire cohort.

23 Q. And that's on page 25 in the right-hand column.
24 How much power is there where the observed expected
25 number is one?

1 A. I have no idea.

2 Q. You're not an epidemiologist?

3 A. I'm not an epidemiologist.

4 Q. I want to look at the first sentence in your --
5 the next paragraph on page 3 where you say the incidence
6 rates of AML in fuel distribution workers is not
7 increased over the incidence of members of the general
8 population. Have you looked at the Terry report?

9 A. It doesn't ring a bell. If you'll show it to
10 me.

11 (Exhibit 75 marked.)

12 Q. (BY MR. SCHMIDT) And when you get there, I'm
13 interested in table 2 on page 1122.

14 A. Okay. I'm looking at this table.

15 Q. And if you look down about two-thirds of the
16 way down the page, petroleum industry or manufacturing
17 petroleum products?

18 A. Okay.

19 Q. And do you see beneath that AML?

20 A. Yes.

21 Q. You have a risk ratio of 7.2 with a confidence
22 of 1.5 to 34 if they had ever worked in the industry and
23 a risk ratio of 6.2 with a statistically significant
24 confidence ratio of 1.3 to 29.8 if they worked in the
25 industry for more than a year?

1 A. Yes.

2 Q. That indicates that there is an increased risk
3 of AML for people who work in the petroleum industry or
4 manufacturing petroleum products?

5 MR. YOUNG: Objection, lack of foundation.
6 The document speaks for itself.

7 A. That's what the article says.

8 Q. (BY MR. SCHMIDT) And the petroleum industry
9 would include fuel distribution workers?

10 MR. YOUNG: Objection, lack of foundation.

11 A. Well, it might.

12 (Exhibit 76 marked.)

13 Q. (BY MR. SCHMIDT) Dr. Natelson, I'm handing you
14 Exhibit Number 76 which is by an author named Jakobsson
15 from 1993, AML Among Petrol Station Attendants. Have
16 you seen this article before?

17 A. No.

18 Q. When you get there on page 256, it's the
19 results paragraph on the left-hand column.

20 A. The only occupational group that showed a
21 significant elevated risk of AML was male petrol station
22 attendants and demonstrators.

23 Q. It says there were ten cases of AML versus 2.8
24 expected?

25 A. Yes.

1 Q. There was a ratio of 3.6 with a confidence
2 index of 1.7 to 6.6 making it statistically significant?

3 A. Yes.

4 Q. Forgive me if I asked you this earlier, did you
5 see Dr. William Sawyer's report in this action?

6 A. Yes, I'm sure I've seen it.

7 Q. Okay. On page 4 you talk about a
8 controversially controlled analysis in reference to the
9 Healthwatch study. Would you explain what you meant by
10 controversially controlled?

11 A. Certainly. What we have here is someone going
12 to 11 people who have acute leukemia and asking them
13 about their exposures and then going to people who don't
14 have acute leukemia and asking them about their
15 exposures. I guarantee that if you deal with people
16 with cancer, you can find someone who has got a 60-pack
17 year history of cigarette smoking and if you start
18 questioning them, they will bring up all of the --
19 anything that could possibly cause that lung cancer
20 aside from that smoking. And that's called recall bias.
21 And I think to do a study like this and take someone who
22 has acute leukemia or any form of cancer and who would
23 like it to have an etiology not of itself or of their
24 diet or of their lifestyle and then you compare it to
25 someone who doesn't have cancer and who has no need to

1 imagine or amplify any chemical exposures, you have a
2 study that has the potential for being meaningless. And
3 if you take a look at that study in comparison with what
4 we've got today and with the entire group from that
5 study, it's very clear there is no increased incidence
6 of leukemia in the Australian petroleum group.

7 Q. Have you read Dr. Glass's 2006 rebuttal?

8 A. I've got one -- yes, I have it right here, I
9 think.

10 Q. I think we just looked at that, didn't we?

11 A. Now, I don't think we looked at this one.

12 Q. No. Her rebuttal to the criticism about bias?

13 A. Well, she says there is no bias, but --

14 Q. So, you have read it?

15 A. Oh, yeah, I've read it, sure.

16 Q. You just disagree with her?

17 A. Well, I take care of people with cancer. I
18 know that when you ask them why they have it, they will
19 come up with a remarkable array of causation other than
20 what the real causation might be. So, unless you
21 actually have measurements on each of these individuals,
22 both in the control group and the patient group, it's
23 not very useful in my opinion.

24 Q. Now, I notice over on page 5, the first full
25 paragraph, I think we dealt with this this morning.

1 That first sentence doesn't have a cite for it but you
2 and I did talk about that and you sent me to some cases.
3 I think it was Morgan?

4 A. Oh, with the latency and the --

5 Q. It was the first one. I'm forgetting the
6 fellow's name. But whether -- making the equivalence
7 between benzene toxicity and chemotherapy?

8 A. Oh, yeah, many papers do that. Morgan is one
9 of those.

10 Q. Was it Jamal?

11 A. Jamal had to do with the carcinogenicity of
12 fuels and the fact that many animal studies have
13 suggested that it depends what your benzene is mixed in,
14 if it's shaken or stirred. And that the competing
15 compounds in fuels make it difficult to compare with
16 pure benzene type studies.

17 Q. I notice that this quote that you have in bold
18 at the bottom of that paragraph indicates that one of
19 the diverse environmental factors that can cause AML in
20 the, parens, it says, e.g., benzene, petroleum, organic
21 solvents, that author seems to believe that petroleum is
22 a cause of AML?

23 A. I don't know what he believes. I just made a
24 quote of what he said in the article.

25 Q. And that's what he said in the article?

1 A. Yes.

2 Q. Did you perform a dose calculation in this
3 case?

4 A. No.

5 Q. Did you review any data, monitoring data
6 regarding tanker driver exposures?

7 A. No.

8 Q. Did you review any tanker epidemiology, tanker
9 driver epidemiology studies?

10 A. Well, some of these articles are distribution
11 workers. So, that would fall under that rubric.

12 Q. Have you been provided documents from
13 ConocoPhillips regarding the health hazards of benzene?

14 A. No.

15 Q. Did they provide you any documents at all?

16 MR. YOUNG: Who is the "they"?

17 Q. (BY MR. SCHMIDT) They, ConocoPhillips, either
18 directly or through its attorneys?

19 A. No.

20 Q. I think you've established you do not disagree
21 with the diagnosis in this case?

22 A. That's correct.

23 Q. And you state the prognosis at the end of your
24 report?

25 A. Yes.

1 Q. You think that Mr. Henricksen has been treated
2 appropriately?

3 A. That's always a tough one to answer. There's
4 no question that his initial treatment was very
5 appropriate. It was about as standard as standard could
6 be. And it had a good result. He went into remission.
7 But we know that people who have normal chromosomes in
8 AML are what we call an intermediate risk group meaning
9 that they don't perform as well as someone with let's
10 say a translocation and have a reasonable potential for
11 a cure with chemotherapy. They're probably going to
12 relapse. And we got a situation here where we have a
13 perfect match in a sibling which is not always found
14 which is a good thing and the question is why wasn't he
15 transplanted during his first remission. Because as the
16 transplanter said, and I just quoted what he said, he
17 said they have a 50 percent two or three-year survival
18 if it's done in first remission and in the second
19 remission when it was done in this case, it drops to
20 30 percent. And, so, obviously I wasn't taking care of
21 him. There may be a lot of factors I don't know about.
22 But to me if I was taking care of this man, I would have
23 tried to transplant him in first remission because he
24 had such a good donor and he's in an intermediate risk
25 group. And certainly if I thought he had a secondary

1 leukemia, I would have done that.

2 Q. Have you formed an opinion that the failure to
3 transplant him in the first remission failed to meet the
4 standard of care?

5 A. No, because I think that's a judgment issue and
6 it's hard to put yourself in the shoes of the treating
7 doctors. But just kind of looking at the numbers about
8 the situation, as I say, I probably would have tended to
9 transplant him and for whatever reason they chose not
10 to. But I don't believe that that would be below the
11 standard of care.

12 Q. And this is a subject about which reasonable
13 doctors could differ?

14 A. Certainly.

15 Q. And you're not going to come in to testify to
16 the jury that the decision not to transplant him the
17 first time was actually the cause of his damages in this
18 case?

19 A. No.

20 Q. You have no personal information about Neil
21 Henricksen, his treatment, his disease or anything about
22 him apart from what you've read?

23 A. That's correct.

24 Q. You did no studies on your own?

25 A. Correct.

1 Q. Apart from reference number 3 in your report,
2 do you have any publications that address the issue of
3 benzene?

4 A. One that has to do with myelodysplasia and
5 benzene.

6 Q. I got your CV right here.

7 A. It's called sideroblastic anemia.

8 Q. It's going to be quicker for you to find it.

9 A. It's called Benzene and Sideroblastic
10 Erythropoiesis. It's number 76 on there.

11 Q. It's number 76 on page 11 of your CV?

12 A. Yes.

13 MR. SCHMIDT: Let's take a break.

14 (Break taken from 3:26 p.m. to 3:34 p.m.)

15 Q. (BY MR. SCHMIDT) Dr. Natelson, do you have any
16 formal training in epidemiology?

17 A. No.

18 Q. Have you ever written an epidemiologic study?

19 A. No.

20 Q. The studies you and I have been talking about
21 this afternoon are epidemiologic studies, however,
22 aren't they?

23 A. Some of them, yes.

24 Q. Have you ever designed an epidemiologic study?

25 A. No.

1 Q. Have you ever implemented one?

2 A. No.

3 Q. Have you ever published one?

4 A. No.

5 Q. Do you have any formal training in either
6 writing, designing or implementing epidemiologic
7 studies?

8 A. No.

9 Q. Do you have any formal training in analyzing
10 epidemiological studies?

11 A. No.

12 Q. Are you on the editorial board of any
13 scientific journals?

14 A. No.

15 Q. Have you ever published on the health effects
16 of benzene?

17 A. Well, only in that these articles address acute
18 leukemia, but not specifically about health effects, no.

19 Q. Have you ever applied for a grant to study the
20 health effects of benzene?

21 A. No.

22 Q. Have you ever spoken at a conference about the
23 health effects of benzene?

24 A. No.

25 Q. Have you ever attended a conference, just

1 attended a conference on benzene and AML?

2 A. No.

3 Q. Have you served on any scientific review
4 committees for the National Institutes of Health?

5 A. No.

6 Q. How about have you served on any scientific
7 review committees for EPA?

8 A. No.

9 Q. Have you ever served on the scientific review
10 committee for any governmental body?

11 A. No.

12 Q. Do you review grants for the National
13 Institutes of Health?

14 A. No.

15 Q. Have any reporters ever solicited your opinions
16 on benzene health effects for any national paper?

17 A. I don't know, but I did get a call from a
18 reporter yesterday, something about this area. It was
19 on whether or not the State of New York should give
20 earmarks of a million and a half dollars for the study
21 of bone marrow damage in soldiers which could be from
22 petroleum products or anything else. And I did talk to
23 this lady on the phone for awhile and then referred her
24 to somebody who knew more about grants is what she was
25 really interested in than I do.

1 Q. Have you ever consulted with the EPA on benzene
2 and its regulation?

3 A. No.

4 Q. How about OSHA?

5 A. No.

6 Q. Have you ever consulted with any state or
7 regulatory agency on benzene and its regulation?

8 A. No.

9 Q. Have you ever received a grant to study
10 benzene?

11 A. No.

12 Q. Have you ever done any animal studies or
13 laboratory studies using benzene or its metabolites?

14 A. No.

15 Q. I believe attached to your report or your CV
16 was a list of cases you've testified to and I saw about
17 25 of them attached?

18 A. I have an updated one which is probably not
19 much different than the one you have.

20 Q. It says the following list of cases since
21 January, 2003 and it is 25 cases?

22 A. Oh, yeah, okay, this is the short version,
23 since '03. I'm with you. I have a longer version since
24 1992. I had forgotten the short version.

25 Q. How many cases are on the 1992 version?

1 A. This is 58 which you're certainly welcome to.

2 Q. And as I understand it, you testify in a number
3 of different arenas, not just benzene cases?

4 A. That's correct.

5 Q. You testify in medical malpractice actions?

6 A. Yes.

7 Q. Benzene cases?

8 A. Yes.

9 Q. What others?

10 A. Cases that had to do with house staff or
11 residency training issues. Testified in deed
12 restriction issues for our subdivision.

13 Q. As an expert?

14 A. No, not as an expert, but we were trying to
15 preserve our deed restrictions.

16 Q. I'm only interested in expert testimony.

17 A. I understand, but it was testimony at trial.
18 But primarily in terms of residency training program,
19 malpractice and benzene issues. One case on sickle cell
20 disease that was not a malpractice that I can think
21 about.

22 Q. How many other cases are benzene cases?

23 A. I don't know. I'd have to count that up.

24 Q. More than ten?

25 A. Yes.

1 Q. More than 20?

2 A. Probably.

3 Q. Have you ever testified on behalf of a
4 plaintiff in a benzene case?

5 A. No.

6 Q. Do you always testify on behalf of petroleum
7 refining companies?

8 MR. YOUNG: Objection, lack of foundation.
9 Argumentative.

10 A. Well, to tell you the truth, I don't pay any
11 attention as to what the company at the basis is. In
12 other words, I deal with the attorneys. I really pay
13 little or no attention and many of these cases have
14 multiple defendants from paint manufacturers to
15 distributors to oil companies. So, the chances are I
16 have testified for many different petrochemical
17 companies.

18 Q. (BY MR. SCHMIDT) But it's always on behalf of
19 companies as opposed to individuals in the benzene
20 litigation that you've testified on behalf of?

21 A. Yes.

22 Q. In what percentage of the benzene cases that
23 you have testified in have you concluded that a
24 plaintiff's disease was benzene-related?

25 A. None of them.

1 Q. In every one of those cases have you testified
2 that the plaintiff's blood-related disorder was not
3 caused by benzene?

4 A. I've testified in all probability it was not
5 caused by benzene.

6 Q. Have you ever been in a fuel loading facility?

7 A. No.

8 MR. SCHMIDT: I think, Dr. Natelson, that's
9 all I have for now.

10 MR. YOUNG: Are you prepared to go on,
11 Doctor? I'm going to ask you about five minutes of
12 questions if you're ready.

13 THE WITNESS: That's fine.

14 (The time is 3:42 p.m.)

15 EXAMINATION

16 BY MR. YOUNG:

17 Q. Dr. Natelson, a few times today you have said
18 in this other stack that's not referenced in your report
19 and you've pointed to this stack. And let the record
20 reflect there's a stack here underneath your report
21 that's a few inches tall and then there's a stack here
22 that's one inch tall. Are you relying on these papers
23 also for your opinion?

24 A. Yes.

25 Q. Can you explain why you brought this stack of

1 papers?

2 A. Yes.

3 Q. Please do.

4 A. The original papers were in support of my
5 report. In subsequently reading Dr. Gardner's report
6 and others' reports, Dr. Gardner raised certain issues
7 about de novo and secondary. And, so, many of these
8 papers read on that issue of what is de novo and what is
9 secondary. And you copied four of those papers, for
10 example.

11 MR. YOUNG: And, Counsel, if you want a
12 copy of these, we will make it happen and get it to you.

13 MR. SCHMIDT: I would like a copy of those.

14 MR. YOUNG: Certainly.

15 Q. (BY MR. YOUNG) On that same topic, Doctor, I
16 have a few questions. Do you have an opinion as to
17 whether Neil Henricksen's AML was de novo or secondary?

18 A. I feel that in all probability he had de novo
19 AML.

20 Q. And can you explain to the jury why you have
21 that opinion?

22 A. Well, I think the evidence indicates that his
23 leukemia was of acute onset without a prior
24 myelodysplasia episode; that he had a normal chromosome
25 array by standard studies; that he had no evidence of

1 dysplasia on the morphology of the bone marrow cells;
2 that he responded well to his initial chemotherapy and
3 entered a prolonged remission and that his occupation
4 was that of a man who had exposures to diesel and
5 gasoline fuels which are not agreed-upon or known
6 carcinogens. And those findings suggest to me that this
7 leukemia is de novo.

8 Q. Dr. Natelson, you understand that in this case
9 Mr. Henricksen's attorneys contend that his exposures to
10 that gasoline with benzene as a component caused his
11 disease. You understand that?

12 A. Yes.

13 Q. So, does such an allegation of benzene exposure
14 make his AML secondary?

15 A. The allegation doesn't make it secondary. What
16 makes it secondary are the fact that his physicians feel
17 that his exposures were such that they caused the
18 leukemia and that there is documented evidence that
19 those exposures to leukemogenic agents were present in
20 the amounts thought to cause that illness.

21 Q. And previously you mentioned one, two, three,
22 four, five clinical factors dealing with secondary
23 versus de novo. It was just in response to my two
24 questions back. You remember those five clinical
25 factors?

1 A. In general terms, yes.

2 Q. All right. And were any of those -- well, let
3 me ask it the other way. Were Mr. Henricksen's clinical
4 factors consistent with de novo AML or with secondary
5 AML?

6 A. They were consistent with de novo AML.

7 Q. Dr. Natelson, for how long has the
8 hematological community applied the terms de novo and
9 secondary to its diagnostic and clinical findings?

10 A. Well, for many, many years, probably at least
11 40, the terms de novo and secondary have been applied to
12 leukemias. But prior to 1992 secondary referred
13 specifically to treatment-related leukemias. But after
14 1992 it became accepted that treatment-related leukemias
15 and environmentally-induced leukemias such as those from
16 benzene were genotypically and phenotypically identical
17 and the medical community lumped benzene-induced
18 leukemia as a form of secondary AML.

19 Q. One of those factors is the presence or absence
20 of cytogenetic abnormalities?

21 A. Yes. In other words, no cytogenetic
22 abnormality proves or disproves primary versus
23 secondary. But cytogenetic abnormalities are the rule
24 in secondary and they're frequently absent in primary or
25 de novo leukemia.

1 Q. And I think that Mr. Schmidt asked you this
2 earlier, but I can't remember, in what percentage of
3 secondary AML's do you see as a clinician the presence
4 of a cytogenic abnormality?

5 A. The literature suggests it's anywhere from 85
6 to 92 percent have associated cytogenetic abnormalities.

7 Q. And of that range, that 85 to 92 percent of
8 patients with the cytogenetic abnormality, do you know
9 what percentage of those present with, for example, a 5,
10 7 change?

11 A. Generally it would be about 50 to 75 percent.

12 Q. If a patient in the hospital reported gasoline
13 exposure or benzene exposure, would that in itself be a
14 requirement to define his or her leukemia as being
15 secondary?

16 A. No. The patient's comment alone would not make
17 that determination. It has to do with the character of
18 the findings and with the type of occupation. We all
19 pump gas or at least most of us do. And we all eat
20 bananas. So, we all have some exposure to benzene. But
21 what the doctor has to determine is whether or not he or
22 she attaches significance to that.

23 Q. You used a term endogenous early in the day.
24 Could you define that term just so the record is clear?

25 A. Yes. Primary or de novo myelodysplasia has

1 also been called endogenous to separate it from
2 secondary which has also been called event-related or
3 exogenous leukemia. In other words, exogenous meaning a
4 chemical caused a hit to the bone marrow, as we earlier
5 described or discussed, that was perpetuated and
6 resulted in the leukemia. Whereas a de novo leukemia
7 may well be endogenous. In other words, there is no
8 external source that caused this. It's a natural event
9 consequent to the need to replace your blood cells at a
10 dramatic rate throughout your lifetime. And mistakes
11 can happen. And that's one reason why the thinking
12 about balanced translocations doesn't change with age is
13 that there's a constant rate of these misadventures,
14 natural misadventures, you might say. And, so, there's
15 going to be a steady occurrence. Eventually a mistake
16 is made and it's sustained. So, another -- I would say
17 the most recent let's say nuance on the term de novo
18 leukemia would be endogenous as opposed to exogenous.

19 Q. In response to Mr. Schmidt's questions earlier
20 today, you described how many, and I don't remember the
21 number, millions or billions or trillions of cell
22 replications the body goes through a day in lymphocytes.
23 Do you remember that?

24 A. Well, lymphocytes actually are longer-lived
25 cells. The myeloid cells, what we think of as your

1 white cells, your granulocytes, the cells that are
2 involved in leukemia, those are replaced three times
3 each day and there are billions of those cells. So,
4 there's an enormous factory for breaking down and
5 rebuilding your DNA all day long every day of your life.

6 Q. So, why is it that people in their 60s develop
7 de novo AML at a greater rate than people in their 50s
8 or 40s or 30s or 20s? I don't understand why that is
9 so.

10 A. Well, nobody knows why that, but one theory is
11 that your repair mechanisms over time become weakened
12 and you're getting this constant breakage of cells all
13 the time but your ability to repair them wears out and
14 bad things happen.

15 Q. I understand.

16 A. That's simply a theory or a hypothesis. We
17 don't really know why that's the case.

18 Q. How old was Neil Henricksen when he was
19 diagnosed with his AML?

20 A. I think he was 60 some-odd. 62.

21 Q. I'm sorry, did you say?

22 A. 62, I believe.

23 Q. And is that within or within the range of when
24 you see the normal onset of increases of AML in the
25 population at large?

1 A. Well, there are more people at age 62 than
2 there are at 20 with AML.

3 Q. Now, this word hit, this one is new to me
4 today. And you and counsel for Mr. Henricksen need to
5 come to some agreement about what that means. When
6 you've answered questions about hit, what has that meant
7 to you?

8 MR. SCHMIDT: I'm going to object. It was
9 clear on the record.

10 A. What it means to me is that something causes
11 damage to a chromosome in the bone marrow and that can
12 be something endogenous or something exogenous. In most
13 instances that hit is repaired very quickly. In some
14 instances that hit may not be repaired. If one sustains
15 a number of non-repairable hits, then the potential for
16 acute leukemia increases.

17 Q. (BY MR. YOUNG) And is that what you meant by
18 perpetuated or sustained hits later when you were
19 discussing that term?

20 A. Yes, in other words, a hit that is not repaired
21 appropriately and then can perpetuate itself.

22 Q. Have you seen any clinical data in the medical
23 records or in the medical histories or in the deposition
24 of Mr. Henricksen or any of the materials you reviewed
25 suggesting that he was individually susceptible to

1 catching AML?

2 A. The only thing in the records was this
3 situation with his mother's breast cancer. And as I say
4 there is some suggestion that the presence of breast
5 cancer in the mother increases the incidence of AML in
6 the offspring.

7 Q. And does that mean taken under that hypothesis,
8 assume for me that that was the case, does that mean
9 he's more individually susceptible to catching benzene-
10 induced AML, any AML, one, the other? What does that
11 mean?

12 A. I have no idea. In other words, I can't define
13 it more than what I've commented on.

14 Q. Is individual susceptibility something that you
15 use as a clinician and as a treater of cancer? Is that
16 something that even factors into your job?

17 A. Usually does not factor into my, into my
18 practice.

19 Q. Last few questions. You discussed a few
20 articles by authors A-u, Au I think is how you pronounce
21 that; Zhang, an author you reference and an investigator
22 whose last name is Lan. And these were papers about, as
23 counsel for Mr. Henricksen said, low dose levels of
24 benzene to individuals and then the investigators were
25 seeing what happened. Do you remember those questions?

1 A. Somewhat.

2 Q. Okay. And without going back through the
3 papers, you used the words not relevant or irrelevant
4 and I just want to make sure the record is clear by what
5 you meant when those papers discussing chromosomal
6 changes in lymphocytes or decreases in peripheral blood,
7 what did you mean that those don't have relevance to
8 this case?

9 A. Just that. That AML is a disease of myeloid
10 cells and aberrations in lymphocyte chromosomes are
11 really not pertinent to this issue. And I've forgotten
12 the second part of your question.

13 Q. The changes in peripheral blood?

14 A. The changes in peripheral blood counts, well,
15 many things can make the white blood cell count drop.
16 And what we're really interested in here is sustained
17 abnormalities in the bone marrow and whether there was
18 any evidence of that in terms of persistent anemias, any
19 evidence of myelodysplasia.

20 Q. When being asked and questioned about a
21 differential diagnosis in the abstract, you were read
22 off a list of a few factors. I can't remember if it was
23 five or seven. I just don't recall how many numbers of
24 factors. Do you recall those questions earlier today?

25 A. I couldn't quote the questions.

1 Q. Do you recall being asked questions about a
2 differential diagnosis and whether or not certain
3 factors were present or absent? Do you remember those
4 questions?

5 A. Yes.

6 Q. What percentage of AML's are reported in the
7 literature to be the result of some environmental
8 stimuli versus being endogenous?

9 A. Very, very small numbers. If you look at what
10 the literature suggests in toto, event-related leukemia
11 is perhaps 15 percent and most of those are people with
12 chemotherapy administration, underlying myelodysplasia,
13 possibly cigarette smoking and the number of leukemias
14 thought to be caused by, let's say, an environmental
15 cause which could include benzene would be very, very
16 small.

17 Q. And, so, if one were to do a differential
18 diagnosis as a hematologist, a clinician, an oncologist,
19 how do you exclude the 85 or so percent of cases that
20 don't have an environmental stimulus?

21 A. Well, they can't be excluded. In other words,
22 in anybody who has AML, an endogenous cause is always a
23 potential possibility.

24 Q. Now, I think the first exhibit to your
25 deposition is from Harrison's, The Principles of

1 Internal Medicine. Do you recall this?

2 MR. SCHMIDT: Brett, the first exhibit was
3 the deposition subpoena.

4 Q. (BY MR. YOUNG) Doctor, would you please find
5 the exhibit, the Harrison's one? And this is the last
6 question. And turn to that very same section where it
7 says chemicals. You see that section, sir?

8 A. Yes.

9 Q. One section was read to you. I'd like to read
10 the other and let you comment on it. Although benzene
11 is no longer generally available as a household solvent,
12 exposure to its metabolites occurs in the normal diet
13 and in the use of lead-free gasoline. Do you see that
14 there, sir?

15 A. Yes.

16 Q. Now, are you aware of any studies that the
17 ingestion of benzene metabolites in the normal diet puts
18 you at increase risks of developing AML?

19 A. No.

20 MR. YOUNG: No further questions.

21 (The time is 3:58 p.m.)

22 EXAMINATION

23 BY MR. SCHMIDT:

24 Q. Dr. Natelson, counsel reminded me about the
25 documents. We've talked about the big stack and the

1 short stack I'm going to get a copy of. What else have
2 you brought here today? What's in the Redwell?

3 A. Well, these are all the medical records that I
4 have. In other words, what I've got here is -- I'll
5 just go through this --

6 Q. You don't need to. You reference those in your
7 report, don't you?

8 A. I've got depositions. I've got expert reports
9 and I've got -- besides the expert reports and
10 depositions I've got disks of all the medical records
11 and then some that I've printed out here. And I've got
12 some e-mails in here between Mr. Young or Mr. Dillard
13 and myself.

14 Q. Could I see the e-mails?

15 A. Yeah. I think that's it for the e-mails.
16 These are the disks. All the records are on the disks.

17 Q. Dr. Natelson, how many people are diagnosed
18 with cancer every year?

19 A. Cancer?

20 Q. In America?

21 A. I don't know that number. I'm better at acute
22 leukemia. I can give you that number, but total cancer
23 I don't know.

24 Q. Hundreds of thousands?

25 A. Probably so.

1 Q. If we assume 300 plus million people in the
2 country?

3 A. Yes.

4 Q. And most of those people get chemotherapy?

5 A. I would say probably not. Many people with
6 cancer are never seen by a doctor. I wouldn't -- I
7 don't know the number, but I would be willing to bet
8 that it's not most get chemotherapy.

9 Q. Do you have any idea what the number of
10 patients who receive chemotherapy every year is in
11 America?

12 A. No.

13 Q. Now, Mr. Young asked you or you said that Mr.
14 Henricksen had no cytogenetic abnormalities. But indeed
15 didn't we establish early this morning that he has AML,
16 had AML and the only way you can have AML is if you have
17 sufficient genetic damage to cause the disease?

18 A. You have genetic damage, but we had no
19 demonstration of it.

20 Q. Right. But that genetic damage is a
21 cytogenetic abnormality?

22 A. It is, but what I made reference to is that
23 what the literature tells us which is that easily
24 demonstrable cytogenetic abnormalities by standard
25 studies are evident in 85 to 90 percent. He didn't have

1 them.

2 Q. Right. That's like the 5, 7 location?

3 A. Or anything. It could be a trisomy 8. It
4 could be 8 to 21 translocations, so on.

5 MR. SCHMIDT: That's it. Thank you.

6 MR. YOUNG: Jackson, one second, please.

7 (The time is 4:01 p.m.)

8 EXAMINATION

9 BY MR. YOUNG:

10 Q. Again, just definitionally, that was my fault.
11 I asked too general a question. What if I rephrase the
12 question to say instead of cytogenetic abnormalities, if
13 I said clonal chromosomal abnormality. If I said a
14 chromosomal abnormality, does that change what we're
15 talking about in terms of the presence or absence of
16 evidence in Mr. Henricksen's case?

17 A. We're talking about a demonstrable chromosomal
18 abnormality by routine cytogenetics.

19 Q. So, if someone asks you a question at trial and
20 says, well, Dr. Natelson, he has AML, therefore, he has
21 to have chromosomal damage, right, that's not what
22 you're talking about?

23 A. That's not the issue here.

24 Q. All right. What is the best available evidence
25 as to the latency for a secondary AML whether caused by

1 chemotherapy or by benzene?

2 A. The best available evidence I think has to do
3 with the vast number of patients who develop secondary
4 AML following chemotherapy.

5 Q. And what does that data suggest?

6 A. That data suggests that the risk of AML is
7 related to a cumulative dose of the drug used and that
8 it typically occurs within a 2 to 10 or 11-year window.

9 MR. YOUNG: Thank you, sir.

1 CHANGES AND SIGNATURE

2 WITNESS: ETHAN A. NATELSON, M.D. DATE: APRIL 11, 2008

3 PAGE LINE CHANGE REASON

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1 I, ETHAN A. NATELSON, M.D., have read the
2 foregoing deposition and hereby affix my signature that
3 same is true and correct, except as noted above.
4

5 _____
6 ETHAN A. NATELSON, M.D.
7
8

9 THE STATE OF _____)

10 COUNTY OF _____)
11

12 Before me, _____, on
13 this day personally appeared ETHAN A. NATELSON, M.D.,
14 known to me (or proved to me under oath or through
15 _____) (description of identity
16 card or other document)) to be the person whose name is
17 subscribed to the foregoing instrument and acknowledged
18 to me that they executed the same for the purposes and
19 consideration therein expressed.

20 Given under my hand and seal of office this
21 _____ day of _____, _____.
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25 _____
NOTARY PUBLIC IN AND FOR
THE STATE OF _____

1 STATE OF TEXAS

2
3 I, Jeanne C. Pearl, Certified Shorthand
4 Reporter in and for the State of Texas, certify that the
5 caption to this deposition correctly states the facts
6 set forth herein; that the examination of the witness
7 named in said caption was correctly reported in
8 shorthand by me at the time and place and under the
9 agreement set forth in said caption and has been
10 transcribed from shorthand into typewriting under my
11 direction and supervision in the foregoing transcript;
12 and that said transcript contains a correct record of
13 the proceedings had at said time and place.

14 I further certify that I am neither attorney
15 or counsel for, nor related to or employed by the
16 parties hereto or financially interested in said action.

17 Given under my hand and seal of office on the
18 15th day of April, 2008.

19
20
21
22 Jeanne C. Pearl, CSR No. 456
Expiration Date: 12/31/08
Firm Registration No. 210
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