CAUSE NO. A-167,693

JAMES COWEY AND RUTH COWEY — IN THE DISTRICT COURT

PLAINTIFFS,

VS. — JEFFERSON COUNTY, TEXAS

COMPANY, ET AL

DEFENDANTS.

58TH JUDICIAL DISTRICT

ORAL AND VIDEOTAPED DEPOSITION OF
RICHARD D. IRONS, Ph.D.
NOVEMBER 21, 2003

ORAL AND VIDEOTAPED DEPOSITION OF RICHARD D. IRONS, Ph.D., produced as a witness at the instance of the DEFENDANTS, and duly sworn, was taken in the above-styled and numbered cause on the 21st of November, 2003, from 9:40 a.m. to 1:19 p.m., before Kathy Miller, CSR in and for the State of Texas, reported by machine shorthand, at the law offices of Fulbright & Jaworski, 1301 McKinney, Suite 4400, Houston, Texas, pursuant to the Texas Rules of Civil Procedure and the provisions stated on the record or attached hereto.

APPEARANCES

FOR THE PLAINTIFFS: MR. LANCE LUBEL
MR. ROBERT BLACK HEARD , ROBINS, CLOUD, LUBEL & GREENWOOD
910 TRAVIS STREET, SUITE 2020 HOUSTON, TEXAS 77002

FOR THE DEFENDANTS UNITED STATES STEEL CORPORATION, ARISTECH CHEMICAL CORPORATION AND USX CORPORATION:
MR. STEPHEN C. DILLARD
FULBRIGHT & JAWORSKI, LLP
1301 MCKINNEY, SUITE 5100
HOUSTON, TEXAS 77010

FOR THE DEFENDANT RADIATOR SPECIALTY COMPANY:
MR. JAMES M. RILEY
COATS ROSE
1001 FANNIN, SUITE 800
HOUSTON, TEXAS 77002-6707

ALSO PRESENT:

MR. ROY LANGLEY, VIDEOGRAPHER

INDEX

EXHIBITS

(Exhibit 1 was marked.)

THE VIDEOGRAPHER: This videotaped deposition of Dr. Richard Irons is being taken on November 21, 2003. The time is approximately 9:45 a.m. We're now on the record.

MR. DILLARD: Good morning, Dr. Irons. Would you raise your hand and be sworn by our court reporter?

RICHARD D. IRONS, Ph.D.,

having been first duly sworn, testified as follows:

EXAMINATION

BY MR. DILLARD:

Q. Tell us your name, please, sir.

A. Richard D. Irons.

Q. Where do you live, sir?

A. In Boulder, Colorado.

Q. And what is your occupation or profession?

A. I am a toxicologist and a pathologist.

Q. How are -- I was going to ask you how you're employed. Where are you employed?

A. I am employed at the University of Colorado Health Science Center in Denver, and at Fudan University in Shanghai, China.

Q. And how long have you been employed by the University of Colorado Health Science Center in Denver?

A. Since 1989. So, approximately 14, 15 years.

Q. You also mentioned another university in Shanghai, China, and I am not sure I can pronounce the name. Would you say it again?

A. Fudan.

Q. Fudang?

A. "Don."

Q. Fudan. How long have you been employed by Fudan Medical Center in Shanghai, China?

A. I have been a member of the faculty there for approximately three years.

Q. You mentioned that you are a toxicologist?

A. Yes, sir.

Q. What is toxicology?

A. Toxicology is the science of poisons, or the adverse effects of drugs and chemicals.

Q. You mentioned that you are a pathologist?

A. Yes.

Q. What is pathology?

A. Pathology is the study of the development of diseases and the laboratory diagnosis of diseases.

Q. What do you do at the University of Colorado HealthScience Center?

A. I am Professor of Toxicology in the School of Pharmacy. I am Professor of Pathology in the School of

Medicine. I am Director of the Cancer Causation Prevention Program in the Comprehensive Cancer Center at the University of Colorado.

Q. I want to get back to that more in just a moment, but first I'd like to ask you about your educational background. If you would tell the jury first of all where you attended school after -- after high school.

A. Raymond College, University of the Pacific. did my undergraduate studies in chemistry, political science, and liberal arts.

Q. And then what additional formal education did you receive?

A. I took graduate training and a masters in medical technology at University of California San Francisco. I then went to the University of Rochester School of Medicine, and obtained a Ph.D. in toxicology. Following that, I did three years of fellowship in pathology at Strong Memorial Hospital, training in general pathology and clinical pathology.

Q. Let's talk about -- and excuse me, what year did you receive your -- your Ph.D. and your doctorate in toxicology?

A. 1974, I believe.

Q. And then you said you completed three years of

additional training --

A. That's correct.

Q. -- in pathology?

A. Yes.

Q. Let's talk about your professional experience after you completed your formal education and the additional three years of training. If you would start in 1976 or '77, and just bring us up to the present time, discussing it briefly, please.

A. From 1977 until 1988, I was a scientist and senior scientist at the Chemical Industry Institute of Toxicology in Research Triangle Park, and a member of the faculty of Duke University.

Q. What did you teach at Duke University?

A. Toxicology and some pathology.

Q. How long did that tenure last?

A. Until I went to the University of Colorado in 1988, '89.

Q. Where you have been ever since?

A. Yes.

Q. Are you certified or licensed as a specialist in your field?

A. Yes. I am board certified by the American Board of Toxicology. I'm certified as a clinical laboratory scientist in the State of California, and as

a laboratory director in China.

Q. How does one become board certified in toxicology?

A. You have training. You have to have training that is -- that qualifies you for sitting for the board exams. You apply to take the exam, and if admitted then you take an examination over a two-day period. It's then renewed every five years by exam.

Q. How long have you been board certified in the field of toxicology?

A. I believe since 1980, although I'm not positive. First -- yes, first examination was in 1980.

Q. And then you take a recertification every five years?

A. Yes.

Q. Tell the Ladies and Gentlemen of the Jury some of the professional organizations and societies of which you are a member.

A. I'm a member of the Society of Toxicology. I'm a member of the Association of Investigative Pathology, Association -- American Society of Hematology, the International Society of Experimental Hematology, among others.

Q. At least one or two of those organizations contain the name -- or the word "hematology" in it.

What is hematology?

A. Hematology is the branch of science and medicine that deals with diseases of the blood and bone marrow.

Q. You're not a medical doctor?

A. No.

Q. Let's talk about your teaching experience. Can you describe for the Ladies and Gentlemen of the Jury, give us an overview of your teaching experience?

A. Depending upon the positions that I've held, I've taught numerous subjects. Currently I teach immunology. I lecture in toxicology, and I lecture in hematopathology, which is the branch of pathology that is specifically -- that specifically deals with the diagnosis of diseases of the blood.

Q. And bone marrow?

A. Bone marrow, yes, that's correct.

Q. And what are your primary areas of professional interests and research?

A. My principal areas of research are on the pathogenesis, studying the -- the development and cause of diseases of the blood and immune systems, and in the differential diagnosis of those diseases. So, looking at the effects of drugs and chemicals on the development of those diseases as well as in the diagnosis of those

diseases.

Q. Let's talk a moment about your professional writing and editorial experience. Can you tell the Ladies and Gentlemen of the Jury some of the professional journals on whose boards you've served, whose editorial boards you've served?

A. Quite a few: Certainly the Journal of Toxicological Sciences, Toxicology and Applied Pharmacology, Journal of Experimental Pathology, several others.

Q. Have you published articles in -- in one or more of these journals and in other professional scientific journals?

A. Yes.

Q. Approximately how many articles, books, and book chapters have you published in professional publications, including professional journals?

A. I think on the order of 100 -- probably 140 peer-reviewed papers and journals, and probably between ten and 20 book chapters or books.

Q. You said peer reviewed. What does that mean?

A. The basic process that scientists use for publication of original research is to publish in journals that basically review manuscripts that are submitted to them by having them reviewed by independent

scientists; and if they satisfy that review process, a review of peers, then they're published.

So, peer review means research and the product of research papers that are reviewed by independent scientists and then accepted for publication.

Q. Have you served as a peer reviewer on -- for articles that obviously where you -- where you were not the author?

A. Yes, many times.

Q. And what is the process there for peer review?

A. Well, the process is that if you submit an article for publication at any of the major scientific or medical journals, then those papers are then forwarded to independent scientists who review them for meeting criteria with respect to rigor, appropriate scientific methodology, appropriate interpretation of results and conclusions, and may make some suggestions on how to improve them; and through the journal and the editorial office of the journal, you have an opportunity to respond to those, and the ultimate product is, in fact, a paper that's been accepted for submission through this process of peer review.

Q. Have any of the professional articles, books, or book chapters that you have authored dealt with subjects including benzene, benzene toxicology, the bone

marrow,bone marrow toxicology, the causation of diseases of the blood, and blood forming organs?

A. Yes.

Q. Approximately how many?

A. Certainly 80, probably between 80 and 90.

Q. And over what period of time?

A. Basically since 1977, so the last 30, 35 years.

Q. I am going to show you what's been marked as Exhibit 1, and ask you if that is a correct copy of your current resume?

A. Yes. I think so.

Q. And does that list these various articles, books,and book chapters that you have authored?

A. Yes.

Q. As well as your work experience, your educational experience, the training you've received, the teaching experience that you've described for us?

A. Yes.

Q. Okay. Thank you.

Dr. Irons, today is November 21, 2003, and we're here taking your deposition. When this testimony, this videotaped testimony, is presented to the jury in this case in December of this year, where will you be at that time, sir?

A. I will be in Shanghai, China.

Q. For what purpose?

A. I am the director of a joint clinical and molecular laboratory in Shanghai that currently has responsibility for diagnosing diseases of the blood and immune system for 23 hospitals in Shanghai; and during the month of December I am on call, so I have to be there.

Q. What is your specific involvement with that project?

A. The laboratory currently supports a series of studies referred to as the Shanghai Health Project that I am principal investigator for, and that is a project that is involved in characterizing the cause and pathogenesis of all hematopoietic and lymphoid diseases that present in Shanghai hospitals over the course of a five-year period; and also is looking directly at the effects of occupational exposure to benzene in the development of diseases of the blood and bone marrow.

Q. What is a hematopoietic or lymphoid disease? What is meant by that?

A. Lymphoid diseases are diseases of the immune system and lymphocytes. The major disease entity that we usually are involved in looking at is lymphoma.

Q. And what is a hematopoietic disease?

A. Hematopoietic is a disease of the blood, blood forming organs. So hemo means blood, and so hematopoietic really is a technical term for diseases of the blood and blood forming organs.

Q. Are you familiar with the category of diseases known as myelodysplastic syndromes?

A. Yes, I am.

Q. Would those qualify as diseases of the blood or blood forming organs?

A. Most certainly.

Q. Who are the major participants in the study that's being conducted in China?

A. The prin -- the study's being conducted through a collaboration between the University of Colorado Health Sciences Center, Fudan University in Shanghai, the Shanghai branch of the Chinese C.D.C., and the Institute of Public Health Supervision, which is the Shanghai -- a -- the Chinese equivalent of OSHA, Occupational Safety and Health Administration.

Q. Many of us may not be familiar with -- with Shanghai, the city where this work is being conducted. Is that a rather large city?

A. Shanghai is a city of 17 million people.

Q. How would that compare to, say, New York City that some of us would at least be familiar with?

A. New York, if you take the greater -- the greater New York metropolitan area, it's probably a little larger; but New York itself is smaller. So, Shanghai is a very, very large city.

Q. How long has this study been underway?

A. It's been three years in development. We've been actively supporting diagnosis in Shanghai since July. We have approximately another four years to go on the study itself. The laboratory which is supporting the study and diagnosis is also intended to continue in perpetuity as a clinical laboratory after the study is complete.

Q. When you say you have been supporting the diagnosis, what -- what do you mean by that?

A. Part of the agreement and collaboration that we're involved in is that during the time of the study, during the period of time where the actual clinical research is being conducted, the laboratory will also be the principal laboratory supporting the diagnosis of blood and lymphoid diseases for the 23 participating hospitals in Shanghai.

Q. And are you involved in that process of diagnosing?

A. Yes, I'm the director of the laboratory.

Q. Who do you report to? Who is overseeing the

study?

A. The -- the study oversight is performed by two international committees. One is an external scientific review panel that's made up of physicians and scientists from around the world who have specific specialization in areas that are covered under the study; and so from a scientific standpoint I report to them in terms of conduct, procedures and operations. There's also an international ethics panel, review panel, that I'm responsible to in terms of meeting the clinical criteria and clinical ethical standards that are defined both by U.S. and Chinese law.

Q. Who is sponsoring this study?

A. The study is sponsored through international consortium that is comprised of the five major petroleum companies worldwide.

Q. And how is independence from the -- of the study from the sponsors maintained?

MR. LUBEL: Objection, form.

A. Well, as I said, the actual reporting line of chain of command, if you will, is that I report to these independent panels with respect to the operation of the study. All clinical trials, on an international basis in general, but specifically in the United States, whether they're performed by government agencies as

sponsors, or pharmaceutical companies, or anyone else, are governed under a set of laws and rules that are established by the U.S. National Institutes of Health and the Food and Drug Administration through an office that's called the Office of Human Research Protection. So, all clinical trials have to meet standards of independence and regulations that are set forth in those guidelines, and we meet those standards.

MR. LUBEL: Objection, nonresponsive.

Q. (BY MR. DILLARD) Dr. Irons, have we asked you to address certain subjects in this case of Mr. James Cowey?

A. Yes.

Q. What specific subject areas have we asked you to address in this case?

A. You've asked me to address the toxicology of benzene, and what's known about the effects of benzene on biological systems and the development of disease; specifically, diseases of the blood forming organs. You've asked me to enunciate and to describe the criteria that scientists use in determining causal inference or the cause of disease associated with different etiologies or exposure to individual agents. You've asked me to evaluate the expert report of Dr. Levy submitted in this case, and you've asked me to

render an opinion with respect to the likelihood that Mr. Cowey's disease could have been caused or contributed by his exposure to benzene.

Q. Okay, sir. I want to go into each of those separately in a moment, but first I want to ask you what in general you have reviewed in connection with your work in this case?

A. I reviewed the materials that were given to me associated with this case, the medical records of Mr. Cowey, the depositions of Mr. and Mrs. Cowey, the expert report of Dr. Levy. I've reviewed the scientific and medical literature concerning the criteria for determining causal inference or causation, the literature concerning the development and pathogenesis of the blood diseases that are at issue in this case. And I've reviewed a report by Mr. Spencer.

Q. Okay, sir. Going back to the subjects that you mentioned that you were asked to address, let's take the first one. What was that again?

A. The toxicology of benzene, what's known about the effects of benzene and the diseases that it causes.

Q. And what specifically have you done in that regard, insofar as Mr. Cowey's case?

A. I reviewed that literature which I am familiar with, in the context of what we know about the effects

of benzene on the blood and blood forming organs, and specifically on the development of acute myelogenous leukemia and myelodysplastic syndrome.

Q. Is it your understanding that Mr. Cowey has a form of myelodysplastic syndrome?

A. Yes.

Q. What -- what form of myelodysplastic syndrome do you understand that he has?

A. The specific subtype of MDS that Mr. Cowey has been diagnosed with is called refractory cytopenia with multilineage dysplasia, or RCMD.

Q. RCMD?

A. Yes.

Q. I want to talk more about RCMD in a moment. The second subject area that we had asked you to address again, sir, was what?

A. The criteria that scientists use in establishing a causal relationship, or determining that a causal relationship, in fact, exists between a given etiology or cause and a disease. In this particular case, the issues pertaining to specifically the exposure to benzene and the development of hematopoietic diseases.

Q. And when you say the -- the scientific criteria that is used, what -- what do you mean by that?

A. There are several different paradigms or patterns that have been described and adopted in the past for use in formalizing criteria that scientists use in determining causation. Science plays by rules and it's necessary to apply a standard set of rules to determining what is an appropriate level of evidence to support a causal relationship between an agent or a potential etiology and a specific disease. Several different criteria have been set forth over the last several decades. All of them basically meet the same standards of criteria that are referred to variously as Bradford Hill criteria, Henle-Koch Postulates, and more recently Evidence Based Medicine. But they all incorporate the same basic standards and criteria.

Q. Would you say that their -- these are rules, did you say, that scientists go by?

A. Basically, yes.

Q. Why -- why is that important, to go by these rules?

A. Because in the absence of setting up criteria that can be generally agreed upon in the scientific and medical communities, we have no basis for developing standards to evaluate causation or to look at the effects of exposure to agents on the development of disease.

These criteria apply not only to causation of disease, but also to evaluating treatment and the use of drugs or other therapies in treating disease. So, the same basic criteria are used in both situations to ascertain the effects of exposure to drugs or chemicals or other agents and the development of disease.

Q. If someone gets a disease and in their past they may have had an exposure to something that is associated with causing that disease, can you conclude that that exposure necessarily caused that person's disease?

A. No.

Q. Why not? Why isn't it that simple?

A. Well, because, first of all, as a toxicologist, I have to consider the fact that there's no such thing as no exposure. There's no such thing as zero. We've all been exposed to an innumerable number of agents in our lifetime at some level or another. We've all been exposed to agents that have the potential to cause different diseases, and the issue or the question of whether or not a specific agent caused a specific disease requires more than simply knowing that under certain circumstances that agent may be associated with development of disease.

Q. Well, how does science go about unraveling it

and getting to the bottom of it in an individual case?

A. One has to look at the criteria in the peer-reviewed literature that relates to the quantitative association of exposure to a given agent.

Q. What's -- now what's that mean now?

A. With respect to the amount of exposure, or the dose that an individual has received, what is that dose? And, with respect to the diseases that have been associated with that agent, what are the specific diseases that have been shown to be significantly increased in terms of incidents, as a result of or associated with specific exposures to that agent? So, quantitative epidemiology, human studies, that characterize the disease processes that are associated with exposure to specific amounts of a given substance.

Q. Is this something in the published literature?

A. By definition, peer-reviewed quantitative epidemiology.

Q. Is published?

A. Yes.

Q. Now, you referred to these scientific principals earlier, Bradford Hill, and one other, and I don't recall the name of it, but where are these set forth, and how did they become the rules of what the scientists go by in determining whether a particular

exposure may have caused a disease?

A. They have been published variously in the published literature. They have been the subject of many conferences and proceedings, and many different bodies and organizations have adopted them in one form or another. They've been described in numerous publications in the past 40 years or so, 40 or 50 years.

Q. Did you note in reviewing Dr. Levy's report that he himself refers to these rules?

A. Yes.

Q. And Dr. Levy, of course, for the benefit of the -- of the jury, is the expert retained by the plaintiff in this case?

A. That's my understanding.

Q. Focusing on the rules that you scientists go by in determining whether a particular substance may have caused a particular disease, can you -- can you walk us through them? And I may have some questions as we go through them, but can you walk us through them and explain what these rules are that you follow in as simple terms as you can for my benefit? Can you do that?

A. Certainly. The first criteria that is an absolute requirement in determining causal relationship is the availability of peer-review quantitative

epidemiologic data, epidemiologic studies in humans that provides strength of evidence, quantitative statistical association between exposure and disease. That's the first one.

A second criteria that is related to that is if you have multiple studies that meet those criteria, that there is consistency, or a general consistency, among those studies. So that if you have more than one study, do you see a consistent pattern or a predominant pattern? Because each of these studies, especially studies involving humans, vary with respect to their design, populations they look at, precise exposure conditions. So, under what conditions of exposure, and what occupations, under what particular circumstances do you see this pattern, and is it consistent?

The third deals with specificity, and specificity is very important in how -- the conclusions you reach based upon the data we've just discussed. Specificity with respect to exposure. Do the studies look at exposure to the specific agent that is in question, or at issue, or do they look at exposure to a variety of different agents, or can you tell whether or not they are looking at a given exposure?

Also, specificity of disease. What are the criteria that were used in measuring outcome in these

epidemiological studies and are they looking at the specific diseases that are in question? Do they look at a variety of different diseases? Are the criteria for diagnosis the same or comparable? And it's not appropriate, for example, to mix or match, to look at exposure to one compound or chemical and assume that it applies to all others; and it's also not appropriate to look at a specific disease and then extrapolate to other diseases that are not the same as the disease you're looking at. So, specificity is a very important criteria.

Another criteria that is important is the issue of a temporal relationship, or the time frame that surrounds the development of disease and exposure, and this is important for determining whether the duration of exposure is appropriate based upon our knowledge of the pathogenesis of the disease, and whether or not the exposure, for instance, preceded the development of disease in some cases. So latency and temporal relationships can be an important issue.

Another very important issue is the issue of dose response.

Q. What is meant by dose response?

A. A cardinal tenet of toxicology is that the response to exposure to a given drug or chemical is

going to be proportionate to the dose that the individual received, that if you increase the dose, you increase the response; you decrease the dose you decrease the response. This applies to populations. It also applies to individuals. The dose response is a cardinal tenet of toxicology and medicine, and epidemiologic studies which are really looking at associations in large groups of individuals have a primary requirement to -- to -- to characterize and establish dose response in order to provide credibility with respect to the relationships that they purport to describe.

Q. I want to ask you some more about dose response. What -- what does a scientist have to know before you can say that an exposure caused a particular disease?

A. Well, as I said, you have to understand what the dose has been to which an individual has been exposed, and whether that dose has been -- that dose has been shown in quantitative studies to be associated with the development of that disease. If the dose that an individual receives is less than a dose range or range of doses that's been shown to be associated with the development of that disease, then you cannot opine that, in fact, that substance caused that specific person's

disease. So, dose response is a very important concept in pharmacology, in drug development, and toxicology. And it has --

MR. LUBEL: Objection, nonresponsive.

Q. (BY MR. DILLARD) Can you give us some everyday examples of dose response, what is meant by dose response, so that we can relate it to -- to our facts?

A. As I said before, to a toxicologist there's no such thing as zero. There's also no such thing as nontoxic. Every substance is potentially toxic under the -- under certain conditions and at certain doses. Water can be lethal. Water can be toxic. If you ingest too much water, too rapidly, it can kill you. It's not easy to do, but it can be done.

Everything follows a dose response, either both in terms of beneficial effects for drugs, as well as adverse effects which can also be associated with drugs and chemicals.

A good example is aspirin, which everyone is familiar with and most people are -- recognize that aspirin can be used to -- as an analgesic, as an agent to reduce pain associated with headache or minor aches and pains. And usually the recommended dose of aspirin, in these -- and under these conditions would be two

typical tablets over a four to six-hour period.

Many people may not be aware that lower doses of aspirin, a half or a third of that, taken every day or every other day, are actually associated with a decreased risk of cardiovascular disease, because aspirin also has an effect on blood clotting, and it minimizes clotting at lower doses. But there are statistical studies, quantitative epidemiology studies, that show that at lower doses than what are normally used to treat headache, can have a very significant impact on the development of cardiovascular disease. It's protective.

Some people who have chronic inflammatory conditions such as arthritis, they may be prescribed larger doses of aspirin than the typical amount we would take for headache. They may be asked to take upwards of maybe five or eight -- equivalent of five or eight aspirins, which would also -- which would have an -- reduce pain but also reduce inflammation. At the same time that people take those doses of aspirin, they may also experience some side effects such as gastrointestinal upset or irritation. That would be an adverse effect that's related to dose.

As they increase taking aspirin, if one were to take say upwards of 12 or 20 aspirin tablets, you

might have some of the same beneficial effects that we've just talked about in terms of analgesia, decreased inflammation, but you're going to begin to have very serious gastrointestinal upset. You're likely to have ringing in the ears, or tinnitus. You may begin to have symptoms associated with dizziness or not feeling right, and as you continue to take more aspirin those symptoms will become much more prominent. Between 20 and 50 aspirin, you're going to become delirious. You're going to have problems relating to your environment. You may lose consciousness, go into coma. And between 50 and 100 aspirin, you may proceed into metabolic and respiratory acidosis. You will go from coma to basically a near death situation and, in fact, you can die from that. It's a very difficult condition to manage from the standpoint of clinical toxicology.

So, there's an example of dose response going from low to high that includes the positive effects of a drug, aspirin, as well as the negative or adverse effects.

MR. LUBEL: Objection, nonresponsive.

Q. (BY MR. DILLARD) If you don't know the dose of a particular exposure, can you say that that exposure caused a particular person's disease?

MR. LUBEL: Objection, form.

A. No.
Q. (BY MR. DILLARD) Why not?
A. As I said before, dose is a very important marker or benchmark with respect to comparing the probability the disease can occur as a function of exposure. If you have no idea what the dose is, you cannot opine that an agent caused the disease.
MR. DILLARD: Mr. Lubel has requested a brief recess.
MR. LUBEL: Thank you.
THE VIDEOGRAPHER: Going off the record. Time is approximately 10:27 a.m.
(A break was taken.)
THE VIDEOGRAPHER: We're now back on the record. Time is approximately 10:31 a.m.
Q. (BY MR. DILLARD) Dr. Irons, the third area that you have told us you had been asked to review in this case had to do with the plaintiffs' expert, Dr. Levy. Have you reviewed his report?
A. Yes, I have.
Q. And I'd like for you to tell us whether or not Dr. Levy followed proper scientific methods as you've described them in reaching his opinions that are expressed in that report?
MR. LUBEL: Objection, form, speculation.

Q. (BY MR. DILLARD) Do you have an opinion as to whether or not he followed proper scientific methods in reaching the opinions that he expresses in his report?

A. Yes, I do.

Q. And what is that opinion?

A. That the methodology that he used in reaching his opinions does not conform to the criteria that I have described, that are variously referred to as Bradford Hill criteria, Evidence Based Medicine, or other paradigms that meet comparable standards.

Q. Why do you say that?

A. He does not rely primarily on peer-reviewed quantitative literature to support his opinions. He includes secondary literature, nonquantitative literature, opinions, editorials, in addition to the quantitative epidemiologic literature.

He also does not perform any type of analysis of dose in arriving at a conclusion -- the conclusions he does with respect to the causation of Mr. Cowey's disease.

Q. Referring back to these scientific rules that scientists follow, the first one you listed a moment ago was peer-reviewed quantitative epidemiologic data --

A. Yes.

Q. -- which finds a statistical association

between an exposure and a disease?

A. That's correct.

Q. What deficiencies does Dr. Levy's opinions -- what deficiencies do Dr. Levy's opinions have in that specific -- in that particular regard?

A. The principal publications that he refers to in reaching his conclusion with respect to Mr. Cowey's disease include papers that did not measure benzene, look specifically at benzene; but instead looked at a variety of different mixed solvent exposures and did not quantitate benzene exposure.

At the same time, these same references did not meet criteria specificity with respect to relating exposures to specific disease, in this particular case the general category called myelodysplastic syndrome. In some cases, there's no basis to conclude that myelodysplastic syndrome was in fact the specific disease in question.

In one particular case, there was no statistically significant increase in myeodysplastic syndrome seen in the paper.

In this particular case, the -- the criticisms that I'm raising don't speak to the general issue of causation, but do speak to the methodology that was used in -- that he used in arriving at his conclusions.

Q. Do you have his report there handy?

A. Yes, I do.

Q. What is your understanding of the allegation that's being made in this case as far as Mr. Cowey is concerned?

A. My understanding is that the allegation is that Mr. Cowey's disease, refractory cytopenia with multilineage dysplasia, a form of myelodysplastic syndrome, was caused as a result of his exposure to benzene over the years, and a product called Liquid Wrench.

Q. Do any of the studies that are cited by what -- well, before I get to that, what is your understanding as far as the allegation that's being made as to the way Mr. Cowey was exposed to benzene from this product called Liquid Wrench.

A. Well, the allegations are that through his use of Liquid Wrench under the conditions in which he employed it, that the -- contamination of the product by benzene provided him with an opportunity for exposure through inhalation from his use of the product, and that that exposure over time lead to the development of his disease.

Q. Is it your understanding that there is some claim also being made that he was exposed to the product

on his skin?

A. Yes.

Q. Do any of the studies that are cited by Dr. Levy apply to that type of an exposure allegation; that is to say, someone on a recreational basis using a product like Liquid Wrench as Mr. Cowey describes using it?

MR. LUBEL: Objection, form.

A. No.

Q. (BY MR. DILLARD) What do the studies cited by Dr. Levy pertain to?

A. They pertain to exposure to solvents and mixed solvents in an occupational setting, in different occupational settings, involving the use of chemicals in refinery situations, in situations associated with making of shoes, in situations associated with exposure to pure benzene in an occupational setting, exposure to mixed solvents in a variety of different occupational settings.

Q. Some involve pure benzene?

A. Yes.

Q. You mention the making of shoes. Which particular study is that, that he -- that he, Levy, refers to?

A. The Aksoy -- the publications by Aksoy that

deal with Turkish shoe workers involve exposure to virtually neat or pure benzene used as a solvent in the preparation of resins for making shoes.

Q. Are you familiar with those studies?

A. Yes.

Q. What type of a work environment were the Turkish --

A. Turkish shoe workers.

Q. -- shoe workers working in where they were using this pure benzene?

A. It was primarily in home environments and sweat-shop environments with -- in confined spaces, either by families, or by groups of individuals, usually groups of families, using benzene-based resins as a glue for the manufacturing of shoes in poorly ventilated and restricted areas.

Q. Do you recall what the general working conditions were in terms of how many hours a day, and that sort of thing?

A. The descriptions by Aksoy describe conditions where people basically lived in those environments, where they basically made these -- they made shoes, and worked and were exposed to solvents in the agents they were using virtually round the clock. They did this in the home. So when they were working, when they weren't

working, they basically were living in and around the materials that they were using.

Q. He cites -- he, Levy, cites a paper by Yin. Are you familiar with that work?

A. Yes, I am.

Q. And what did that involve?

A. Yin did a virtual cross-sectional study of exposure of workers in China to a variety -- in a variety of settings, thousands of facilities and hundreds of thousands of workers where benzene was not directly measured but, in fact, the assessment of exposure was made indirectly.

This involved, again, shoe workers. It involved industrial workers, factory workers, petroleum refinery workers, rubber workers, painters, a variety of different occupational settings, usually involving quite large facilities.

Q. Do you believe that that -- that Mr. Cowey's alleged exposure scenario is comparable to the Aksoy or the Yin studies?

MR. LUBEL: Objection, form.

Q. (BY MR. DILLARD) Do you have an opinion in that regard?

A. My opinion is that the description of Mr. Cowey's use of solvents in the course of his

activities is not reflected or related to the types of occupational exposure that has been the subject of these studies.

Q. You also mentioned that some of the studies that Dr. Levy cites, or other studies that Dr. Levy cites, involve petrochemical plants?

A. Yes.

Q. Refineries?

A. Yes.

Q. Do you have an opinion as to whether or not those studies would be applicable to the type of usage that Mr. Cowey -- would the exposures in those studies be comparable to Mr. Cowey's alleged use of the Liquid Wrench product?

MR. LUBEL: Objection, form.

Q. (BY MR. DILLARD) Do you have an opinion in that regard?

A. It's my opinion that those exposures are not relevant to that of Mr. Cowey's.

Q. Looking back at the -- at the scientific rules that you described for us earlier, another of the rules you mentioned was specificity. With respect to Mr. Cowey's alleged exposures to the Liquid Wrench product, do the studies cited by Dr. Levy, in your opinion, meet, or do they not meet the specificity

requirements?

A. They do not meet the specificity requirements.

Q. Why not?

A. They've looked at mixed solvent exposures, a variety of different exposures, and do not quantitate benzene exposure either in the context of mixed exposure or potentially heavy exposure to pure benzene. So, from the standpoint of providing a quantitative basis to relate exposure or dose to the cause of disease, they do not meet those criteria.

Q. You mentioned the consistency requirement of the scientific rules. Do you have an opinion as to whether or not Dr. Levy has satisfied that requirement?

MR. LUBEL: Objection, form.

A. He has not. In fact, as I mentioned, some of the studies that he cites specifically with respect to the question of the relationship between myelodysplastic syndrome and exposure to solvents don't reach a statistical -- don't provide evidence of a statistical association between exposure and the development of the disease.

Q. (BY MR. DILLARD) That's a point I want to ask you about. Do some of the studies that Dr. Levy has cited refer to or involve myelodysplastic syndrome --

A. Yes, they do.

Q. -- the condition that Mr. Cowey has?

A. Yes, they do.

Q. And is there a consistency across those studies that meets the scientific requirements?

A. No. Neither with respect to specificity or consistency for those specific citations.

Q. With regard to the dose response requirement, does Dr. Levy satisfy that requirement, in your opinion?

MR. LUBEL: Objection, form.

A. No, he does not. He does not address the issue of dose.

Q. (BY MR. DILLARD) Okay. Let me ask it -- ask it again. Does he even address the issue of dose response in his opinions?

A. No, sir.

MR. LUBEL: Objection, form.

MR. RILEY: What's your objection basis on that last question?

MR. DILLARD: Yeah.

MR. LUBEL: I'll tell you what primarily my basis has been for a little while, which is Steve's been referring to whether Dr. Levy has addressed certain things, and he's not been specific to his report. And as I appreciate what Dr. Irons is talking about, is what is contained in his report. Steve's question doesn't

focus in on the report. It focuses in on what Dr. Levy has addressed, when it would be speculation for one, because neither Steve nor Dr. Irons have talked to Dr. Levy about what he's done in this case.

MR. DILLARD: Well, that's not a form objection. And I believe --

MR. LUBEL: Well, maybe I am making a poor objection but that's -- you asked for what I was doing.

MR. DILLARD: That's not a form objection.

MR. RILEY: True.

MR. DILLARD: But I appreciate the clarification. We will certainly expect that he'll remain hitched to the report he produced in this case, since we've been required to produce reports, right? Agree with me on that?

MR. LUBEL: Upon what?

MR. DILLARD: On that he has to stay -- the subject matter he's covering is covered in his report, right?

MR. LUBEL: I think by and large his

MR. DILLARD: Okay.

Q. (BY MR. DILLARD) Dr. Irons, let me a

you have an opinion, sir, whether or not -- first of all, you're familiar with the opinions that Dr. Levy expresses in his report; is that correct?

A. Yes.

Q. Okay. And that's his report dated -- what's the date on it?

A. September 18th.

Q. It was produced to us by the plaintiffs, pursuant to the requirements of the court back in September.

In reviewing that report, do you have an opinion whether or not Dr. Levy has ruled out with reasonable certainty other factors that would explain Mr. Cowey's disease?

A. Not at all.

Q. Why not?

A. Because the principal risk factor associated with the development of myelodysplastic syndrome in the vast majority of individuals is age, and that's not even addressed in Dr. Levy's report.

Q. Let's talk for a moment about myelodysplastic syndromes. How does the -- how does the disease get its name, if you know?

A. Myelodysplastic syndrome is a relatively new classification of diseases within the hemopoietic blood

forming system that's evolved over the past 30 years. It is a neoplastic condition. It is a --

Q. What does that mean?

A. It means that it is a cancer.

Q. Okay.

A. It is a type of cancer on a spectrum that includes acute myelogenous leukemias, a specific subclass of leukemias. So, myelodysplastic syndromes and acute myelogenous leukemias represent a spectrum of diseases that involve the altered maturation, growth, and regulation of the cells of the bone marrow that make our blood cells.

Q. Are all acute myelogenous leukemias considered to be myelodysplastic syndrome?

A. No.

Q. Are all myelodysplastic syndromes considered to be acute myelogenous leukemia?

A. No. As a matter of fact, the vast majority are not. There is overlap in these diseases, but the specific diseases within these classifications represent distinct entities as defined by the scientific and medical literature.

Q. Are there different forms of myelodysplastic syndrome?

A. Yes.

Q. Can we refer to it as MDS? Is that an --

A. Yes, MDS is -- is useful.

Q. How are cases of MDS diagnosed?

A. Cases of MDS are diagnosed using criteria and techniques that are the same ones that are used in the diagnosis of acute myelogenous leukemias. The basic criterias in their -- there are three major components to the laboratory diagnosis of these diseases. One is to examine the cells and look at them to see what they look like. It's called morphology.

So you look at the bone marrow, either in smear or section, and evaluate what the cells in the bone marrow look like.

Another is to use a technique that allows us to look at a fingerprint of the molecules on the surface of the cells that help us determine what they are, and that's called immunophenotyping or flow cytometry. So we're looking at fingerprinting on the surface, morphology of the cells, what they look like, and also we look at the DNA in these cells. We look at DNA to see if there are structural changes in the DNA, and this is what we talk about when we talk about chromosome or chromosome abnormalities. Chromosomes are packets of DNA, and if they are rearranged, absent or missing in one form or another, this is also a criteria that's used

in the differential diagnosis of these diseases.

Q. Have you been -- you yourself been involved in diagnosing these diseases?

A. Yes.

Q. As opposed to treating them like a doctor would do?

A. I don't treat these diseases, but I diagnose them and I supervise the laboratory that diagnoses them.

Q. With respect to the type of MDS that Mr. Cowey is reported to have had, RCMD, is that a common or uncommon form?

A. Very common. Probably the most common. It is among the most common forms of MDS.

Q. And what -- what are the main risk factors for MDS?

A. The principal risk factor for 85 percent of the cases of MDS that are diagnosed is age.

Q. What's your understanding of the -- of the age -- the peak age range when this disease is diagnosed?

A. Well, the data is fairly dramatic. Below the age of 50, the incidence of MDS in the general population is on the order of a half of a -- one to -- a half to one or two per 100,000 people. At the age of 50, studies variously report an incidence of five to maybe 12 per 100,000 people. And as you go up in

decade, it increases logarithmically. At the age between 70 and 79, the incidence is on the order of 49 to 50 or even higher per 100,000. So, between the age of 50 and the age of 80, you have a change that's about ten-fold in terms of the incidence of the disease, and above 80 it rises to 20-fold higher.

Q. So it continues to rise with increasing age?

A. Yes.

Q. What was Mr. Cowey's age when he was diagnosed, if you recall?

A. I believe it was 72, 73, in that area.

Q. Would that be in a peak age range for this disease?

A. Yes. Much higher than either the 50s or the 60s, obviously less than the 80s, or the 8th decade, but extremely high. On the order of about 49 per 100,000.

Q. You were explaining this a moment ago, but just very briefly, how does -- how does one tell one form of MDS, say like the kind that Mr. Cowey has, from another form?

A. With respect to Mr. Cowey's disease, the issues that are important are the types of cells that are present by morphology, so the number of blast cells that are present in the bone marrow; as well as data from flow cytometry or immunophenotyping looking at

molecules on the surface of the cells; and also cytogenetics, genetics, looking at chromosomes, and changes in the DNA.

Q. Are you familiar from reviewing Mr. Cowey's medical records as to whether he had any particular chromosome pattern that was found when his was diagnosed?

A. Yes. He had three of the cells that were examined for cellular genetic damage or chromosome aberrations, possessed an extra chromosome 8, which is referred to as trisomy 8. And the fact that it was found in three cells establishes that it is a clonal lesion, and is most likely associated with the development of his disease.

Q. Do you have an opinion as to whether Mr. Cowey's chromosome pattern, this trisomy 8, would fit into the pattern seen in the 85 percent of MDS cases where the cause is not known as opposed to the 15 percent of cases where it is?

A. The pattern of presentation of his disease, including trisomy 8, is a pattern that's most frequently found in the 85 percent for which we -- there's no known cause, or that's commonly called idiopathic MDS; and is much less frequently found, in fact, is rare, in cases of MDS that have -- that are known to be associated with

other causes.

Q. The 15 percent?

A. Yes. And that -- that particular pattern has become increasingly prominent over the last several years, and certainly the most recent literature looking at the development of MDS occurring secondary to exposure to toxic agents, the -- there's a clear deficit or rarity of trisomy 8 in those cases.

MR. LUBEL: Objection, nonresponsive.

Q. (BY MR. DILLARD) Do you have some published literature, peer-reviewed literature, that you have here with you today that supports the opinions that you've expressed?

A. Yes.

Q. You said that this was becoming more increasing -- excuse me, that this was increasingly becoming known in the literature in the last few years. What specifically are you talking about?

A. Well, for example, in the early '90s, it was well recognized that there were patterns of chromosome abnormalities that were found in acute myelogenous leukemia, AML and MDS, that was associated with exposure to toxic agents that were clearly more likely to be found in those cases than in idiopathic cases.

Q. And what --

A. The majority of cases.
Q. What does idiopathic mean?
A. No known cause.
At the same time there are chromosome abnormalities that were reported occasionally occurring in either, those that were idiopathic, no known cause; or those that developed secondary to exposure to toxic agents.
Q. Such as what --
MR. LUBEL: Objection, nonresponsive.
Q. (BY MR. DILLARD) -- type of toxic agents?
A. Alkylating chemotherapeutic agents, radiation.
Q. Cancer drugs?
A. Cancer drugs.
Q. Radiation?
A. Radiation. Also, in solvent exposure where these lesions have been found in individuals who have been occupationally exposed to solvents, including benzene.
Q. Now, is that -- is that group, the chemotherapy, the radiation, and the benzene exposure, is that the 85 percent category or is that the 15 percent?
A. That's the 15 percent category.
Q. All right.

A. What we've seen over the last several years with increasing -- with studies that look at larger numbers and have focused on primarily the chemotherapeutic literature, it's become clear that this difference in the pattern of the frequency of chromosome abnormalities that are seen in those developing secondary to exposure and those that are idiopathic is much greater than was considered in the past. So, we now have recent studies looking at very large numbers of cases where that pattern of differences in the types of chromosome lesions that are found between those exposed to alkylating agents and those that are not is a dramatic difference.

MR. LUBEL: Objection, nonresponsive

Q. (BY MR. DILLARD) What is the predominant pattern that is seen in the 85 percent of cases where age is the risk factor and there's no known external cause?

MR. LUBEL: Objection, form.

MR. DILLARD: What's the form objection there?

MR. LUBEL: Compound. Age is the risk factor and there is no external cause.

Q. (BY MR. DILLARD) Okay. What is the predominant pattern that is seen in the 85 -- first of

all, let's go back to the 85 percent of cases.

Is this the group where there is a known risk factor or -- excuse me, where there is a known cause or not a known cause?

A. Not a known cause.

Q. Okay. And what's the main risk factor in that group?

A. Age.

Q. All right. What is the predominant chromosome pattern that is seen in that category?

A. Reoccurring chromosome lesions that are found and described in acute myelogenous leukemia and in MDS that are associated with no known cause; and there are a series of reoccurring lesions that are described in the diagnostic classification of these, included among them would be trisomy 8, or involvement of translocations involving chromosome 8. Also, other types of abnormalities as well, most of them involving translocations or inversions.

Q. Now, let's talk about the 15 percent category, where there's a known cause. What's the predominant pattern that is seen in those?

A. The predominant pattern is the loss of all or part of chromosome 5 and/or chromosome 7 and sometimes both; so involving the chromosome 5 and chromosome 7 and

deletions of those chromosomes. And studies over the years suggest that the incidence of those in AML and MDS preceding AML following exposure to alkylating agents is higher than 70 percent. The most recent study by Larson in Chicago suggests 76 percent.

Q. Did James Cowey have that chromosome pattern?

A. No, he did not.

Q. Is the MDS that is in this 85 percent category considered to be the same disease or a different disease from the MDS in the 15 percent category?

A. The World Health Organization classification of diseases, which has become the world bench standard for the classification of these over the last couple of years, distinguishes MDS into several different categories; and it distinguishes AML, acute myelogenous leukemia, into several different categories. The specific type of AML associated with exposure to alkylating agents is preceded by a type of MDS, and so the -- they're referred to together as MDS/AML developing secondary to exposure to these agents. So it has a specific disease classification all by itself.

Q. Is that the same as or different from --

A. It's different from.

Q. -- the 85 percent?

A. That's correct.

Q. Incidentally, did you note the treatment that Mr. Cowey had received, the medication that he had received?

A. Yes.

Q. Okay. What did he -- what did he receive?

A. He was entered into an experimental protocol that involved the use of a derivative of Dideoxycytidine, 5-Aza-2'-Deoxycytidine, and Cytosine Arabinoside, or Ara-C. Ara-C is routinely used in treating myelodysplasia and acute myelogenous leukemia, usually in combination with other drugs. In this particular case, the use of the Dideoxycytidine derivative was an experimental protocol.

Q. Have you had any involvement with that drug?

A. Yes. I worked on the development of the parent compound Dideoxycytidine, 2'3'-Dideoxycytidine, prior to its approval as a drug.

Q. Have you published on that drug?

A. Yes, I have.

Q. Do you have that paper here with you in the event someone wants to ask you questions about it?

A. Yes, I do.

Q. Do you also have here available the papers that you referred to earlier involving this 85 percent category and the chromosome pattern seen there, and the

15 percent category and the chromosome pattern seen there?

A. Yes.

Q. Let me turn now to the last of the subjects that you were asked to address, Dr. Irons, and if you could remind us again what that was.

A. Specifically with respect to the probability that Mr. Cowey's disease was caused by his exposure to benzene over the years in his use of Liquid Wrench.

Q. Applying the scientific methodology that you've described, do you have an opinion as to whether there is reliable scientific evidence that Mr. Cowey's use of Liquid Wrench, assuming it contained benzene for purposes of this question, was a cause of his disease?

A. Yes, I do.

Q. And what is that opinion?

A. That there is no reliable scientific basis to conclude that his exposure to benzene Liquid Wrench was the cause of his myelodysplasia.

Q. Why do you say that?

A. First of all, because the presentation of his myelodysplasia, as I've just said, is consistent with presentation that's seen in vast majority of individuals who develop idiopathic myelodysplastic syndrome, the major risk factor of which is age, and his age at

diagnosis is consistent with that.

Independently, there's no basis upon which the information I have been provided with that I can quantitate a -- make a meaningful assessment of his exposure to benzene, given the information that's been presented to me. So, it's impossible for me to provide a quantitative analysis of his exposure to benzene.

Independent of that, the quantitative epidemiologic literature that demonstrates an association between exposure to benzene and the development of AML or MDS involves exposure scenarios and occupations that are not relevant to Mr. Cowey's specific situation and use of the product Liquid Wrench.

Q. Assuming that he was last using Liquid Wrench at a time when it might have contained benzene, in 1978, and his diagnosis was in 2001, do you have an opinion as to whether or not that would be consistent with the Liquid Wrench usage explaining his disease?

A. The vast majority of the quantitative epidemiology -- epidemiologic literature dealing with the development of acute myelogenous leukemia following exposure to benzene defines a latency, or period, or interval between opportunity for exposure and development of disease that has a median of about nine-and-a-half to ten years. More recent follow-up

studies of those same populations suggest that it may be possible that that latency may extend for a period of, say, 15 years at the latest, or the longest. But I know of no basis to conclude that on -- certainly on the basis of latency that exposures exceeding that, or certainly exceeding 20 years, are associated with the development of acute myelogenous leukemia.

Q. How about MDS?

A. MDS is subsumed within diagnosis of AML when we're talking about AML secondary to exposure to toxic agents. They're part of the same paradigm or process.

Again, in contrast, if you look at MDS/AML developing secondary to alkylating chemotherapy, the latency interval is on the order of two to seven years.

MR. LUBEL: Objection, nonresponsive.

Q. (BY MR. DILLARD) What is the latency period for the development of the MDS/AML disease that is at -- that's this 15 percent, what is the latency in those individuals receiving chemotherapy?

A. Two to seven years.

Q. Do you have an opinion as to the most likely factor in explaining Mr. Cowey's disease?

A. His age.

MR. DILLARD: Thank you, sir.

I think that's all the questions I have right

now.

EXAMINATION

BY MR. LUBEL:

Q. Dr. Irons, my name is Lance Lubel, and you and I briefly met right before we started this deposition, correct?

A. That's correct.

Q. We had never met before?

A. That's correct.

Q. True? And as I appreciate it, you have been retained by the lawyers for United States Steel Corporation to serve as an expert witness for them, is that true?

A. That's correct.

Q. When were you retained?

A. I believe it was this summer, may have been August.

Q. Mr. Steve Dillard from the law firm of Fulbright and Jaworski, did you have discussions with him about this?

A. I had discussions with Mr. Dillard and with Mr. Kemp. Kemp.

Q. Another lawyer from their Dallas office?

A. I believe so, yes.

Q. Is -- is benzene a carcinogen, in your

opinion?

A. Yes.

Q. What does the term carcinogen mean?

A. That it is a substance or chemical or an agent that can cause certain types of cancer.

Q. If I heard you correctly when Mr. Dillard from Fulbright was asking you questions, I believe that you said that MDS, or myelodysplastic syndrome, was a cancer, in your opinion?

A. Yes. It is a neoplastic disease. It is by definition clonal, which means it is a cancer.

Q. Is there any dispute amongst good scientists such as yourself as to whether benzene is, in fact, a cancer-causing agent?

A. No.

Q. Would it be fair to say that it is generally accepted in both the medical and the scientific community that benzene can cause cancer if exposures are correct?

A. If the exposures are sufficient, benzene has been demonstrated to cause specific kinds of human cancer, principally the acute myelogenous leukemias.

Q. And, in fact, sir, is it true that benzene has been known in the medical and scientific community to cause serious -- or can cause serious health

consequences for many, many decades?

A. Certainly since the -- benzene's been known for many, many years to be -- to be able to cause bone marrow suppression, and toxicity to the blood forming organs. Certainly, by the mid '70s, the mid to late '70s, it was generally appreciated and understood that benzene could also cause acute myelogenous leukemia.

Q. Are you aware, Dr. Irons, from all of your research regarding benzene, that adverse health consequences have been reported in the literature back in the 1920s and '30s regarding benzene exposures?

A. Yes.

Q. And, in fact, I am sure you're aware, and since you have been in this field for some period of time, that the American Petroleum Institute that was made of large oil companies such as United States Steel Corporation, that they issued a report in about 1948 that found that benzene was a hazardous substance.

MR. DILLARD: Object to the form of the question.

Q. (BY MR. LUBEL) Are you aware of that, sir?

A. I'm generally aware that the American Petroleum Institute recognized the potential toxicity of benzene, certainly as early as the '40s.

Q. And you have no reason to dispute that -- that

companies that were interested in finding out what the potential hazardous health effects from benzene exposure were, that there was some information that was available as early as the 40s concerning benzene exposures, true?

MR. RILEY: Objection, form.

A. As a matter of fact, there were several anecdotal reports going back at least that far, that described bone marrow suppression and the development of blood disease associated with very high level exposure to benzene.

Q. (BY MR. LUBEL) And I'm sure that you're aware that the 1948 report by the American Petroleum Institute was actually authored by a gentleman from the Harvard Medical School by the name of Dr. Phillip Drinker?

A. That I couldn't tell you one way or the other.

Q. Do you know who Dr. Drinker is or was?

A. He was a prominent hematologist, I believe.

Q. He was a good and reputable doctor in his field of blood disorders, correct?

A. To my understanding, yes. I wasn't there at the time.

Q. But --

A. Yes, he's well-known.

Q. In your years of researching and writing on the topic of benzene exposures, you've come across

Dr. Drinker's name on more than one occasion, I take it?

A. Yes.

Q. And he's well written in that area, true?

A. Yes.

Q. And were you aware that the 1948 American Petroleum Institute study that Dr. Drinker authored on behalf of oil companies stated that there was -- there was absolutely no safe level of benzene exposure?

A. I do recall that it said that.

Q. And, in fact, you acknowledge that that study talked about blood and blood forming disorders, correct?

A. Yes.

Q. And would you agree that MDS, the disease that you acknowledge Mr. Cowey has, is a blood or blood forming disorder?

A. It is. It's probably important to point out that at that particular point in time, the state-of-the-art was such that myelodysplastic syndrome wasn't recognized as a disease process, and that the exposures that were at issue with respect to the toxicity of benzene in the '40s were several fold higher than those that we now are concerned about with respect to benzene exposure and toxicity.

MR. LUBEL: I object to everything after "It is" as being nonresponsive.

Q. (BY MR. LUBEL) Have you brought with you, Dr. Irons, the peer-reviewed published articles that state that there are -- there -- there is a safe level of benzene exposure?

A. I am not sure what you're referring to.

Q. Well, we talked just a minute ago briefly about the American Petroleum Institute study in 1948 that said there was absolutely no safe level of benzene exposure, short of zero. And so my question is: Have you brought with you today any peer-reviewed published literature that tells us what the safe level is?

A. There is no literature that I can point to, including the API report, which incidentally wasn't a peer-reviewed study either, that defines a safe level. There are many studies that in the context of quantifying the relationship between exposure and disease, that have provided a characterization of dose response. But in science we can't prove a negative; and therefore, you won't find any studies that point to a specific level and say that it is safe. That's not something that science does.

Q. So, you don't have, at least with you today, a study that says what level of exposure to benzene is considered safe by the relevant medical and scientific community, correct?

A. As I said, in science we can't prove a negative, so there are no studies that exist that will affirmatively say that there is a quantitative level that has been proven to be safe.

Q. So, the information that was published in the 1948 American Petroleum Institute, where they said that there is absolutely no safe level of benzene exposure, that still holds true today, correct?

A. No. I don't believe so. I don't believe that you can say there's absolutely no level that does not produce adverse health effects. There clearly are. But pointing to a specific level and saying that there is a study or a body of literature that states that this level is safe is not something that scientists do.

Q. What are the accepted risk factors of MDS, Mr. Cowey's disease? And by accepted I mean generally accepted in your field, medical people and scientists.

MR. DILLARD: I'm sorry, would you state it again?

Q. (BY MR. LUBEL) I'll be happy to. What are considered to be in your community, the medical and scientific community, the generally accepted risk factors for MDS, myelodysplastic syndrome?

A. Depending upon the specific type of myelodysplastic syndrome, as I have -- as I've discussed

previous today, the risk factors include age, which is the predominant risk factor certainly for idiopathic myelodysplastic syndrome. With respect to MDS developing in the context of acute myelogenous leukemia, or in combination of acute myelogenous leukemia, exposure to alkylating chemotherapeutic agents, exposure to radiation, and with some controversy, exposure to benzene.

There are other agents that have been generally -- other agents and drugs that have been variously suggested to be associated with it, but in general those are the major causes.

Q. Well, other than age, exposure to alkylating agents, which I think you've referred to as basically chemotherapy?

A. Yes.

Q. Radiation is accepted, true?

A. Yes.

Q. True?

A. Yes.

Q. And is that ionizing radiation?

A. Yes, definitely.

Q. And then certain benzene exposures?

A. There -- there's at least one report that implies electromagnetic radiation. That certainly has

not been confirmed and has not been demonstrated with respect to biologically plausible mechanisms.

Q. So, as you sit here today, do you have the opinion that electromagnetic exposures -- is that what you referred to it as? Electromagnetic --

A. Electromagnetic fields.

Q. At this point in time, as you sit here, is the information sufficient for scientists such as yourself to conclude that that causes MDS?

A. No.

Q. And as you sit here today, are you aware of any exposures that Mr. Cowey had to electromagnetic fields?

A. No.

Q. So, other than age, chemotherapy, ionizing radiation, and benzene, are you offering any opinions as to the major accepted risk factors for MDS other than those?

A. No.

Q. How much benzene was Mr. Cowey exposed to --

MR. DILLARD: Object to --

Q (BY MR. LUBEL) -- during his lifetime?

MR. DILLARD: Object to the form.

A. I don't know.

Q. (BY MR. LUBEL) How many years did Mr. Cowey

use benzene-containing products?

MR. DILLARD: Object to the form.

A. As a toxicologist, the only responsible answer I can give to that is as long as he worked, he was exposed to products that to some degree or some form contained benzene because it's ubiquitous. You can't exclude for -- assume that at any time he or any of the rest of us have not had some exposure to benzene.

Q. (BY MR. LUBEL) But as you sit here today, can you offer to the jury, based upon the information that the United States steel lawyers have provided you, either on a qualitative basis or quantitative basis, what Mr. Cowey's exposures to benzene were over his lifetime?

A. No, I can't.

Q. Did -- did the lawyers for United States Steel Corporation advise you that on a fairly regular basis Mr. Cowey used benzene-containing products for approximately 25 years?

MR. DILLARD: Object to the form.

MR. RILEY: Same objection.

A. I am aware and was provided with information that related to the allegation that he had used Liquid Wrench, and Liquid Wrench is a solvent mixture.

Q. (BY MR. LUBEL) But did they tell you that

there was benzene as an ingredient in that product?

A. I have seen reports that document that at various times the product contained mixtures of raffinates that included some benzene, yes.

Q. And that varied, based upon the information you were provided? Would you agree with that?

A. Yes.

Q. Not every batch was exactly the same, true?

A. That's correct.

Q. And that wouldn't surprise you as a scientist?

A. No.

Q. Have you done work for any Exxon or Mobil entities during your career as a scientist?

A. I've consulted with Exxon before.

Q. Have you done any work for Mobil?

A. Yes, I believe so.

Q. And did you find your experience with the Mobil people to be enlightening?

MR. DILLARD: Object to the form.

A. I'm afraid I don't know what you mean.

Q. (BY MR. LUBEL) Let me tell you what I'm driving at, Dr. Irons.

The lawyers in this case have -- have seen studies performed by Mobil employees that demonstrate that Liquid Wrench, at least in the late '70s, had a

benzene content of 7 to 30 percent. Have you seen those studies?

MR. RILEY: Objection, form.

A. I've seen references to analysis of raffinate in at least one occasion that would comport with those -- that level of benzene.

Q. (BY MR. LUBEL) And I am trying to be more specific. As you -- you understand that raffinate is a component of Liquid Wrench, correct?

A. Yes.

Q. What I'm telling you is, is that the lawyers in this case have been provided Mobil documents that indicate that Liquid Wrench itself had a benzene content between 7 percent and 30 percent, and I am asking you if you have seen those?

A. What I -- what I recall seeing is the -- is various anal -- various analyses of raffinate in at least one occasion that would be consistent with those levels.

Q. Do you have any reason to disagree or differ with what those documents tell us about the benzene component of Liquid Wrench?

A. No.

Q. There was a period of time where you did work for the -- I think you called it the Chemical Industry

Institute of Toxicology?

A. Yes.

Q. Where were they based?

A. Research Triangle Park, North Carolina.

Q. And who owned that group, if you will?

A. It was a nonprofit independent research institute that conducted research on commodity -- toxicology, research on commodity chemicals. It was funded when I was there through a group of chemical companies.

Q. Do you know the name of those chemical companies?

A. There was something like 20 or 23. I know some of them but I certainly couldn't give you an exhaustive list.

Q. Just tell me the ones you can remember.

A. Dow, Dupont, Exxon, Mobil, Chevron, Conoco, W. R. Grace, Phillips -- I don't know what number I'm at -- Shell, Monsanto, many different companies.

Q. When did you do work for -- for those companies?

A. I worked for the Chemical Industry Institute. I didn't work for the companies.

Q. That's what I mean. What -- what time period are we talking about?

A. 1977 to 1987, '88.
Q. And I take it during this roughly -- that's a ten-year period, am I right?
A. Yes.
Q. -- that you would have fairly frequent communication with representatives of these various chemical companies you've told us about, correct?
A. Only within the context of restrictions that the Institute guidelines placed on me. We did not have routine interaction with company representatives outside of the normal activities of the institute.
Q. Were you aware that Mr. Dillard and his law firm of Fulbright & Jaworski do a lot of work for those companies?
A. At that time --
MR. DILLARD: Object to the form.
A. -- no, I didn't know Mr. Dillard then.
Q. (BY MR. LUBEL) Talking about now. Are you aware of it as you sit here now?
MR. DILLARD: Object to the form. It's not right, but --
A. For which companies?
Q. (BY MR. LUBEL) Well, when did you meet Mr. Dillard?
A. Probably I first met Mr. Dillard 1989, 1990,

1 1991, somewhere in that time frame.
2 Q. And how did you meet him?
3 A. I don't remember the first time I met him. It
4 might have been in conjunction with a lawsuit in which I
5 was an expert, but I couldn't tell you specifically the
6 first time I met him.
7 Q. Do you recall that -- at any rate that it was
8 a lawsuit that had something to do with chemical
9 exposures?
10 A. If it was a lawsuit, I -- I think that would
11 be safe assumption.
12 Q. And has it been your experience since you've
13 been doing work for Mr. Dillard that oftentimes he
14 represents chemical companies?
15 A. Yes.
16 Q. Have you ever been an expert witness for
17 Mr. Dillard or his law firm in cases where they did not
18 represent a chemical company?
19 A. I don't believe so.
20 Q. Now, when were you first introduced to
21 litigation?
22 A. 1989, I believe.
23 Q. And who was the first person that introduced
24 you to lawsuits and potential expert work you could
25 provide in that area?

A. Well, the first attorney that I ever agreed to talk to on this would have been Mr. Robert Scott.

Q. And who put y'all two together as you appreciate it?

A. He called me.

Q. And did he tell you who he got your name from?

A. Got my name, I believe, from Dr. Daniel Teitelbaum.

Q. And who is Dr. Daniel Teitelbaum?

A. He's a toxicologist in Denver.

Q. He does similar work to you, similar field?

A. I think that's probably a stretch, but he -- he's involved primarily -- I think his background is in drug abuse and toxicity of drugs and glues and things like that.

Q. Is he a good doctor?

A. I have no idea.

Q. Have you met him before?

A. Yes, I have.

Q. Is he reputable in his field?

A. I'm not sure how you would define his field I really can't speak to what his reputation is as a doctor.

Q. So, tell me what you can recall about your first conversation with Mr. Robert Scott, about you

getting involved in these lawsuits.

A. I think it's --

MR. DILLARD: Object to the form.

A. At the time, as I recall, he asked me if I knew that my work, my research, was being used to support opinions that were being offered in litigation; and I said, no, I wasn't. And he asked me to -- if I would take a look at some testimony and call him back if I felt like it, and send him a bill otherwise. But simply just to review testimony that had been presented in a case relating to my own work, and the interpretation of that work, and after some give and take I agreed to do that.

Q. (BY MR. LUBEL) Did you at some point in time learn that Mr. Robert Scott, in fact, represents companies similar to Mr. Dillard and his law firm; that is, chemical companies?

MR. RILEY: Objection, form.

A. Mr. Scott asked me if I would be willing to serve as an expert in a case that involved the allegation of disease caused by exposure to benzene.

Q. (BY MR. LUBEL) My question is -- it's a little bit more specific, and that is at some point in your time -- in time, did you learn that Mr. Scott, like Mr. Dillard, typically represents chemical companies in

these chemical exposure cases?

MR. RILEY: Objection, form.

A. I think he does. He represents a number of clients, some of which include chemical companies.

Q. (BY MR. LUBEL) Can you think of any clients that Mr. Scott has had in the number of cases that you've worked with him on, where he represented companies that were not in the chemical company field, if you will?

A. It's my understanding -- I know that he has been involved and has represented companies that aren't chemical companies, but I couldn't tell you in which particular cases or who they are.

Q. Dr. Irons, do you hold yourself out as an expert epidemiologist?

A. No. I'm a toxicologist.

Q. And what is the difference between toxicology and epidemiology?

A. Epidemiology is the science that deals with the design and conduct of population-based studies relating to the cause of disease and the incidence of disease.

It's distinguished from toxicology in that toxicology is primarily focused on understanding the specific relationships and pathogenesis of disease

caused by exposure to chemicals. Toxicology uses epidemiology extensively in evaluating the cause of disease.

Q. Are you a hematologist?

A. I'm an experimental hematologist, and I'm a clinical laboratory scientist that uses hematology in differential diagnosis.

Q. Do you hold yourself out as a hematologist?

A. Yes. As an experimental hematologist, I do.

Q. Now, is there a difference between a medical doctor hematologist and an experimental hematologist?

A. Yes.

Q. What is the difference?

A. A medical doctor as a hematologist is involved in the treatment of diseases involving the blood system. I am not involved in the treatment of blood diseases. An experimental hematologist is an individual who is concerned with the understanding the mechanisms of diseases involving the blood forming organ.

Q. Now, if I understood you correctly, you're not a medical doctor, correct?

A. That's correct.

Q. And you did not go through a complete -- all the courses that medical students have to go through, correct?

A. That's correct.
Q. And you don't hold yourself out as an expert in -- as a physician?
A. No.
Q. Is that true?
A. That's correct.
Q. Now, if I heard you correct, the work that you're doing over in China is funded by some chemical companies, too; is that correct?
A. It's -- it's funded by a consortium that is made up of companies that are involved in petroleum.
Q. Okay. And there's a difference between -- at least in your mind between petroleum companies and chemical companies?
A. In general, yes.
Q. But your work even in China that you talked to the jury about so far today is being funded by petroleum companies?
A. That's correct.
Q. So, would it be fair to say that between 1977 through roughly today, in 2003, that much of your work has been funded by either the chemical or the petrochemical industry?
A. A great deal of it has. A great deal has also been supported by federal funds and pharmaceutical

companies, and a variety of other sponsors. Certainly because my focus and focus of my research is -- involves primarily drugs and chemicals, much of my research funding has come from the makers of those products.

Q. And I didn't mean to imply that you have not done any other work in your career as a scientist other than for the chemical and the petrochemical industry. My only point was much of your work has been funded by those industries? Is that true?

A. That's correct.

Q. Now, I am curious, because in your report, and I have seen a report -- is your report dated October 24th of 2003?

A. Let me look at the date here. Yes, it is.

Q. In your report, it's a number of pages, you -- you do make some opinions based upon Mr. Cowey's exposures within the report, is that a fair statement?

A. I make some opinions on exposure that are based upon a report that I reviewed by Mr. Spencer.

Q. All right. Now, I think what you've told me so far, I want to make sure we're on the same page, is that you don't feel as you sit here today that you have seen competent evidence, if you will, or proof, of what Mr. Cowey's exposures to benzene or benzene-containing products has been throughout his life, is that a fair

assessment?

A. No. Not exactly. Based on the materials that I've reviewed in this case, I cannot make a reasonable quantitative assessment of what his exposure was. I did review Mr. Spencer's report which provided me with a worst-case scenario, and I did reach a conclusion based upon that with respect to given a worst-case scenario, what, in fact, the relationship would have been between Mr. Cowey's exposure to benzene and potential development of his disease.

Q. And that's what I want to visit with you about for -- for a moment is the report that you relied upon that Mr. Spencer provided you. Do you have that with you?

MR. RILEY: Objection, form.

A. I don't know whether I do or not.

MR. LUBEL: We're going to take a short break, Dr. Irons, and if -- I am not saying you can't do anything else; but over the break, will you look for that report?

THE WITNESS: Yes.

MR. LUBEL: Thank you.

THE VIDEOGRAPHER: Going off the record. Time is approximately 11:41 a.m.

(A break was taken.)

THE VIDEOGRAPHER: This is the beginning of tape 2. The time is approximately 11:55 a.m. We're now back on the record.

Q. (BY MR. LUBEL) Dr. Irons, before we took the break, I asked you to try and locate the Mr. Spencer report that you -- that you've addressed earlier, correct?

A. Yes.

Q. Did you find it?

A. Yes, I did.

Q. What product did Mr. Spencer test?

A. Liquid Wrench, I believe.

Q. And do you know if the components of the Liquid Wrench that he tested were the components in the Liquid Wrench that Mr. Cowey used?

A. I can't say that on the basis of my review of the report.

Q. Can you tell if the product called Liquid Wrench that Mr. Spencer tested was a 2003 product?

A. No. I have no idea.

Q. Do you see the reference in Mr. Spencer's report about how he added benzene or had benzene added to the Liquid Wrench product?

A. Certainly -- well, what I have is the amounts that were -- were in the formulations. I don't know

exactly how he compounded those.

Q. But, as you sit here today as an expert witness for United States Steel Corporation, you can't tell us under oath whether or not the product that Mr. Spencer tested was in fact a product that had the same or substantially similar ingredients to that that Mr. Cowey used, correct?

A. I can't say that. No.

Q. And I take it that it's -- there's those kind of deficiencies, if you will, or shortcomings, in Mr. Spencer's report that have put you in a position to say, I don't have any meaningful information, I think is the word you used, or I can't make a meaningful evaluation of Mr. Cowey's benzene exposures?

MR. DILLARD: Object to the form of the question.

Q. (BY MR. LUBEL) Is that what you said?

MR. DILLARD: Object to that question.

A. I reviewed this report and I've reviewed the testimony of Dr. Rose, and Dr. Rose's testimony provides me with absolutely no basis or quantitation or estimate of what Mr. Cowey's exposure to benzene might have been. Mr. Spencer's report is a -- is to my understanding an estimate of worst-case exposure scenario based upon the modeling conditions that he used in deriving this

report. So, I have independently used these numbers in evaluating worst-case scenario for potential exposure. But I have seen, in certainly Dr. Rose's report, no information, nor in Mr. Spencer's report, information that would allow me to evaluate specifically what Mr. Cowey's personal exposure would have been.

MR. LUBEL: Objection, nonresponsive

Q. (BY MR. LUBEL) Did you earlier today in your testimony make a statement that you didn't feel as though you were in a position to make a meaningful evaluation of Mr. Cowey's benzene exposures based upon the information that had been provided to you?

A. That's correct.

Q. Do you stick by that statement now that I'm asking you questions?

A. Yes. That's correct.

Q. Now, my question is: Is part of the reason that you have that opinion that you can't make a meaningful evaluation of Mr. Cowey's exposures to benzene -- is part of the basis for that because of Mr. Spencer's report does not give you the detail you need to know whether, in fact, he's even testing a product that, in fact, Mr. Cowey used?

A. No.

Q. That's not part of it?

A. My evaluation of Mr. Spencer -- I used Mr. Spencer's report in providing an independent evaluation of potential worst-case scenario for exposure to Liquid Wrench given different formulations of benzene in modeling that Mr. Spencer did. It's independent and separate from my opinion, which is that I have no basis to make a meaningful assessment of what Mr. Cowey's specific exposure to benzene is.

Q. Can you tell the jury how much benzene Mr. Cowey was exposed to when he would be underneath the houses using Liquid Wrench, in what he called, I believe, crawl spaces?

A. No, I can't.

Q. Does Mr. Spencer within his report provide you any information regarding that particular task, what Mr. Cowey was exposed to, for the Liquid Wrench he was using?

A. Mr. Spencer uses a couple of different mathematical models and assumes certain conditions with respect to ventilation and air flow. I can -- I am not an industrial hygienist and I can't tell you whether or not those comport with conditions that would be representative of a crawl space or not.

Q. But in Mr. Spencer's report, does he make any reference to Mr. Cowey's exposures in the crawl spaces

underneath the houses? Do you see that in there?

A. Not specifically, no.

Q. I want to talk to you for a minute about your -- one of the major pieces of work that you said that you've done over your career, is do work for pharmaceutical companies.

A. Yes.

Q. Which companies?

A. Roche, Astra, Fujisawa, Lily, Sandoz. I'm probably leaving a couple out.

Q. How about Bayer?

A. No. Not that I'm aware of. They may own somebody. I mean in this business, I can't tell.

Q. Now, when you did work on behalf of the pharmaceutical companies, would those companies actually fund your work?

A. Well, they paid me. On occasion -- on occasion I have consulted specifically in -- on issues related to drug development or certification. Other times I've done research on products with respect to evaluating mechanisms of toxicity. I've done both, sometimes interchangeably.

Q. Are you familiar with any asbestos-related diseases?

A. Yes, in general.

Q. Have you done any reading on the disease mesothelioma?

A. Yes.

Q. Do you recognize mesothelioma to be an asbestos-related malignancy or cancer?

A. It is generally considered to be that, yes.

Q. Are you aware of any other known and accepted causes of mesothelioma other than asbestos?

A. No, with the proviso that other fibers with asbestos-related properties, I think, probably, have the potential to do the same.

Q. Are you familiar with the studies that concern housewives contracting mesothelioma from washing their husband's clothes that contained asbestos, after work?

A. No, I'm not.

Q. Would it surprise you if there were, in fact, studies of housewives contracting asbestos-related malignancies such as mesothelioma from simply washing out the clothes of their husbands after they had returned from work?

MR. RILEY: Objection, form.

A. I would have to review those papers before I could give you a meaningful opinion on then. I haven't seen them and I'm not familiar with them.

Q. (BY MR. LUBEL) Would it surprise you,

Dr. Irons, that in those studies that conclude that housewives exposed to asbestos while washing out their spouse's clothes could contract the disease, or did, in fact, contract the disease mesothelioma, that in those studies there was no quantitative exposure -

MR. RILEY: Objection, form.

Q. (BY MR. LUBEL) -- that was referenced in the study?

A. Without referring -- without having a chance to review the papers, I couldn't give you an informed opinion on them.

Q. Now, one of the things that you brought with you is a three-ring binder that has multiple documents including studies in it, correct?

A. Yes.

Q. And I'd like to mark that as Exhibit Number 2 to your deposition and have either Mr. Dillard's office or the court reporter make a copy of that and then return the original to you, is that okay?

A. That's acceptable.

Q. Now, you were kind enough over the last break we took to let me see that thick book of studies, correct?

A. Yes.

Q. And if we look at, I believe, the first or

second study is a 1965 article about the Bradford Hill -- Hill criteria that you have discussed today. Do you see that?

A. That would probably be the first -- that's the first address given by Sir Austin Bradford Hill, yeah.

Q. And what number is that in your book? Is that the second cite -- tab, if you will?

A. It's Number 1.

Q. It's Number 1? Now, you -- you have referred on many occasions to those particular scientific criteria, if you will, today?

A. Yes.

Q. Is that a fair statement?

A. Yes.

Q. And one of the statements that I believe that you've made is that the Sir Bradford Hill criteria require quantitative exposure levels to establish or make an inference of causation; is that true?

A. One of the criteria within the rubric of Evidence Based Medicine and the Bradford Hill criteria is dose response, and that is what requires quantitative analysis of exposure.

Q. That there is, in fact, a dose response?

A. In order to establish that there is a dose response, you have to know what the dose is, and that

requires quantitative analysis.

Q. Well, let me ask you this. Is there a dose response between benzene and AML?

A. Yes.

Q. In your opinion, has that been successfully plowed through, if you will, or discussed in the literature?

A. We have a literature that provides us with a quantitative dose response for benzene.

Q. And, in fact, dose response means, and correct me if I am wrong, is that you would expect if a person is exposed to more of a chemical, that the response would be greater, is that generally what it means? Or am I misstating that? I don't want to put words in your mouth.

A. That requires -- in order -- in order for me to answer that requires a little bit more specificity. Dose response applies to populations, and it also applies to individuals, but there are differences.

In a population dose response refers to, in general, certainly given the design of most epidemiology studies, the frequency of a given disease in the population as a function of what they were exposed to. So the number of cases or the incidence.

In an individual, dose response either refers

to the probability that they developed a certain disease, or to the severity of the symptoms that they may encounter if, in fact, they're related to dose. So, in other words, if you increase the dose, you increase the severity of the symptoms.

Q. And there's what's referred to as a dose response curve; is that true?

A. That's correct.

Q. And if you would go ahead and draw out on your yellow sheet of paper what curve you would expect to see, in general, to fulfill this dose response criteria of the Sir Bradford Hill criteria, or test.

A. I'm not exactly sure what you're asking me to do.

Q. It was a poorly phrased question. Let me -- let me start over on that, so that you and I are talking the same language to the extent that that's even possible.

Can I borrow your piece of paper?

A. Sure.

Q. I have drawn on the sheet of paper two axis, if you will, correct? Do you see that?

A. Yes.

Q. If you would just point -- hold that up to the jury so they can see what you and I are talking about.

All right. Now, if I can have that back, let me draw another line.

Now, if you would take a look at that and hold that up. If the -- and the line I've drawn that angles upward, if your dose goes up, you would expect a greater response to chemicals such as benzene; is that true?

A. If your -- if your dose response curve is linear, which is a major assumption, then that's true.

Q. All right. Now, will you draw for us on a separate piece of paper, or below that if you can, what the dose response chart looks like for benzene?

A. With respect to a complete dose response going from zero effect to a measurable effect, I can't do that, because we don't know basically what the dose response is at concentrations below which we can see an effect. The observable effect is one that has to be quantitated on the basis of appropriate statistics and industrial hygiene.

Q. But would you agree, Dr. Irons, that there is a dose response for benzene and MDS when you take into account the Sir Bradford Hill criteria?

A. We have a dose response for benzene based on Bradford Hill, Evidence Based Medicine, Henle-Koch. There's a clear-cut dose response in the sense that there are specific cumulative exposures that have been

associated with a statistically significant increase in acute myelogenous leukemia; and there are exposures, cumulative exposures, below which we don't have any evidence of a significant increase.

Q. But my question is: Is there a dose response with respect to benzene and MDS, the disease that Mr. Cowey has?

A. Only in the context of MDS/AML, not in the context of MDS itself.

Q. All right. Now, can -- looking at the actual 1965 paper that you have before you on the Bradford Hill criteria, can you locate the section for us that talks about dose response?

A. Biological grading.

Q. What page?

A. Dose response.

Q. What page are you on?

A. 298.

Q. And can you read for us the relevant section on the dose response criteria that you have been talking about with the jury at some length today?

A. Well, certainly in the original Bradford Hill criteria, he says, "Fifthly, if the association is one which can reveal a biological gradient or dose response curve, then we should look most carefully for such

evidence. For instance, the fact that the death rate from cancer of the lung rises linearly with the number of cigarettes smoked daily adds a very great deal to the simpler evidence that cigarette smokers have a higher death rate than nonsmokers. That comparison would be weakened, though not necessarily destroyed, if it depended upon, say, a much heavier death rate in light smokers and a lower rate in heavier smokers. We should then need to envisage some more complex relationship to satisfy the cause and effect hypothesis. The clear dose response curve admits of a simple explanation and obviously puts the case in a clearer light."

Q. All right. Now, let me stop you there and talk to you about that for a second. The example that's given in that Sir Bradford Hill criteria document is cigarette smoking, correct?

A. That's correct.

Q. And does it stand for the proposition that people that smoke more are more -- or at greater risk of developing lung cancer?

A. Yes.

Q. And would it also hold true, if we applied that same concept to people that are exposed to benzene, that people that are exposed to benzene would be at greater risk if they're exposed to more benzene?

A. Yes.
Q. You don't disagree with that, do you?
A. No.
Q. And did the studies bear that out, that in fact there is a relationship?
A. Yes.
Q. Now, Where in the Sir Bradford Hill criteria document that you have before you does it get into the quantitative issues with regard to the individual as opposed to the quantitative issues regarding a population?
A. That is the basic -- Bradford Hill does not address dose response in that context. It addresses it in terms of the gradient I've just described as a criteria. Dose response with respect to population versus individual, severity of response is subsumed in the entire field of toxicology.
Q. Can you find for us any peer-reviewed publication in your three-ring book there that stands for that proposition?
A. Probably not. But I could cite to several text books that describe it in extreme detail. I didn't bring my toxicology -- basic toxicology literature with me. Pharmacology toxicology, the concept of dose response is extremely well exhaustively described.

Q. Are any of the studies that you have with you studies that address the specific product Liquid Wrench?

A. No.

Q. There is no such study, correct?

A. Not to my knowledge.

Q. Are there any studies that you brought with you that addressed solvents, products that contained benzene?

A. Yes.

Q. And can you just tell us the tab numbers of the studies that discuss mixed solvents, if you will?

A. This could take a little while.

MR. LUBEL: Do you-all mind if we go off the record while he is doing this?

THE VIDEOGRAPHER: Going off the record. Time is approximately 12:19 p.m.

(A break was taken.)

THE VIDEOGRAPHER: We're now back on the record. Time is approximately 12:25 p.m.

Q. (BY MR. LUBEL) You can proceed, Dr. Irons.

A. Yes.

Q. Were you able to give us the tab numbers?

A. There are several that deal with solvents and/or benzene and solvents: 30, 31, 32, 35, 39, 40, 41, 42, 43, 44, 46, 47, 48; 51 is an error in that the

title page is correct but the chapter that was copied is not the correct chapter. And for which I apologize.

Q. Now, would it be fair to say that the remaining studies that you didn't read us off the tab numbers within your three-ring binder involved pure benzene?

A. No. There are studies in here that deal with a variety of different issues, not just benzene, including disease causation, specificity, and other issues. There are three that deal specifically with -- that quantitatively deal specifically with pure benzene exposure.

Q. Within your references that you brought with you, do you have the study by Hayes, Yin, and others, from 2000, that was in the Journal of toxicology and Environmental Health?

A. I don't believe so.

Q. The title is, "Benzene and lymphohematopoietic malignancies in China."

A. I don't believe it's in here.

Q. Have you seen that study before?

A. Yes, definitely.

Q. Are you aware that that is a -- a study that concludes that benzene exposures cause MDS?

A. It includes MDS/AML as a subcategory. It

includes them together as a form of AML that is -- that develops secondary to exposure to alkylating agents.

Q. But were you aware that this particular study states that benzene exposure causes MDS?

A. It causes -- that particular study quantitates the relationship between exposure to benzene by the criteria that they use, and the development of MDS/AML.

Q. Do you have any criticisms of this study?

A. Yes, I do. The -- the exposure analyses are extremely sparse, and, in fact, don't actually measure exposure, direct exposure, in majority of individuals, which makes it very limited for use in evaluating risk, quantitative risk. It does, however, reaffirm and confirm some of the other findings that have been described in other more reliable quantitative studies, including the relationship between benzene exposure and AML and AML/MDS.

Q. Were you aware that that particular study stated that there were significant excess risks for MDS from benzene exposure?

A. Yes.

Q. You don't disagree with that statement, do you?

A. No.

Q. How long have you known about the study that

was published apparently in the year 2000?

A. That study is one of several that was -- that basically describes the -- that paper is one of several that describes the same study that was conducted by the NCI in China. I have been aware of it for quite a long time.

Q. What is the NCI in China? What do you mean by that?

A. The National Cancer Institute.

Q. Is that a Chinese governmental agency?

A. No. It's a U.S. Governmental agency. U.S.

Q. Oh, the National Cancer Institute?

A. Yes.

Q. Okay. Were there Chinese scientists that were involved in this study?

A. Yes. Yin Song Nian was the Chinese principal investigator.

Q. Were you aware that that particular study was a collaborative study that involved the Chinese Academy of Preventive Medicine?

A. Yes.

Q. And as you stated, the United States National Cancer -- Cancer Institute?

A. Yes.

Q. And were there, in fact, good scientists that

worked on this particular study?

A. Certainly.

Q. And good scientists can disagree, correct?

A. Yes.

Q. And remain good scientists?

A. Yes.

Q. You don't agree with everything that Dr. Yin or Dr. Hayes have stated about benzene, I take it?

A. No.

Q. And that doesn't make them bad scientists, does it?

A. No.

Q. Have you made your criticisms regarding this particular study known to the National Cancer Institute, and the Chinese Academy of Preventative Medicine?

A. Oh, yes, several times. My criticisms of that study are widely known, and are consistent with some of the general criticisms that have been made about that study. I don't know why they even published it.

Q. And your criticisms about this particular study, are they in writing anywhere?

A. I've referred -- well, I know that I certainly referred to criticisms that have been made with respect to the quantitative limitations of that particular study, because they have been made in government

publications, and I've referred to them. The EPA, for instance, has -- won't use that for risk assessment because of the quantitative limitations in it.

That's widely known. I've commented on it, and I think several other people have as well.

MR. LUBEL: Objection, nonresponsive.

Q. (BY MR. LUBEL) My question simply is: Have your criticisms of this 2000 study by Yin and Hayes and others, have you made those criticisms known to them in writing? Do you have a document, a letter, another article that you published that talks about these criticisms?

A. I've referred to them before. I am certain of it. Precisely where, I would have to review my writings to tell you exactly. I've also publicly commented on them at meetings, and I'm -- specifically one in Ottawa conducted several years ago.

There -- they're certainly not arcane or esoteric.

Q. Let me ask you this: There's a discussion in this article that talks about how cases of MDS have been reported in prior exposure to solvents, and they refer to a 1990 study by -- is it Venisse?

A. I'd have to look at it to comment on that. I -- I don't know who you're referring to.

Q. How about Ciccone, C I C C 0 N E?
A. Ciccone.
Q. Ciccone?
A. Yes.
Q. Have you seen that study?
A. Yes, I have.
Q. Do you have that with you?
A. Yes, I do.
Q. All right. And then they reference a case control study in Great Britain by Mehlman, 1987. Do you have that study with you?
A. No. I don't.
Q. Have you looked at that study?
A. I don't know what specific study it is. I may have, may not have.
Q. They cite it for showing an association of MDS with a history of exposure to gasoline and diesel fumes or liquids. Does that spark your memory?
A. No.
Q. Have you seen the -- the Rothman work on benzene?
A. Rothman is one of the authors on the NCI series of papers that all refer to this same study.
Q. Have you seen his 1996 work?
A. There are numerous publications dealing with

the same study in different forms and different formats. If you want to refer to a specific paper and you've got it, I can give you an informed response; but, the fact is there are numerous articles that have been published by that group. In fact, I'm a coauthor on at least one, if not more of them. So, I can't speak to a specific date and know precisely which publication you're talking about.

Q. Are you familiar with the scientist named Dosemeci?

A. Yes.

Q. Is he a good doctor, good scientist?

A. He's a statistician. I don't know much more about him than that.

Q. Have you seen any of his work on benzene?

A Yes.

Q. Do you have any criticisms of that work?

A. He's attempted to use mathematical models instead of actually measuring benzene. I think in general if you're going to try to develop an accurate dose response, especially when you're looking at fa -- thousands of facilities, that you have to have some basis for understanding what the exposures were on a quantitative basis and what the confounders are. A math -- mathematical model is not a surrogate for measuring

exposure.

Q. And I take it that you've seen the -- the work out of Australia by their petroleum institute that was at least sponsored in part by ExxonMobil Corporation?

A. If you're talking about the Health Watch Study, I am generally familiar with that study.

Q. And were you aware that in that study, they concluded that excess risk of leukemia appears to be associated with lower cumulative exposures, and exposure intensities when compared to other petroleum industry studies where an excess of leukemia risk had been found? Are you familiar with that conclusion?

A. I'm familiar with that, and I'm also familiar with the design and issues related to that study, one of which you mentioned, which is the relative inability to segregate or to distinguish one type of anemia from another. Excuse me, leukemia.

Q. So, you -- you disagree with the Australian Petroleum Institute study that found that there was an excess risk of leukemias even in lower exposure -- at lower exposure levels than had previously been reported?

A. I think that that subject is some question. They confirmed previous studies with respect to risks associated with acute myelogenous leukemia at higher concentrations, but they are -- significance is seeing

lower concentrations for nonspecific leukemia and they have extremely few -- low numbers, so they have difficulty in distinguishing between the disease types and the exposures.

Q. Do you have any other criticisms or complaints with that study other than what you've told us about?

A. Well, it would depend on what you're referring to. That study itself, and the document that I have read, is probably 200 pages long. If you're asking me whether the only statement or criticism I have of it is which I just said, is probably not. But, with respect to the issues of exposure analysis and dose response, those are my principal criticisms. It's unstable for specific disease association in exposure at the lower doses.

Q. Do you agree with the finding in that study that smoking does not increase the risk of developing AML?

A. There are other studies out -- there are a number of studies, including some government studies looking at meta-analysis of smokers involving huge numbers of smokers, that does show an increased risk of AML associated with smoking, so I would disagree with the conclusion of this -- of the Health Watch study insofar as it doesn't comport with much larger studies

that have seen an excess risk associated with smoking.

Q. Now, in your report in this case, you don't conclude that Mr. Cowey's MDS is caused by any prior smoking history he may have had, correct?

A. I think by and -- by and large and far away the most significant risk factor associated with Mr. Cowey's disease is age. That doesn't --

Q. My question --

A. -- exclude the possibility that smoking might play a role, but I did not consider in my evaluation of Mr. Cowey that smoking played a prominent role in the development of his disease.

Q. Does your report anywhere in there state or make reference to smoking playing a role in his MDS?

A. No. I just said I did not conclude that.

Q. Well, can you find for us the studies that you brought with you that demonstrate that age causes MDS?

MR. DILLARD: Object to form.

A. As a risk factor, yes. Age as the -- a risk factor for MDS is described several times in the literature. The most recent one, I've got an excerpt from a monograph by Neal Young in which he cites a Birmingham study. That's one.

Q. (BY MR. LUBEL) But is it your opinion --

MR. DILLARD: Why don't we get those

marked so we know what we're talking about?

A. And independently, as stated by Williamson, et al, that is actually from the mid '90s showing -- establishing the incidence of myelodysplastic syndrome with age.

Q. (BY MR. LUBEL) My question, Dr. Irons, is, is it your testimony and your opinion that age causes MDS?

A. Age is a co-factor. It is a confounder, a risk factor. It is understanding the relationship between confounders and risk factors is an important tenet in Bradford Hill and Evidence Based Medicine. It does not mean that one can say that age is a cause. It is an important influence and co-factor that has to be evaluated in determining causation, and in excluding other potential etiologies.

Q. So, if I understand you correctly, what you're saying is that as a person's age increases, or a person gets older, they're at an increased risk of developing MDS?

A. Absolutely.

Q. But you're not saying that age itself causes MDS?

A. I think that's semantic. I could say the same thing with respect to exposure to alkylating agents; that as you're exposed to alkylating agents, your risk

factor increases, or your risk of developing disease increases. Do the alkylating agents directly cause it? That involves understanding the pathogenesis and molecular mechanisms of toxicity, and to that extent I can't say with respect to alkylating chemotherapeutic agents or age what is the defining factor that's associated with that increased risk, but it's clearly established in the quantitative literature.

Q. Do you have any quantitative literature that states, that concludes, that age causes MDS?

A. No.

Q. Is there, in fact, literature that -- that is peer reviewed that states that chemotherapy agents can cause MDS?

A. Yes.

Q. Peer-reviewed studies?

A. Yes.

Q. Have you brought with you all of your file materials regarding your opinions and the bases for your opinions today?

A. I believe so. Other than references you've made to general textbook concepts that I haven't documented in the material that I have brought with me.

Q. Other than that, have you brought the documentation?

A. Yes.
Q. Do you have your billing records?
A. That I don't believe I have.
Q. Have you been paid for your services yet?
A. To date, yes.
Q. And do you know approximately how much you have billed prior to this deposition starting?
A. Total fees and expenses, I believe, is on the order of $10,000.
Q. Would that include today or just before today?
A. No, that's before today.
Q. And what is your billing arrangement? How do you bill and how much?
A. I bill personally $500 an hour for time.
Q. Does that include travel time?
A. Yes.
Q. Does that include time where you're reviewing materials?
A. Yes.
Q. Does that include testimony time, like here today?
A. Yes.
Q. I understand that you're not going to make it to this trial, if it goes forward in December, correct, because you're going to be out of the country?

A. That's correct.

Q. But if you -- if this case for some reason were to get continued, and you were to make it to trial, do you have a different rate for attending trial?

A. No.

Q. You charge by the hourly basis for coming to trial, or do you have a day rate?

A. Hourly basis.

Q. And would it be fair to say that Mr. Dillard's law firm, Fulbright & Jaworski, has paid your bills up through the beginning of today?

A. Yes.

Q. When did you arrive for your deposition?

A. Yesterday evening.

Q. And have you had a chance to visit with Mr. Dillard or other representatives from United States Steel Corporation to discuss your testimony in this case?

A. I met with Mr. Dillard last night.

Q. Did you-all go to dinner?

A. Yes, we did.

Q. And did you-all visit about the case?

A. Yes.

Q. That's not uncommon between experts and the lawyers that hire them, is it?

A. No.
Q. Have you been provided with the reports by Dr. Nettleson and Dr. Raabe?
A. Yes, I have seen them.
Q. Did you review those?
A. Yes.
Q. And were you aware that some of the opinions that they give are different than what you say?
MR. DILLARD: Object to the form.
A. In some minor degree, yes.
Q. (BY MR. LUBEL) In other words, were you aware that Dr. Raabe has taken the position that benzene exposure does not cause MDS?
MR. DILLARD: Object to the form.
A. That's -- that wasn't -- that's not exactly my impression of Dr. Raabe's -- what I've read in Dr. Raabe's report. I think he correctly points out that there are no quantitative -- there's no quantitative basis to specifically demonstrate the quantitative exposure to benzene, specifically as associated with the development of MDS specifically. A great deal of the basis for concluding that MDS is associated with benzene exposure comes from our knowledge of MDS as a part of secondary AML, and the enormous data base we have with respect to alkylating

chemotherapeutic agents and the development of that disease.

MR. LUBEL: Objection to the nonresponsive portion.

Q. (BY MR. LUBEL) Is it fair, Doctor, for scientists such as yourself to review and rely upon literature on AML in assessing MDS?

A. To the extent that we're talking about AML that is preceded by MDS, and that is described as a specific entity, yes. It's actually a di -- a specific diagnostic paradigm within the WHO classification of hematopoietic lymphoid diseases.

Q. And I take it that one of the reasons for which you're able to hold the opinion that benzene exposures can cause MDS is based upon the AML literature that you're familiar with?

A. That's correct.

Q. All right. Let's talk for a minute about latency period. And I believe that you made a statement that the outside time limit -- limit for latency period is 15 years?

A. It's certainly in terms of the quantitative literature that -- that appears to be an outside number.

Q. Can you pull for us the peer-reviewed studies that state that in order for a malignancy to be related

to benzene, that the malignancy must manifest itself within 15 years of the last exposure?

A. There's no literature that's specifically going to say that. The way in which latency is determined is by looking at the distribution of cases that -- and the time that they occur relative to exposure in studies that have demonstrated a quantitative relationship.

The only study that infers and does not specifically indicate -- actually implies is the proper term -- a latency as late as 15 years, would be Wong update of the original pliofilm study in which the follow-up cases included at least one case that appeared 15 years after exposure. The vast majority of cases conform to the nine-and-a-half to ten-year period that I referred to, and certainly prior to that study, that was the general consensus and can be found in several different places and documents.

Q. But you -- you don't have with you a peer-reviewed published study that states that?

A. States that? No.

Q. Now, if we go back and we look at the Sir Bradford Hill criteria, one of the criteria -- criteria, I believe you referenced was temporal relationship?

A. Yes.

Q. And you've subsumed the term "latency" within that criteria, correct?

A. Latency is in -- is included within temporal relationship.

Q. And the temporal relationship can be important because one of the things that scientists need to look at is whether, in fact, there's been an exposure before the disease onset?

A. That would be the extreme temporal -- I mean, it's a spectrum. But, yes, obviously it's easier to illustrate that temporal relationship than many others. But if the exposure does not precede the onset of the disease, you obviously have a temporal issue.

Q. And that's an important criteria that Sir Bradford Hill surely recognized?

A. Yes.

Q. And you don't differ with that?

A. No.

Q. Let me talk to you about dose response for a minute. Are you familiar with any substances for which there is a dose response relationship; however, at a certain point, as the dose increases, it can overwhelm the system and -- and, in fact, can change the mechanics, if you will, of causation? In other words, a person can have a greater exposure at a certain level

and, in fact, have a reduced risk?

A. In populations, yes. For individuals, it's not really biologically plausible, but for populations, yes. That's well described.

Q. Can you give us some examples of that?

A. Radiation, ionizing radiation. The dose response for leukemia and ionizing radiation has a bell curve at the extreme end of the spectrum.

Q. And what is the bell curve? For people that don't know, where did that --

A. It means that at extremely higher doses, the actual incidence rate goes down. That's well described for agents that are extremely cytotoxic, immunogenic.

Q. What is the scientific explanation for the bell curve?

A. There are two potential explanations, both of which are plausible.

One is that in the case of radiation that the radiation itself is causing other injuries that compete with the incidence of the disease for survival and/or sickness. The other is that they, in fact -- that radiation may, in fact, influence the expression of the disease in individuals as a function of damage.

Q. Have you seen anyone determine Mr. Cowey's dermal exposures?

A. Specifically, no.

Q. Do you have an opinion as to whether or not dermal exposures can contribute to hema -- hematological disorders?

A. Unless a person is wearing respiratory protective equipment, dermal exposure almost never for solvent exposure represents an important factor relative to inhalation.

Q. My point is, is can it contribute to the disease process?

A. Yes, and studies that have basically looked at quantitative benzene exposure, by definition, include dermal as well as inhalation exposure.

Q. And have you brought those studies with you?

A. They -- any of the studies that looked at the epidemiology of benzene, including those I have brought, have as a matter of -- of fact contained within the exposure scenario dermal exposure.

Q. How do they quantify the dermal exposure?

A. The dermal exposure is part and parcel of what the individual is exposed to. Most of the studies are quantitative only airborne exposure, but the dermal exposure is part of those exposure scenarios.

Q. I am not disagreeing with you. I am just asking you in those studies, how did they actually

quantify the dermal exposures?

A. Those studies don't. There are an independent set of studies that have looked at the physical chemical properties of solvent flux through the skin and quantitated benzene, and other solvents specifically, and those studies, as a group, confirm that solvent exposure through the skin, especially for benzene, is a relatively minor component, even at high levels of exposure, inhalation being the dominant exposure.

Q. But you're not suggesting to this jury that dermal exposures are safe and inhalation exposures are not, are you?

A. I am saying that chronic exposure to benzene at concentration -- or to deliver a dose of benzene via the skin that would be consistent with airborne exposures that are associated with adverse health effects, is an extreme phenomenon, and one that's going to be -- that is inconsistent with typical dermal exposure even under conditions of high level inhalation exposure.

Q. But if somebody has got -- has received both inhalation exposures and dermal exposures, you're not telling this jury that the dermal exposures are of zero consequence?

A. I am saying that the major consequence, and

certainly the consequence associated with chronic effects of benzene, is predominantly due to inhalation, and that dermal exposure, to be consistent with levels that we know, or doses that we know cause, for instance, chronic toxicity to the blood or bone marrow, are only consistent with extreme pathology to the skin and are not consistent with relatively short-term or low-level exposure to the skin.

Q. So, if I understand you correctly, in your opinion, the inhalation exposures are far more important than the dermal exposures to the disease process, but you do acknowledge that the dermal exposures may contribute to it?

A. Dermal exposure is going to contribute to a minor extent to the overall body burden or dose of benzene. The predominant exposure -- the root that I believe is most consistent with chronic toxicity of the blood or bone marrow is via inhalation.

Q. All right. Now, I want to talk to you about the studies that you talked about with regard to the shoes.

A. Yes.

Q. How do you refer to those? The shoe making studies?

A. Shoe worker studies is --

Q. What --

A. -- an accurate description.

Q. -- benzene-containing product were they using in those studies?

A. Benzene.

Q. Pure benzene?

A. Pure benzene used as a solvent for dissolving resins, Arbetar-based resins for use as glues.

Q. All right. Well, some -- somewhere in your testimony, I got the impression that you said that they were using benzene-based resins.

A. It's basically -- the same thing is seen in China. You take a resin which is basically an organic substance derived from glue factories, like where they used to take old horses, and you use benzene as the solvent to resuspend and dissolve that, and that's used as a glue for making shoes. It apparently is a very efficient substance for gluing leather.

Q. What percentage of the glue contains benzene?

A. I'm not sure what you're asking me.

Q. Well, you're not saying that the glue was 100 percent benzene, are you?

A. I am saying the glue was made by taking resin and dissolving it in benzene, and using it in an open pot. So, the solvent was benzene.

Q But, how much of the glue was benzene?
MR. DILLARD: You're not understanding him, I don't think, Lance.
MR. LUBEL: I'm probably not. I am not trying to be --
MR. DILLARD: I think you-all are crossing paths.
Q. (BY MR. LUBEL) Let me start over. Were the workers in these studies using glue to manufacture shoes?
A. Yes. And they were making the glue as they went by taking and dissolving resin in benzene.
Q. But are you saying that those studies -- they state that every worker was making the glue, or were there some workers that were just applying the glue, or do you know?
A. The typical situation you're talking about would be a group of people sitting around a table such as this in which they are -- they have a bowl, and they have resin, and they keep pouring the benzene into the resin to keep it in a slurry, and they're spreading it on soles and putting the shoes together. And when they need to do more, they -- then, it begins to get dry, they pour some more benzene in it. So it's basically -- it's a maw-and-paw-type operation.

Q. All right. And what size areas were they working in?

A. Houses, living rooms, kitchens.

Q. How big were these areas?

A. It varies. It varies from individual -- if you read -- if you read the descriptions, the anecdotal descriptions, some of the situations I've seen in China, they vary from very small facilities to extremely large facilities.

Q. Facilities, you mean rooms, houses, kitchens?

A. Rooms, houses, kitchens, factories, workshops.

Q. I am talking about these houses right now. Were any of the -- do you know if any of the windows were open in them?

A. I have no idea what those conditions were other than the descriptions that Aksoy provides.

Q. And in the study does it say whether the windows were open?

A. There are -- they're simply descriptions about the fact that these were family-run businesses, with the -- basically the manufacture of shoes within the house.

Q. Are you familiar with the Paci study?

A. I am not sure what you're referring to.

Q. The Italian study.

A. Paci?

Q. Paci, sorry.
A. Yes. I am in general.
Q. Do you have that with you?
A. No, I don't.
Q. Were you aware that the substance being used in those studies that were -- that was pure benzene?
A. If you've got a copy of it, I would be happy to review it. I am generally familiar with it, but I don't remember the specific with -- it certainly is a -- a -- a work that discusses benzene exposure.
Q. We will just move on. I don't have a copy of it with me.
Did you rule out radiation as a cause of Mr. Cowey's disease?
A. I didn't see any basis to conclude that he had exposure to radiation in the materials that I reviewed.
Q. Did you rule out chemotherapy agents as being a cause of his MDS?
A. In general, as I -- as I recall, in his medical history, if you let me refer to my summary, he received surgery for prostate adenocarcinoma but didn't receive any radiation or chemotherapy. So I did not consider that a potential cause of his disease.
Q. As we sit here today, it's not -- it's your opinion that neither radiation nor chemotherapy induced

his MDS?

A. Yes.

Q. You agree with that?

A. Yes.

Q. All right. Do you agree with Dr. Youman's diagnosis of MDS for Mr. Cowey?

A. The description that he provides is consistent with the diagnosis refractory cytopenia, multilineage dysplasia.

Q. So you agree -- you agree with him on the particular cell type, too?

A. Based on the description, yes. I haven't reviewed the slides, but the description is entirely consistent.

Q. Now, I take it based upon what you told us earlier that you disagree with Dr. Youman when he says that this chromosome 8 defect is common in benzene exposed workers?

MR. DILLARD: Object to the form.

A. It's certainly not consistent with the secondary literature in -- specifically, and the literature concerning solvent exposure in which benzene is a major component.

Q. (BY MR. LUBEL) Have you brought with you any peer-reviewed published studies that state that the

chromosome 8 defect that Mr. Cowey has should not happen from benzene exposure?

A. Again, you're asking me to prove a negative. What I have brought with me are peer-reviewed studies that evaluate the cytogenetic abnormalities, the clonal abnormalities found in individuals exposed to solvents, and trisomy 8, involvement of 8, is extremely rare in exposed individuals and much more frequent in the control.

Q. Now, Mr. Dillard asked you some questions about this 85 percent group --

A. Yes.

Q. -- that I think you've talked about as being the idiopathic group?

A. Yes.

Q. Is that correct?

A. Yes.

Q. Do you know how many people in the idiopathic group, this 85 percent, that were exposed to benzene?

A. All of them at some level of exposure, the question is how much, which is the basic question of dose.

Q. And do you know -- do you have any reliable data that provides us any meaningful information regarding what those people's benzene exposure levels

were within this 85 percent idiopathic group, you have called it?

A. No, neither that nor -- neither any other potential cause.

Q. Have you understood my questions today, and when you didn't, did you try to tell me?

A. Yes.

Q. Have I been courteous to you?

A. Yes.

MR. LUBEL: Thank you for your time. Your turn. Need another break or are you ready?

MR. DILLARD: No, I'm ready. Do you have any questions? Why don't you go ahead with yours?

EXAMINATION

BY MR. RILEY:

Q. Dr. Irons, my name is Jim Riley. I represent Radiator Specialty in this case. I just want to ask you a few questions, basically because of some objections that were made.

My first question is: Dr. Levy has not given his deposition in this case yet pertaining to Mr. Cowey, so obviously you have not reviewed Dr. Levy's testimony pertaining to Mr. Cowey in giving your deposition here today, correct?

A. No, I have not.

Q. And you have -- have you spoken to Dr. Levy about his opinions pertaining to Mr. Cowey?

A. No.

Q. Okay. So, basically, Mr. Dillard was asking you questions about Dr. Levy's opinions, his methodology and his articles, can you tell us whether or not you understood that to mean his eight-page report which you have reviewed?

A. Yes. That was my understanding.

Q. Now, Doctor, I want to ask you one other question, or actually two, it will be. Do you have an opinion that based upon the scientific literature that you have referred -- that you have reviewed in the course of your research, on whether the industrial uses of benzene differed from the 1940s versus say the 1970s?

A. Yes.

Q. And what is that opinion, sir?

A. It differed dramatically.

Q. Dramatically in what way?

A. In the '40s, the accepted levels of exposure, or the permissible levels of exposure to benzene were huge compared to what they were in the '70s, and enormous compared to what they are today. Common usage was much higher.

MR. RILEY: That's all the questions I

have, sir. Thank you for your courtesy.

MR. DILLARD: Dr. Irons, I would like to have marked as exhibits some of the articles to which you have referred in your testimony, and so perhaps we ought to take a quick break in order to do that, and not take up the court or jury's time with it. So let's go off the record for just a couple of moments if we could.

THE VIDEOGRAPHER: Going off the record, time is approximately 1:08 p.m.

(A break was taken.)

(Exhibits 2 through 6 marked.)

THE VIDEOGRAPHER: We're now back on the record. The time is approximately 1:16 p.m.

RE-EXAMINATION

BY MR. DILLARD:

Q. Dr. Irons, I'd like to have marked as exhibits some of the articles to which you have made reference to in the course of your testimony. Can you hand me the stack?

A. Yes, sir.

Q. Thank you. I'll first show you Exhibits 3 and 4, and ask you what those articles -- or for what proposition do those articles stand as you have cited them?

A. Both of these articles describe the

age-dependent incidence of myelodysplastic syndrome in the general population.

Q. All right. I'll next show you Exhibit Number 5, and ask you what -- what that is?

A. That is a publication of mine that deals with Dideoxycytidine, which is the parent compound in the experimental drug that Mr. Alley was treated with.

Q. Mr. Cally -- Cowey?

A. Cowey, I'm sorry.

Q. And then what is Exhibit 6, please, sir?

A. This is a recent publication out of the University of Chicago that deals with the clinical and cytogenetic associations of therapy-related myelodysplastic syndrome and acute myelogenous leukemia.

Q. There is also a collection of articles to -- just to your right, what -- what are those?

A. They're simply copies of some of -- a few of the articles that are in the binder of articles that I provided.

Q. Okay. What are their reference numbers, of those articles in your binder which has been marked as Exhibit Number 2?

A. 30, 31, 32, and 39.

Q. For what proposition do those articles stand?

A. These articles describe the relative incidence

of cytogenetic abnormalities in individuals developing leukemia associated with solvent exposure versus those who developed leukemia without any known exposure.

Q. Is this this 85 percent versus 15 percent that was talked about earlier?

A. In relation to MDS, yes.

Q. And did they -- do these articles that you have just referred to support the opinions that you expressed?

A. Yes.

Q. I want to ask you about the Hayes paper published in the year 2000. You're familiar with it?

A. Yes.

Q. Does the United States Environmental Protection Agency use that study for evaluating the risk of benzene exposure?

A. No. They don't.

Q. What has the United States Environmental Protection Agency said about the value of that study in evaluating the risk of benzene exposure?

A. Based upon the lack of direct industrial hygiene and analysis of benzene exposure, in that overall study, the U.S. EPA has determined that it's not a reliable tool for use in quantitative risk assessment of benzene.

Q. Was myelodysplasia, or MDS, as we've referred to it here, recognized as a disease entity in the 1940s?
A. No.
Q. What benzene exposure levels were considered harmful in the 1940s?
A. Depending upon exactly when acceptable exposure levels were at 100 parts per million, and by the end of the '40s, they were -- it was generally accepted that they should be reduced to below 50 parts per million.
Q. And what did the API say in the 1948 publication about exposure levels that were recommended?
A. My recollection is they recommended that exposures be reduced to below 50 parts per million.
Q. And how was -- how would that compare to the recognized exposure levels today?
A. The PEL in the United States today is one.
Q. What is PEL?
A. The permissible exposure limit in an occupational setting. So that would be 50 times higher.
Q. Are you familiar with the testimony of Dr. Vernon Rose on behalf of Mr. Lubel in this case?
A. Yes.
Q. Did Dr. Rose state that he was asked to address an exposure assessment in this case?

A. I don't recall specifically what he said he was asked to do. I do recall specifically that he indicated he had not done so.

Q. I was going to ask you that. Did Dr. Rose provide an exposure assessment of Mr. Cowey's alleged exposure to benzene from Liquid Wrench?

A. My recollection is he said that he couldn't.

Q. Did Dr. Levy in his report provide such an assessment?

A. No, sir.

Q. Based upon the literature, which you've referred to as the quantitative literature that's published in the reliable scientific journals, what is the observed cumulative benzene level that is associated with a significant excess of the disease that is called AML/MDS?

A. Well, if you look at -- if you look at the quantitative studies combined, and you look at statistical significance, the lowest cumulative exposure level that's been consistently demonstrated to produce a significant excess is 60 ppm years, 60-per-part-million years.

Q. Is there any scientific evidence that Mr. Cowey's benzene exposure, if any, met or exceeded that level?

A. Not to my knowledge, no.

MR. DILLARD: Thank you, sir. Pass the witness.

RE-EXAMINATION

BY MR. LUBEL:

Q. Dr. Irons, can you go ahead and pull out your reference that -- I think you made a statement that the EPA does not follow the 2000 Hayes and Yin study. Do you have that with you?

A. No, I don't.

Q. Okay. Is there a study that says that study is not of any value?

A. It's an official EPA publication, and it does state that in performing risk assessments, quantitative risk assessments associated with benzene and leukemogenesis, that the Hayes study is not an appropriate tool.

Q. Now, do you know whether this EPA, this alleged EPA statement, refers to one of the older studies as opposed to the 2000 version?

A. It refers to the study. There are numerous papers relating to the study, but the original study criteria and design and analysis remain the same. I believe the EPA ruling was 1996.

Q. Okay. Were you aware that the paper that was

actually published in 2000 had refined information from the previous work?

A. I couldn't speak to that. Whether or not they performed any additional analyses or not, I couldn't say.

MR. LUBEL: That's it. Thank you.

MR. DILLARD: Thank you, sir.

THE VIDEOGRAPHER: Going off the record, time is approximately 1:24 p.m.