IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF TEXAS
GALVESTON DIVISION

FLOYD L. CHAMBERS, ET UX,
VS. C. A. NO. G-S9-306
MONSANTO CHEMICAL COMPANY ET AL.

INSTANT ACCESS TRANSCRIPTION

VIDEO DEPOSITION OF:
RICHARD D. IRONS, PH.D.
FEBRUARY 4, 1991

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VIDEO DEPOSITION OF RICHARD D. IRONS, Ph.D., called as a witness by Defendant Marathon Petroleum Company, taken before Emanuel A. Fontana, Jr., Certified Shorthand Reporter in and for the State of Texas, in the law offices of Goforth & Lewis, 2200 Texaco Heritage Tower, 1111 Bagby, Houston, Texas, on the 4th day of February, 1991, beginning at 10:12 a.m., pursuant to Notice, the Federal Rules of Civil Procedure and the following stipulation and waiver of counsel:

A P P E A R A N C E S

Mr. Martin D. Barrie, of the law firm of Messrs. Umphrey, Burrow, Reaud, Williams & Bailey, 8441 Gulf Freeway, Suite 600, Houston, Texas, 77017-5001, appearing for the Plaintiffs.

Mr. James B. Galbraith, of the law firm of Messrs. McLeod, Alexander, Powel & Apffel, 802 Rosenberg, Galveston, Texas, 77553, appearing for Defendant Marathon Petroleum Company.

Mr. Joe G. Hollingsworth and Ms. Evelyn J. Pulliam, of the law firm of Messrs. Spriggs & Hollingsworth, 1350 I Street, N.W., Washington, D.C., 20005-3305, appearing for Defendant Marathon Petroleum Company.

Mr. Robert P. Scott, of the law firm of Messrs. Sewell.& Riggs, 333 Clay Avenue, Suite 800, Houston, Texas, 77002, appearing for Defendant Monsanto Chemical Company.

Mr. Daniel O. Goforth, of the law firm of Goforth & Lewis, 2200 Texaco Heritage Plaza, 1111 Bagby, Houston, Texas, 77002, appearing for Defendant Monsanto Chemical Company.

ALSO PRESENT:
Mr. Steve Schuller, Videographer
Mr. Stephen L. Moll

IT IS STIPULATED and agreed by and between counsel for the respective parties hereto that the deposition of the witness named-in the caption hereto may be taken at this time and place before the officer named in the caption hereto; that said deposition, or any part thereof, when so taken, may be used on the trial of this case with the same force and effect as if the witness were present in court and testifying in person;

THAT the necessity for preserving objections at the time of taking is waived, and that any and all legal objections to this deposition, or any part thereof, may be urged at the time same is sought to be offered in evidence on the trial of this cause; except, however, that objections to the form of the question and/or responsiveness of the answer must be made at the time of taking, or else such objections are waived;

THAT the original of this deposition shall be presented to Mr. Galbraith, who shall in turn submit it to the witness for his examination and signing and, thereafter, shall return same to the officer taking this deposition;

THAT if the signed original is not presented to Mr. Galbraith prior to the time of trial, a copy may be used in lieu thereof.

RICHARD D. IRONS; Ph.D.,
was called as a witness by Defendant Marathon
Petroleum Company and, being first duly sworn,
testified as follows:

DIRECT EXAMINATION
QUESTIONS BY MR. GALBRAITH:

Q. Can you please tell your name, please,
sir?
A. Richard D. Irons.
Q. How old a man are you, sir?
A. I'm 43.
Q. Where do you live?
A. Boulder, Colorado.
Q. Dr. Irons, you understand that you're
called upon to give your testimony in a
deposition here today in a lawsuit that's been
filed against my client, Marathon, and Union
Carbide and Monsanto --
A. Yes, sir.
Q. -- three chemical plants?
And you have been contacted by us,
attorneys for Marathon in this lawsuit, to give
your opinions based upon your review of certain

documents and your experience in this field?
A. That's correct.
Q. Tell us about your -- well, I guess what I want to ask now is: What is your field? And tell me about your background, your educational background and your present employment.
A. Well, I'm a toxicologist. I am Director of the Molecular Toxicology and Environmental Health Sciences Program at the University of Colorado Health Sciences Center. I have a Ph.D. in Toxicology from the University of Rochester, in Rochester, New York. And I have spent the last 14 years studying the mechanisms of toxicity to the blood and bone marrow primarily associated with benzene and the mechanisms of benzene leukemogenesis.
Q. Okay. First of all, let me back you up there. You said Director of the Department of Molecular Tech -- Toxicology. Excuse me. Tell me what that entails.
A. Well, the Molecular Toxicology Program at the University of Colorado is a program that involves research, teaching and service associated with toxicology and environmental health. It is based in the School of Pharmacy,

and I have appointments as Professor of Toxicology in the School of Pharmacy and as Professor of Pathology in the School of Medicine.
The major teaching obligations we have are to train Ph.D. level toxicologists, to provide teaching in toxicology for individuals training in epidemiology. This will be graduate students and/or clinicians and these that wish. additional training in occupational health and epidemiology.
And we provide teaching and training in toxicology for graduate students undergraduate students in pharmacy, and medical students.
Q. Okay. Teaching students of medicine as well as students of pharmacy and pharmacology?
A. Yes, sir. 18 Q. In addition to your -- you said three things, research, teaching and service --
A. Yes. 21 Q. -- were involved in your position as Director of Molecular Toxicology and Environmental Health Sciences.
Tell me what-you mean when you say your position involved service, first of all.

A. Oh, the service we provide involves a variety of different activities. It involves providing expertise to the public and state agencies related to environmental health issues n toxicology, to the Department of Health, to the Governor's office on issues of concern to the public and Government agencies related to environmental health within the State. It involves providing, actually, expertise for the University, in terms of meeting its commitments with respect to occupational and environmental health.
Q. Okay. And research, the third leg of your --
A. Yes. 16 Q. -- involvement, tell me about that. What does that involve?
A. The program itself has very broad-based research activities in the general area of toxicology, with an emphasis on mechanisms of toxicity, how chemicals cause adverse effects. My own research program involves three major areas. First and foremost, again, is an extension of the work I've done for the past 14 years or so studying the role of the regulation

of stem cells in the development of diseases of the blood, principally leukemia. Stem cells are the cells that are responsible for making all of our blood cells, and they are intimately involved in a variety of processes, both normal and abnormal. And a -- a good part of my work involves studying the alterations that occur in stem cells following exposure to toxic agents, be they chemical, such as benzene, or drugs.

I have two other programs that I'm currently working on. One involves, again, characterizing changes in the blood-forming organs that are associated with extended space flight. It's been found that -- that the immune system and the blood system is susceptible to alterations that are associated with conditions in space that are of importance to understand in the design of future extended space missions.

Another area that, again, is related involves developing strategies for the purification, separation of stem cells from patients for use in bone marrow transplantation. And that's another area that we're actively working on at the present time.

Q. All right. How long have you been the Director of the Department of Molecular Toxicology and Environmental Health Sciences at the University of Colorado Health Sciences Center?
A. It's a program technically, not a department.
For the last slightly over two years.
Q. Okay. Now, you mentioned that your research regarding cause of diseases, in terms of chemical causes of diseases, has gone on for longer than that.
A. Yes, sir.
Q. Tell me what preceded your directorship of the department -- of the Program of Molecular Toxicology and Environmental Health Sciences.
A. Well, following my graduation from the Toxicology Program at Rochester, I was a fellow in the Department of Pathology at Strong Memorial Hospital in Rochester, New York. And there I trained in general pathology, immunopathology and hematopathology.
General pathology is pathology - general pathology, pathology covering a wide range of topics, nothing in particular.

Q. Pathology, in your t6rms, meaning exactly what?
A. The pathogenesis of disease. The structural and functional alterations that occur in the body and the body tissues, as a function of disease in the progression of disease.
In addition, I trained, in terms of specialty, in immunopathology and hematopathology, which is pathology that is special -- a specialized area of pathology that deals with diseases of the immune system and the blood-forming organs.
I then went to the Chemical Industry Institute of Toxicology in Research Triangle Park, North Carolina, where, for 12 years, I was responsible for and directed studies to understand the mechanisms of benzene toxicity in particular, as well as the effects of a variety of other compounds on the blood and the immune system.
Q. Okay. You mentioned that you had your doctorate degree, Ph.D., in pharmacology and toxicology.
A. Toxicology. Q. Okay. Tell me, what preceded that, in

terms of education? You don't just jump out there and get your Ph.D. as your first degree. What preceded?
A. I obtained my bachelor's degree from Raymond College, University of the Pacific in Stockton, California, where I specialized in liberal arts, chemistry and political science. I then obtained advanced training and certification in medical technology and diagnostic hematology, laboratory diagnostics, before going to the University of Rochester.
Q. All right. At the Chemical Industry Institute of Tech -- Toxicology, tell me what that organization is, first of all, in Research Triangle Park, North Carolina.
A. It's a nonprofit institute that is dedicated to research and training in toxicology. It was founded by the chemical industry as an institute that could provide basic mechanistic, basic research studies on mechanisms of toxicity of hazardous agents and initially was funded solely by the chemical industry. It's now diversified in its support and is, as I understand it today, funded from a variety of different sources, including Federal

Government, industry, and what have you.
Q. The purpose is solely to do scientific research?
A. Yes, sir. Q. Okay. And while you were there, your area of scientific research included what?
A. As I said before, my principal area of research involved studying the mechanisms of toxicity to the blood and bone marrow, primarily associated with benzene, as well as a variety of other compounds and chemicals that produce effects on the blood and immune system.
Q. Looking at how benzene acts on blood and bone marrow?
A. Yes, sir. Q. Okay. Do you have any particular licenses or board certifications within your field?
A. I'm certified in medical technology, and I'm also board certified by the American Board of Toxicology.
Q. Tell me what it means to be board certified by the American Board of Toxicology.
A. The American Board of Toxicology is an organization that reviews the academic and

training credentials of toxicologists and
administers a board examination to determine
their qualifications to practice toxicology.
Q. How long have you been certified, board
certified?
A. I was certified in, I believe, 1981, so
ten years.
Q. Okay. Tell me about some of the
Government activities or Government -- Government
programs you have been involved in, please.
A. Well, I have had considerable experience
in what we call the peer-review process, which is
the process whereby scientists review the
scientific merit of other scientists' research
proposals that are submitted to various agencies
for consideration for funding, grants, if you
will.
I've served on a number of Government
bodies that are responsible for reviewing these
applications. For example, I've served as
Chairman of the NIH Toxicology Study Section.
This is the -
Q. First of all, excuse me. What is the
NIH?
A. National Institutes of Health.

Q. Okay. 2 A. The National Institutes of Health is --
is probably the single most important funding
source for research in the medical sciences, and
also one of the major sources of funding for
research in toxicology.
I served as the Chairman of the body
that is responsible for reviewing those
applications on the basis of their scientific
merit.
I also currently serve as a member of
the Environmental Protection Agency Health
Effects Review Panel, which has a similar
function for the Environmental Protection Agency.
Q. How is it that you came to be called
upon to serve in the peer-review capacity; in
other words, to look at other scientists'
projects and determine whether they have merit or
not?
A. A peer review is a very important aspect
of the whole process of research and the
publication of scientific research in the United
States. Papers that are submitted for
publication, manuscripts, if you will, that are
submitted by scientists to a journal will be

reviewed by independent reviewers to determine whether or not it's accurate, whether it's well presented, whether the experiment has been designed properly, and basically that the work says what the author thinks it says.
Peer review is a necessary pre -- prerequisite for maintaining the quality of the scientific literature, and also to evaluate the quality of proposed research.
As a scientist enters a field, he will be -- as he publishes work, he will be recognized for that. And as he publishes high quality science, he will be recognized by being asked, first of all, to review papers for a journal.
And this will continue. And, in fact, he may be asked by a Government body to participate in this kind of activity, based upon his experience in the field and his publication record.
MR. BARRIE: Let me object to the nonresponsiveness of the answer.
Q. (By Mr. Galbraith) Okay. If I understand correctly what you're telling me, then, it's you get asked to serve on these peer-review committees, passing upon the merit of other scientists' work, based upon, first, you

having published, successfully, I guess, with recognition --
A. That -- that is a prerequisite, yes.
Q. Okay. Are there any authoritative periodicals in your field to which you contribute?
A. Oh, yes, several. Probably first and foremost is the -- is "Toxicology and Applied Pharmacology," which is the premier journal in toxicology today. And I serve as an associate editor for that journal at the present time.
Q. What do you do, in your capacity as Associate Editor of "Toxicology and Applied Pharmacology"?
A. As an Associate Editor, I'm responsible for selecting reviewers, for reading the comments of reviewers and making my own evaluation of manuscripts that are submitted and rendering a judgment as to whether or not the manuscripts are appropriate for publication, whether they are not, or whether they need to be revised in some fashion prior to publication.
Q. Okay. Do you contribute in this fashion to any other publications?
A. I serve as an editor for the journal,

"Cell Biology and Toxicology. I serve on the editorial board of a number of other journals, including the journal of "Experimental and Molecular Pathology." I've served on review boards and in various editorial roles on a number of journals in the past, as well.
Q. I confess to having been given a copy of your curriculum -- your resume, and I would ask that that copy be marked as Exhibit 1. Could I present it to you now?
Is that a copy of your curriculum vitae or resume?
A. Yes, it is. I believe it is not the most current version.
Q. Okay. Approximately how up-to-date is that copy?
A. I suspect it's a year old.
MR. GALBRAITH: Okay. Let me hand it to the court reporter now and ask that it be marked, please, sir.

(Whereupon, the instrument referred to by counsel was marked for identification as Irons Exhibit No. 1.)

MR. GALBRAITH: Thank you.
Q. (By Mr. Galbraith) Refer to it, I guess, if you need to.
Are there organizations, scientific organizations or organizations involving those in similar research and in similar scientific study that you have participated in?
A. I'm a member of several professional societies. The Society of. Toxicology, which is a -- the principal professional group to which toxicologists in the United States belong. I belong to the American Association of Pathologists, which is the principal academic society that pathologists belong to.
I've been elected a member of the International Society of Experimental Hematology, which is a group of -- it's an international society that includes individuals who are active in doing research in hematology.
Q. Okay. Let me ask you about that International Society of Experimental Hematology.
First of all, what's hematology?
A. Hematology is the study of diseases of the blood and normal blood production. It's the

study of the blood, both normal and abnormal.
Q. Okay. How was it that you came to be involved in the International Society of" Experimental Hematology?
A. On the basis of the research that I've done, I was asked to join by some of the members of the Society, and was elected to membership in that Society.
Q. What does that membership involve? What does it do for you, and what do you do for it, I guess?
A. I attend meetings, annual meetings in which research in hematology is discussed. I correspond with and occasionally collaborate with other members of the Society on research we have a mutual interest in. And I take the journal that is published by the Society.
Q. Okay. You have mentioned that in your present position, you have some academic teaching responsibilities of medical students and pharmacology students. Have you had any other academic-type positions or experience?
A. I've -- I'm involved, at the present time, in designing a course in toxicologic pathology, which is pathology specializing -

that specializes in the adverse effects of chemicals or agents on the body and its tissues.
I lecture frequently in a variety of different courses. I've lectured at Duke University in toxicology and in occupational medicine. This past year, most recently, I've lectured at the University of Nebraska, at Johns Hopkins University and at Rutgers University.
I lecture probably four or five times a year in other programs and universities, and I'm currently lecturing in the Epidemiology Program in the School of Medicine at the University of Colorado.
Q. Okay. What does it mean -- I notice in your resume here you've got a number of post-doctoral fellows. Tell me what those are and what they mean.
A. Those are individuals that have trained in my laboratory after obtaining their doctoral degrees, either an M.D. or a Ph.D., and have gone on to careers in the field.
Q. Okay. Tell me -- I notice in your resume you've got a number of research interests, some in sciences and some in applied sciences.

Tell me what the distinction is there.
A. Well, basic science really deals with understanding mechanisms of how the body and the cells of the body work, how they are regulated and how they function, and how diseases are initiated and how they progress and, hopefully, in some respects, what strategies can be used for treating them.
Applied -- applied science deals with the use of this knowledge in a more practical vein, if you will, in terms of some immediate practical objectives, such as the use of a method to obtain an end such as diagnosis, or the development of techniques for use in basic science.
Q. Okay. I'm looking through the pages here of the books, book chapters and published articles, and I keep seeing recurrent themes, such as, first of all, toxicology, hematology, blood, bone marrow, and even some leukemia or leukemogenesis. And here's a benzene or two sprinkled around among the titles of these books and articles.
Tell me, what's the interrelationship between all those things, and why do I keep

seeing them here?
A. Well, the reason you keep seeing them is because my principal area of research interest is the blood and bone marrow and the immune system, which are all interrelated. And it's well known that, at high concentrations of exposure, chronic exposure, benzene will cause toxicity to the bone marrow. And that's been one of my principal areas of research and expertise now for many years.
Q. Okay. What is the relationship between leukemia and blood or bone marrow?
A. Leukemia is, in -- to put it very crudely, or simply, cancer of the blood or bone marrow. And there are several different types of leukemia that differ with respect to their origin, their prognosis, what the process of the disease is, the cells they involve, and their ultimate -- the ultimate outcome of the disease. Leukemia is one of my principle areas of research interest.
Q. Okay. Do you have any particular scientific research project ongoing at present, that is, occupying a good bit -- bit of your interest?

A. Yes. As I mentioned earlier, I have three different research projects that are underway at the present time.
Q. Okay. Talking about regulation of stem cells?
A. Yes.
Q. Okay. I remember that now.
As a result of us calling upon you in this lawsuit, what documents have you had an opportunity to review, as they might relate ;to this case?
A. I reviewed the -- what I believe is the First Amended Complaint. I reviewed the medical records of Mr. Chambers. I reviewed summaries of the depositions of Mr. and Mrs. Chambers. I reviewed the depositions of Dr. Savitz and Dr. Fehir, and I've reviewed the medical literature and scientific literature that I feel pertains to the issues that are involved here.
Q. Okay. Have you come to a conclusion -- or what is the basis of your understanding about what exposures, if any, Mr. Chambers is alleging?
A. It's my understanding, from my review of those records and from discussions that I've had both with you and with Mr. Scott, that the --

there are alleged exposures to benzene Mr. Chambers had while -- during the course of his employment.
Some of those seem quite remarkable or unique to me, in terms of my experience with the industry, so he has alleged that he has been exposed to benzene under some fairly outrageous circumstances.
Q. Okay. Which exposure do you reference there?
A. I believe there's -- there's a reference to 55-gallon drums of benzene that were made available for washing hands and tools, which --
Q. Why -- why do you find that outrageous, I believe, as you said?
A. Well, in my experience, I've never known that to be a practice of the industry. That would be outlandish to me.
Q. What is your knowledge about 55-gallon drums of benzene?
A. Knowledge of fifty-five thousand -
Q. Fifty-five -
A. Fifty-five gallon -
Q. -- gallon drums.
A. It would be an extremely -- I can't

think of a use for that much benzene except in an industrial commodity use. I can't -- using it in those quantities for -- for cleaning is outrageous, to me.
Q. Okay. Well, let me just ask you: As a result of your review of these documents in this case and a result of your prior experience and your research itself, have you arrived at any opinions as they relate to this lawsuit?
A. Yes.
Q. What -- what are those opinions or conclusions?
A. I have reached two opinions in this case.
The first is that chronic lymphocytic leukemia is not caused by exposure to benzene.
And the second is that more probably than not Mr. Chambers' chronic lymphocytic leukemia began shortly after birth, or before.
Q. Okay. Let me take those one at a time.
You first concluded that in this case, or in general, I guess you would say, chronic lymphocytic leukemia is not caused by exposure to the chemical benzene?
A. That's correct.

Q. What is the basis for that opinion?
A. There's no reliable evidence to suggest that CLL or chronic lymphocytic leukemia is caused by benzene or, for that matter, any other agent, and there's considerable evidence to indicate that it is not.
This is a widely held view in the medical and scientific community. It appears in -- it's supported by the original literature. It's supported by the review literature. It is a textbook concept as recent as this year. This is a widely held opinion.
Q. Okay. You said two things. Number one, there's never been evidence, reliable evidence to support a relationship between benzene and chronic lymphocytic leukemia.
And, two, there is evidence to show the absence of a relation -- of a causal relationship.
A. That's correct.
MR. BARRIE: I object to counsel testifying for this expert.
Q. (By Mr. Galbraith) Did I understand that correctly?
A. Yes, sir.

Q. Okay. First of all, when you said even textbooks as recent as this year have refuted the relationship between chronic lymphocytic leukemia and benzene, to what did you refer?
A. There -- well, I can show you, if you would like. There are a number of recent reviews in textbooks which reiterate a commonly held opinion that, in fact, there are no known causes of chronic lymphocytic leukemia.
For example, radiation, which is generally regarded as a universal leukemogen, an ionizing radiation, and exposure to ionizing radiation is known to lead to the development of a variety of different types of leukemia.
Chronic lymphocytic leukemia is distinguished among these in not being caused by even exposure to radiation.
Q. So -- I want to make sure I understand that. So things like radiation that cause other leukemias are known not to cause chronic lymphocytic leukemia?
A. Yes, sir. Q. And radiation is one you cited, and benzene --
A. Right.

Q. -- is another you cited?
A. Yes.
Q. Okay. Go ahead, if you would, tend point to me the textbooks that -- to which you can now have reference, let's say.
And recent reviews, I believe, is what you referred to.
A. Yes. Well, the first one that reflects on this is a review by Drs. Foon, Rai and Gale that was published in October of 1990 in the "Annals of Internal Medicine." And it's a review article on Chronic Lymphocytic Leukemia: New Insights into Biology and Therapy."
Q. What is the significance of that publication?
A. It's representative of any number of recent publications that review the state-of-the-art with respect to CLL. And it's very consistent with -- it's representative of all of them. I can --
Q. What does it provide or say that is consistent with other research?
A. Well, the -- with respect to the questions that we're discussing now, there's a statement here which I think summarizes it quite

succinctly. Can I read it?
Q. I wish you would, please.
A. Okay.
"The cause of chronic lymphocytic
leukemia is unknown. Unlike other forms of
leukemia, the incidence of chronic lymphocytic
leukemia is not increased by exposure to
alkylating drugs, radiation or chemicals." I,
Q. Okay. All right. You've got before you
there a three-ring binder. What is -- what is
 that?
A. It's a collection of articles from the
literature that I put together in support of the
views that I presented here.
Q. Could I -- could I take a look at that?
A. Certainly.
Q. All right. This -- this constitutes
articles that you have pulled from what types of
 sources?
A. Primary scientific literature, the
medical literature. There are also some reviews
this there, recent reviews of the literature.
A review would be an article that
summarizes existing knowledge, as opposed to
being an original scientific article.

I also have some expert -- excuse me, excerpts from a recent pathology textbook which simply illustrates that the -- the current -- our current understanding of biology and nature of CLL is, as I have said, and, in fact, is what is taught as state-of-the-art in the typical general pathology textbook.
Q. Is that what I'm looking at here, entitled "Pathology" by Drs. Rubin and Farber?
A. Yes. 11 Q. Okay. I see something from the "American Industrial Hygiene Association Journal."
A. What -15 Q. Do you recall that? It's abbreviated, and I take that to be "American Industrial Hygiene --
A. Yes.
Q. -- "Association Journal"?
A. Yes, yes, yes.
Q. Okay. I'm not going to go through these individually. "American Journal of Industrial Medicine," is that also referenced?
A. Yes. 25 Q. What is the "American Journal of

Industrial Medicine"?
A. It's a journal that publishes articles on medicine, that is, basically specialties in occupational medicine or diseases and/or problems associated with occupational exposure.
Q. You've got here an article on chronic lymphocytic leukemia in the "American Journal of Hematology." What is the "American Journal of Hematology," if I can ask?
A. The "American Journal of Hematology" is one of the premier journals in hematology. It publishes clinical studies on hematology, as well as some experimental work. Primarily clinical work.
Q. Okay. Apparently, you have articles from a hematology journal entitled "Blood," as well as from a textbook entitled "Blood." Is that right?
A. "Blood" is, again, another very well-regarded journal in hematology.
Q. There are a large number of articles. Could I simply ask -- could we, with your permission, have this marked as Dr. Irons' Exhibit No. 2?
A. Yes. I should mention, as well, that

I've brought a very recent version of a text which is entitled "Leukemia" and is devoted entirely to the issue of the biology and clinical manifestations of leukemia and the various types of leukemia that also reflects the opinions that I have in this case.
Q. That you've told us about a moment ago?
A. Yes.
Q. In fact, that's a 1990, as a matter of fact.
A. Yes. It's a very recent edition.
Q. Published by a Dr. Edward S. Henderson, a medical doctor of the State University of New York at Buffalo, in Buffalo, New York, and T. Andrew Lister, a medical doctor from the Department of Medical Oncology, St. Bartholomew's Hospital in London, England.
A. Yes. 19 Q. Okay.

(Whereupon, the instrument referred to by counsel was marked for identification as Irons Exhibit No. 2.)

Q. (By Mr. Galbraith) You said that there

was no known cause of CLL. I've heard chronic lymphocytic leukemia referred to as "idiopathic." Are you familiar with that term?
A. Yes.
Q. What does it mean?
A. That is a fancy word that simply means there's no known cause.
Q. Okay. Has benzene itself been looked at as a possible cause for chronic lymphocytic leukemia?
A. Oh, yes. Benzene is known to cause acute myelogenous leukemia, which is a different type of leukemia in some people who are exposed to high concentrations for long periods of time. That relationship is generally accepted and widely established.
As a result of that, the hypothesis, or the suggestion that benzene might be the cause of other types of leukemia, specifically CLL, has been the point of departure, if you will, for a number of different studies, studies of individuals in industry, a wide variety of different types of studies, and epidemiology studies. So that it's a reasonable -- it has been a reasonable hypothesis that that might be

the case.
But these studies have not borne that out. And, in fact, there are a number of studies which suggest that benzene is not associated with CLL.
Q. Okay. If you can, quickly, in a shorthand fashion, if it's possible, tell me the difference between a myelogenous leukemia and a lymphocytic leukemia?
A. In shorthand fashion? Okay.
Q. I apologize for the question, but I don't withdraw it.
A. There are bone marrows responsible for making all the different type of blood cells that we have, and it's ultimately responsible for also making the cells of our immune system, the lymphocytes. These all are produced, ultimately, by a single type of cell, called the pluripotential stem cell. It's capable of giving rise to all the different types of blood cells through a fairly complicated process of development.
The first step in this development is the production of two different types of progenitor cells, or -- or stem cells, lymphoid

cells and myeloid cells.
Myeloid stem cells are the cells that are responsible for making red cells that carry our oxygen; white cells, the granulocytes and macrophages, these are cells that are associated with helping us fight off infections; and platelets, which keep our -- which cause our -- which cause clotting and keep us from bleeding.
On the other side of the coin, there's a cell called the lymphoid progenitor cell, or stem cell, that is responsible for giving rise to lymphocytes, which are our immune system, comprise our immune system.
And these are two separate lineages or directions or pathways that these cells-can take. So our blood, in terms of its origin, is separated into two major compartments, the lymphoid compartment and the myeloid compartment, and then there are a number of other compartments that branch out from these.
¢. What you're telling me is such things as radiation and certain chemicals like benzene may have an impact or an effect upon myeloid cells, that radiation or chem -- certain chemicals don't have on lymphoid cells?

A. And -- yes. Yes. Well, not exactly to that degree. Radiation can have effects on -- on the development of a variety of different leukemias, principally myeloid, but not restricted entirely to the myeloid lineage. But it has never been associated with chronic lymphocytic leukemia.
Q. Okay. All right. You mentioned that there was considerable evidence to show that benzene doesn't cause chronic lymphocytic leukemia.
A. Yes.
Q. To what did you refer?
A. The principal quantitative studies that have been conducted in this area have been conducted in the rubber industry, and the rubber industry is unique in -- with respect to the types of neoplasms that have been seen in the rubber industry, compared to those that have been seen in conditions where you have relatively pure exposure to benzene, because it's a very complicated work environment and numerous agents and numerous compounds to which an individual is potentially exposed in that situation.
Initial -- as I said, the hypothesis, if

you will, that benzene was associated with lymphoid neoplasms formed the point of departure for studies in this area. The most --
Q. Meaning studies were undertaken to see if --
A. If
Q. -- benzene had a relationship with chronic lymphocytic leukemia?
A. That's correct.
Q. Okay.
A. Or lymphoid neoplasms in general.
Q. Okay.
A. Many of these studies, most of them have not distinguished between chronic lymphocytic leukemia and acute lymphatic leukemia or lymphosarcomas, a variety of lymphoid neoplasms, so it's difficult to segregate out the various diseases within the broad category.
One study that purported to show a -- a potential effect with respect to benzene and lymphoid neoplasms, and maybe CLL was a study by McMichaels at the University of North Carolina.
Now, this study, a major criticism of this study is that efforts were not made to really quantitate or evaluate potential exposure

to benzene very well. And this study suggested that there might be an increased incidence of lymphoid neoplasms in the population of tubber workers.
Now, this study was followed up by the same group with some case control studies that looked very carefully at the exposure histories of these individuals. And the -- the principal authors on these two studies were a Dr. Wilcosky and a Dr. Checkoway. And these are all from the University of North Carolina.
These studies determined that, in fact, the greatest association with the lymphoid neoplasms was not benzene, but was, in fact, related to other solvents. Whether or not those findings will bear up under the test of time is anybody's guess, because those particular agents have never been associated previously with leukemia. But the principal importance of those studies is that they demonstrate, that with very careful evaluation of the exposure groups, benzene was not associated with any increased incidence of lymphoid neoplasms.
That's consistent with the fact that the pattern of neoplasms seen in rubber workers is

not the same as is seen in individuals who have been exposed chronically to benzene in the past.
Q. Okay. Any others that you can point to me?
A. Well, I think -- I think that summarizes, in general, the -- the most reliable datasets that we have.
There are numerous other studies that have impacted on this subject. There are, for instance, nonquantitative studies involving collections of cases which are not very useful for quantitating or determining causation, but, nevertheless, point to the same pattern, where the hypothesis was, in fact, that one would expect to see a relationship between benzene exposure and CLL. And, in fact, when populations have been examined where the exposures were very high, you, in fact, see fewer CLL than you do in the normal population.
So there's really no substantive evidence to support that link.
Q. Okay. All right. Now, I want to ask you about your second opinion that you mentioned some time ago.
You said that it was your opinion, based

on your review of information in this case, that the chronic lymphocytic leukemia process in Mr. Chambers himself started before birth or shortly thereafter. Tell me what you mean by that, first of all.
A. Well, I arrived at this opinion by performing what is called a "lymphocyte doubling time analysis."
Q. What is a "lymphocyte doubling time analysis"?
A. Well, chronic lymphocytic leukemia is unique amongst the leukemias in that the rate at which the tumor cells increase in number is very constant, the kinetics of cell replication, when cells -- cells make other cells simply by dividing. And this process, in some leukemias, such as acute myelogenous leukemia, is very fast and very rapid and very complex, in terms of the rate at which the cells divide. In --
Q. In other words, the rate at which the myelogenous leukemia progresses?
A. Yes.
Q. Okay.
A. Yes. In the case of CLL, the cells replicate at, that is, they divide at a

relatively slow rate. And the principal cell type that's seen, that's associated with the disease, is actually a very long-lived cell that does not divide very rapidly at all.
The total cell number, abnormal cell number in a patient increases slowly as the di -- disease progresses. It's been demonstrated that a very reliable indicator of the -- the prognosis, or the.-- how the patient is likely to fair, is the lymphocyte doubling time.
This involves making an estimate of the patient's total tumor cell body burden, the number of cells in his body, based on his peripheral blood count, with time.
If you look at any individual blood value, especially in a patient with CLL, it may or may not really reflect, at that moment, what the overall progress of the disease is. And, in fact, the lymphocyte count, if you will, this is a disease of lymphocytes, is not a very reliable indicator of how the patient is doing or will do.
The doubling time, however, relates to an estimate of the total number of cells that are abnormal within the person, and with time, that's

proven to be a very reliable prognostic indicator, and it's reliable because it's so constant.
Q. Okay. You -- where has it -- where does it come from, that you have the -- your information about the doubling time and its constancy --
A. Well -9 Q. -- or how reliable doubling time is with chronic lymphocytic leukemia?
A. There's considerable literature on the subject that has been published over the last decade or two. And this -- the interest here is developing very useful indicators of how a patient will fair.
One of the -- the history behind this is -- is that CLL is the most frequent type of leukemia seen, certainly in the western world, representing about 30 percent of total leukemias.
It is really a disease of old age, in that the disease becomes manifest after the age of 40. Over 90 percent of the cases appear after the age of 40. The median age is about 60. So it's a disease of old age, basically. And it is

very heterogeneous with respect to its prognosis. Some patients can do very well for over 10 years without any treatment, where other patients may need very aggressive therapy and may, in fact, die within a year or two of diagnosis.
So it's been important, in the course of studying the disease and studying patients with the disease, to develop means of predicting how a patient is going to do early on. And one of the -- in -- in current practice, one of the techniques that has -- that is receiving a great deal of interest, in terms of its potential value, is the lymphocyte doubling time, because by using the doubling time, it's been demonstrated that you can distinguish individuals into two broad categories, those that have a relatively poor prognosis and those that have a relatively good prognosis.
MR. BARRIE: I'm going to object to the nonresponsive portion of the answer.
Q. (By Mr. Galbraith) Okay. I want to make sure I understand what you've just said.
Certain patients with chronic lymphocytic leukemia will have a doubling time

where the number of cells, leukemic cells will double more quickly than others.
A. It's the -- the total population of tumor cells that a patient has is a function of two things: how fast the cells divide and how fast they disappear, or how long they live -- excuse me.
In the case of chronic lymphocytic leukemia, this is a very dynamic process. You actually -- the cells are actually dividing slower than normal lymphocytes would. The rate of division, the rate -- the proportion of cells that are actively dividing is relatively less than in a normal individual, but you have many more cells present, and so you have a larger total entry of cells into that compartment. They also live a long time. And so you slowly build up a larger tumor load.
Q. Okay. So to get a prediction on the future, in other words, how someone will do after a diagnosis of chronic lymphocytic leukemia, you look at this doubling time?
A. Yes. 24 Q. Okay. How do you get the information, on a specific patient basis, for doubling time?

A. The principal tool that you use is the peripheral blood count, and you determine the -- actually, the number of lymphocytes in the peripheral blood count.
Using data that's been published in the literature in the characterization and study of lymphocyte doubling time, one can estimate, based on the patient's weight, what the total body burden is. This is a rough estimate. It's not necessarily an exact figure, in terms of the precise estimate of the number of cells.
What is most useful about this technique is if you have data on which to calculate the rate at which the tumor cells double, en masse, it is more reliable than any individual datapoints. You're calculating the number of years or months that it takes for the total tumor mass to double.
Q. Okay. And if you can calculate that rate, that gives you an indication of when the disease process started, itself?
A. It's principal use at present, in a clinic, is to project the rate at which the cells will double for prognostic reasons.
Q. To predict how the patient is going to

do in the future?
A. Right. Now, the reason it is reliable in that context is that the doubling times is a very constant feature of CLL.
Now, another piece of information you have to have, to reach the conclusion that I have in this case, is the fact that CLL is what is called a "monoclonal disease." It is derived from a single cell. All the cells that are tumor cells are ultimately derived from a single malignant cell. And in order to do that, that cell had to be initiated, it had to become a cancer cell, and it then had to undergo divisions.
The first doubling time is the second cell, and then progressively, with time. This rate in CLL is very constant.
Q. Okay. So tell me what you have done in this case to look into or to calculate that rate and that doubling time to lead to your opinions about when Mr. Chambers' chronic lymphocytic leukemia process started?
A. Now, the first thing that I did was to review his medical record and to look at all the blood tests that have been done that were

reported in the record on Mr. Chambers dating back to 1967.
Q. And what did that tell you?
A. That gave me the -- what's called the - I calculated the absolute lymphocyte could, which is the number of lymphocytes circulating in his peripheral blood. In this case, it's -- it's measured in microliters, or cubic millimeters, if you will.
Q. Okay.
A. And then, in order to -- because this - the estimates of body burden were first made by Dr. Stryckmans -- and his article is in here - and I used his nomogram for calculating or estimating the total body burden.
Q. Okay. You've come out with a sheet of paper, and I guess I'd like to have that marked as Exhibit 3. Could we do that before we start referring to what's on it? How about it?
A. Yes.

(Whereupon, the instrument referred to by counsel was marked for identification as Irons Exhibit No. 3.)

Q. (By Mr. Galbraith) A11 right. Taking a look at Exhibit 3, that is your tabulation of his blood counts back to nineteen -- May 9th of 1967 was the first one?
A. That's correct.
Q. And it-has what entries?
A. The white blood cell count, or WBC, the differential lymphocyte count or percent lymphocytes as determined on the smear, the absolute lymphocyte count, which is basically -- this is a percentage, and so this simply represents the total white cell count times the fraction that are lymphocytes, to give us a total lymphocyte number.
Now, the work by Stryckmans and colleagues has determined, or has demonstrated that it is -- you can obtain a more reliable indicator of the estimated body burden of tumor cells if you relate this to the individual's weight, because, obviously, fluctuations in weight could alter the respective body burden that is reflected in the cell counts in the blood.
So just in case there were fluctuations in weight, I used that estimation based on weight

to -- for the rest of my analysis. I actually could have just used, as it turns out, the peripheral lymphocyte count, because Mr. Chambers' weight has not varied that much over the course of the last twenty some years.
Q. Okay. So, from the medical records, you had the blood counts, you had the percent lymphocytes and you had the weights?
A. Yes. 10 Q. Okay. And from that, you arrive at what conclusion or what figures?
A. Well, basically what I did, was I plotted the average yearly body burden, as determined from these analyses. And when you do that --
Q. Over time?
A. Over time.
MR. GALBRAITH: All right. Could we take that plot and refer to it as Exhibit No. 4, please?

(Whereupon, the instrument referred to by counsel was marked for identification as Irons Exhibit No. 4.)

Q. (By Mr. Galbraith) Sb Exhibit 3 has --
so Exhibit 3 has the actual numbers from
Mr. Chambers' medical records, from actual blood
counts?
A. Yes, sir.
Q. And then Exhibit 4 takes that
information and puts it on a -- a graph over
time?
A. Yes. I think you need to include this,
as well. These are the average values for each
year.
Q. Okay. 13 A. Mr. Chambers had several blood tests
done in the course of some of these years, and I
averaged those to come up with estimated body
burden for this purpose.
Q. On a year-by-year basis?
A. A year-by-year basis.
Q. Okay. Could we refer to that, then,
your average cell body burdens, as Exhibit 5?

(Whereupon, the instrument referred to
by counsel was marked for identification as Irons
Exhibit No. 5.)

Q. And so these numbers from Mr. Chambers' medical records are plotted on Exhibit 4?
A. Yes.
Q. What does -- what does Exhibit 4 do for you?
A. Well, this analyses, in total, tells me a number of things.
First of all, the data suggests a very reliable doubling time analysis, because the points clearly depict an increase that is constant and progressive with time, and the doubling time is over three years by this analysis, 3.31 years, actually.
Q. What does that mean, the doubling time of chronic lymphocytic leukemia in Mr. Chambers' case is 3.31 years?
A. It means, first of all, that it takes over three years for the tumor cells that he has to double in number, for the mass to increase by two. So every 3.31 years, it has been increasing in size by twice.
Q. Okay.
A. That's number one.
Number two, because it's well over one year, the time it takes for this to happen, it

places him in a very good pro4nostic category.
The doubling time analyses that have been conducted by Montserrat and others in the literature have indicated there are two major groups of individuals: those that have a very rapid doubling time of less than a year; and those that have a slower doubling time of greater than a year.
Those that have a slower doubling time of greater than a year show a more favorable prognosis and go for a much longer period of time before they need treatment, in general, than individuals with a more rapid period of time.
This is -- this is consistent with the lack of problems that Mr. Chambers has had related to his CLL in his medical history.
Q. Okay. I take it this chart indicates that you can graph backwards through time, as well, that it's constant and reliable in reverse.
A. At this point, we are basically looking at the state-of-the-art with respect to our understanding of the biology of CLL. It's clear that CLL has, compared to other leukemias, a very -- a very decided familial disposition.

There's a tendency on the part of different family members within the same family to develop CLL.
The doubling time is very constant. And because the slope of this line is very reliable in projecting and/or predicting the outcome of the patient, it is reasonable to project a line, as well, going the other direction, in terms of developing an understanding of where this event may have occurred.
Other leukemias, you can't do this, because the kinetics are far too complicated, and there are events that are going on during the course of the progression of the disease that change the rate of division. Since the rate of division is so constant in CLL, it's reasonable to project backwards to determine, within some reasonable margin of error, where the initial event might have occurred that led to the development of the disease.
Q. Okay. A. And if you do this with Mr. Chambers, you arrive at a conclusion that the initial cell population either was present before he was born, or shortly thereafter.

Q. And carrying that slime reasoning forward, in terms of the rate of the progression of Mr. Chambers' disease, he is one of those individuals who has an unfavorable future in terms of the progression of the disease, or a more favorable prognosis or future?
A. Certainly, based on the literature, he has a favorable prognosis.
Q. Dr. Irons, thank you.
MR. GALBRAITH: And I'll pass the witness at this time.
Might this be a good time for a break?
MR. SCOTT: I need to take one.
THE VIDEOGRAPHER: It's 11:17.
We're off the record.

(Whereupon, after a brief recess, the video deposition continued as follows:)

THE VIDEOGRAPHER: It's now 11:32.
We're back on the record.

EXAMINATION
QUESTIONS BY MR. BARRIE:

Q. Good morning, sir. How are you?
A. Hi.
Q. My name is Martin Barrie, and I represent Mr. Chambers and his wife in this cause of action. And I understand, sir, you've been retained as an expert in this case by the Marathon Oil Company, correct?
A. That's correct.
Q. All right,. Is it Dr. Irons?
A. Yes.
Q. Is that a title conferred upon you, sir, by virtue of a doctorate of philosophy?
A. Yes.
Q. You, sir, are not a medical doctor?
A. No, I'm not.
Q. May I call you "Doctor"?
A. Yes.
Q. Dr. Irons, I'd like to have a few general agreements with you, if I can, during this deposition.
Sir, if you don't understand any of my questions during his deposition, I want you to stop me. I want to be sure that I can rely on your answers that you have given in answer to my questions. So if you don't understand them, will

you stop and ask me to rephrase it?
A. Yes. 3 Q. Dr. Irons, have you ever had occasion to
give your deposition before?
A. Yes, I have.
Q. Would you tell the jury, sir, how many
times you've been giving your deposition
testimony?
A. Three or four,, I believe.
Q. Were those on behalf of individuals who
were injured, or were they on behalf of
corporations, or can you tell the jury any sort
of distribution about those depositions?
A. Three have been for corporations who
have been defendants in cases, and one has been
for a plaintiff.
Q. Let's talk about these three depositions
you've given for corporations. Can you tell me,
sir, who those corporations were?
A. Monsanto. And one case involving
multiple defendants. I believe one of them was
Shell.
Q. Can you tell, me, sir, when the
deposition testimony was given?
A. I gave two depositions in a case called

Skeen, Skeen 2, which was approximately -- it was over two years ago. One was in November or December, I believe -- or January, January of 1989. And the other one was in the fall of '88, I believe.
I gave a deposition in a case called Buchaj, which I failed to mention. I'm sorry. And the defendant in that case was Texaco. And that was in November of this last year.
Q. Can you recall any other names, other than the Skeen trial, in which you were an expert for a defendant, or the Buchaj case that you were, again, an expert for a defendant. Can you recall any other styles or names of cases, sir?
A. Yes. One. It's -- there are three plaintiffs, Carter, Sleuter and Riddle. And I gave that deposition in August of 1990.
Q. Where was that case filed, sir?
A. It's in Roan Oak, Virginia.
Q. Were you representing these three plaintiffs, or were you representing a corporate entity?
MR. SCOTT: I object to the form of the question. Lawyers represent people. Witnesses appear behalf of parties.

Q. (By Mr. Barrie) Well, when you were retained by a party, were you retained by these three plaintiffs, or were you retained by a corporate entity?
A. By the corporations that are defendants in the case.
Q. Can you tell me, sir, what those corporations were --
A. I
Q. -- by name?
A. I believe I mentioned Shell is one of them. I'm afraid I can't remember exactly who the others are. It's not Monsanto.
Q. Would it have been Marathon?
A. No. I don't think so.
Q. Union Carbide?
A. I don't think so. To the best of my recollection, it's not.
Q. Do you keep copies of your deposition testimony, sir?
A. Yes, I do.
Q. Are they in your office in Colorado?
A. I believe so, yes.
Q. This Skeen trial, was this the Skeen trial, sir, where there was another gentleman who

worked at Monsanto who got leukemia?
MR. SCOTT: Object to the form of the question. "Another" implies that there is some in this case. There's certainly no evidence of that.
Q. (By Mr. Barrie) Dr. Irons, was the person involved in the Skeen case, was he an individual who had leukemia who worked in the Monsanto facility?
A. I believe he worked in the Monsanto facility, yes.
Q. Did the plaintiff in the case have leukemia?
A. Yes, he did.
Q. And was one of the issues in that case, sir, that you were looking at was whether benzene caused that gentleman's leukemia?
A. That's correct.
Q. And you came to a conclusion, sir, that that leukemia wasn't caused by benzene exposure; is that correct?
A. That's correct.
Q. The Buchaj case, was that a case involving a gentleman with a leukemia?
A. Yes.

Q. Was that case also, sir, involving one of the allegations whereby that gentleman was exposed to benzene and whether that was the result of his leukemia?
A. Yes, sir.
Q. And did you testify, also, in that case, sir, that that gentleman's leukemia was not caused by benzene exposure?
A. Yes, I did.
Q. So the jury is able to understand what we're talking about in this case when we use the word "benzene," benzene is a chemical, is it not, sir?
A. Yes.
Q. And it is true, is it not, sir, that benzene is a constituent or is found in other types of solids, correct?
A. On occasion, yes, it is.
Q. Well, you're aware, sir, that benzene is found in various concentrations in gasoline, correct?
A. Yes.
Q. And you're certainly aware that benzene is found in naphtha, correct, in some concentration?

A. It can, yes.
Q. And you're also aware, sir, that benzene is found in distillate that may be coming off of a distillation column in a refinery, correct, sir?
A. It can. It depends on the particular distillate fraction.
Q. You're not suggesting that there's distillate that contains no benzene, are you?
A. There's virtually no distillate or a variety of other compounds or substances that contain no benzene. "No" is a -- is an absolute term, and in toxicology, we think in terms of relative terms.
There's benzene in distillate fractions, there's measurable benzene in eggs, there's benzene in cigarette smoke.
MR. BARRIE: Well, I'll object to the nonresponsiveness.
Q. (By Mr. Barrie) But there is benzene found in distillate, correct?
A. Technically, yes. You can measure benzene in a variety of different fractions, including distillate.
Q. Looking at your resume, sir, I notice

that you've been in the academic arena, the academic world, from approximately 1965 until you completed your doctorate of philosophy in about 1974, '75; is that fairly correct?
A. Yes.
Q. Have you ever had an occasion, sir, to work in a refinery?
A. No, sir, I have not.
Q. Have you ever had occasion to do any air monitoring or monitoring of an individual's blood or urine to do assessment of any potential blood-forming organ crises as a result of exposures in refineries?
A. In refineries, no, sir.
Q. Have you ever had an occasion to visit the Monsanto refinery?
A. I don't believe I have.
Q. Have you ever visited the Marathon Oil Company refinery or chemical facility?
A. Marathon? No. No, sir.
Q. You certainly don't know Mr. Chambers personally, do you, sir?
A. No, sir, I do not.
Q. You've never worked with Mr. Chambers in a refinery or chemical plant at all, have you?

A. No, sir.
Q. You certainly haven't worked with any of his co-workers who have worked with him on a day-to-day basis and performed tasks with him, have you, sir?
A. No, sir.
Q. In your doctorate of philosophy, did you have an occasion to write a dissertation, sir?
A., Yes, sir, I did.
Q. Would you be so kind as to tell me the title?
A. "Characterization of Low Molecular Weight Cadmium and Copper-Containing Proteins."
Q. Essentially, if we can just reduce that to fairly simplistic terms, for my benefit, are we talking about heavy metals --
A. Yes.
Q. -- and what effects they may have?
A. Yes.
Q. Do you have a copy of that dissertation in your files?
A. Someplace, yes, I do.
Q. In your offices in Colorado?
A. I'm not certain where it is, but I'm sure I have it someplace.

Q. You've identified, sir, that Exhibit No. 1 is a copy of your curriculum vitae, am I correct?
A. That's correct.
Q. And I think you've already told the jury that this is not an up-to-date copy. Am I correct?
A. That's correct.
Q. Do you have an up-to-date copy?
A. Oh, yes.
Q. Okay. Would you be so kind as to provide me a copy, so I can take a look at it?
A. I'd be happy to.
Q. Let me just hand you your curriculum vitae. It's Exhibit No. 1, Doctor. And let me just ask you if there's anything that's omitted from that particular CV, whether it be an article, whether it be experience, whether it be training, or anything of that nature, that I need to know about that you may be relying on in the formation of any opinion in this case?
A. Certainly not that I'm aware of.
Q. Are you going to be relying, sir, on some specific article at the trial of this case that's not reported in that CV?

MR. GALBRAITH: I guess I object to the form of the question because he's already referred to articles here today that aren't authored by himself or in his CV. So the answer -- I guess -- I guess I don't object to the form because the answer is "Yes." He's already indicated "Yes." That makes me think I don't understand the question. That's all -- the reason for my interjection.
Q. (By Mr. Barrie) With regard to your CV, is there any article that you have in a CV, whether it's that CV or one that's more recent, that you're going to cite to some book, cite to some article, cite to some training, or any other experience in the formation of an opinion in this case?
A. If I understand your question, I intend to rely on the articles and the documents that I have provided, the background that's in my curriculum vitae. If you, or anyone else, asks me questions that require that I rely on other documentation or books or articles within my knowledge, I will, but it's not my intention to do so, based upon the opinions that I've rendered here.

Q. So with regard to the opinions that you're going to render in this case, I'm going to be able to rely on the articles that you've brought and the text that you're brought here before us today, as well as what's in your resume in the formation of those opinions; am I correct?
A. Yes, sir.
Q. Can you cite me, sir, to any specific article within your CV that you're going to be relying on in rendering those two opinions that you've already expressed to us today?
A. Specifically, no, sir. Not specifically. With respect to my background, I'm relying on my experience. I've published in several of the areas that are germane to the analyses and my opinions -
Q. There's not an article specifically you can say, "This is an article I'm going to be relying on at the time of the trial of this case because it helps support my opinion"?
A. Not specifically, no, sir.
Q. Thank you, sir.
Your activity at the Colorado Health Science Center, can you tell me, sir, how much time you devote to teaching?

A. Somewhere between 10 and 20 percent.
Q. That leaves us somewhere in the order of between 80 percent and 90 percent of the time you're doing something else, right?
A. That's correct.
Q. Would you tell me what else you are doing, other than teaching, those 10 percent or 20 percent of the time?
A. I would say I spend somewhere between 10 and 20 percent doing administrative -- what I would call administrative duties related to the program or the University: I spend approximately 10 percent of my time consulting and in providing advice to external agencies and parties. And the remainder of my time is spent in research.
Q. Would it be fair to say approximately 50 percent of your time or less would be devoted to research?
A. About half -- that's -- that's about right.
Q. You mentioned that approximately 10 percent of your time is involved in consulting. Do you devote some of your time within that framework to legal consulting?
A. Yes, sir.

Q. How much of a percentage does that take up of that 10 percent of your time, in terms of providing expert opinions to lawyers involved in cases?
A. Last year, I think it was about nine percent. It's -- it -- I can't give you an absolute precise figure, but I'd say that certainly in terms of guidelines, we're talking between 10 and 15 percent. Last year, it was nine. This year, I don't know what it would be. It's about that.
Q. Would it be fair to say, that of the consulting activities you do, a majority of it is spent in providing benefits and services to lawyers involved in cases?
A. In that fraction we're talking about, yes. The remainder of it is spent consulting with attorneys general, health departments, the Governor's office, a variety of different -- the EPA, a variety of different Government bodies, as well.
MR. BARRIE: I'll object to the nonresponsive portion of the answer.
Q. (By Mr. Barrie) Can you tell me, sir, what fees that you charge to provide legal

services?
A. Well, I don't provide legal services, in the sense that I'm not an attorney. I provide expertise related to areas of concern to the various parties. I charge a fee of three hundred dollars an hour.
Q. Is this three hundred dollars an hour that you charge for your services, is that for deposition testimony only?
A. It's for anything. It's for review of the literature, it's for travel, it's for testimony, whatever.
Q. Can you tell me, sir, how much have you billed, to date, the attorney representing Marathon --
A. I haven't
Q. -- for your services?
A. I haven't billed him yet at all. I have -- at this point, oh, I guess I've probably worked two days.
Q. Forty-eight hours?
A. No, no. Sixteen -- two days, eight hours a day, roughly, I think. I'm not sure. But certainly before coming here, that was about right.

Q. So the amount owing to you is sixteen hours, approximately, times three hundred dollars an hour?
A. Approximately, for that work, yes.
Q. You mentioned you were involved with the molecular toxicology Environmental Health Sciences in Colorado.
Can you tell me, sir, does that group, if you will, require funding from outside services or companies in order to provide your activities, grants, if you will?
A. Yes.
Q. Who provides the grants to the Molecular Toxicology and Environmental Health Sciences -
A. We have a number -
Q. -- Group?
A. We have a number of different sources of funding for various activities.
Q. Do chemical companies provide grants for you?
A. Yes.
Q. That's the money, sir, that you rely on in order to perform your services and activities within that department or that group?
A. It's primarily for teaching and

training. It's really not used for other activity, per se. The program funds and/or gifts or donations to the program are used for -- in support of training graduate students in toxicology.
Q. Are you saying, sir, that none of the grants or monies provided by chemical companies are going to the running of any of this activities that takes place under this Molecular Toxicology Environmental Health Group?
A. No, sir, that's not what I said. I said that the monies that are obtained as gifts for use by the program itself are dedicated to training and education.
All of us in academia, certainly within my program, have grants for research that are obtained from a variety of different organizations in support of the work we do. It's very expensive. I personally have grants from both Government and corporate entities in support of my research.
Q. You mentioned that for a period of time, approximately ten years or so, you were involved in the Chemical Industry Institute of Toxicology at Research Park, North Carolina. Am I correct?

A. I was employed by CIIT, yes.
Q. And you mentioned that the funding for that institute came primarily, in the -- in the initial period of time, from chemical companies, correct?
A. That's correct.
Q. Do you have any idea, sir, when the transition took place from major funding from chemical companies to funding from chemical companies plus other agencies?
A. Well, it began gradually. I couldn't put a precise date on it, but to my best recollection, the Institute was accepting some Federal funds as early as, say, 1987, maybe 1986. I can't -- I really wasn't involved in those decisions, so I couldn't tell you precisely.
Q. All right. That's the first time period that you're aware of that funds outside of the chemical industry were being provided to that Institute?
A. Yes.
Q. And it's fair to say, even today, as we speak, sir, that industry is a major supplier of funds to that particular Institute, correct?

A. I would hesitate to speak about the funding profile for CIIT today, because I really have no idea. I would expect that they are receiving a considerable amount of support from the industry, but I also am generally aware that they have been active and successful in obtaining Federal funding, as well.
Q. You mentioned that when you were at the Chemical Industry Institute, you performed or did some investigation in the mechanism of toxicology and the toxicity of the chemical benzene. Did I understand that correctly?
A. That's correct.
Q. Did you perform any studies, sir, that would fall under the umbrella term of "epidemiological investigations;" that is to say, identifying the sorts of individuals, such as workers, who were working in an industry that may have exposure to the chemical benzene or other products containing benzene and matching them to similarly situated individuals with the exception that they weren't exposed?
A. For benzene, no, I didn't. I have done that for other compounds, however.
Q. When you were at the Chemical Industry

Institute?
A. Yes.
Q. What compounds did you perform that type of an epidemiological investigation for?
A. I performed the initial feasibility studies of conducting such a study as you described on butadiene in the People's Republic of China.
Q. Butadiene has been linked with causing specific types of cancers, has it not?
MR. SCOTT: I object to the form of the question. What do you mean "linked"?
Q. (By Mr. Barrie) There's a, causal relationship between butadiene exposure and some cancers, is there not?
A. In my -- yes.
Q. Is it your testimony that butadiene does not have a causal relationship to any cancers in humans?
A. It's my opinion that a causal relationship between butadiene and human cancer has not been definitively established.
Q. Well, what about the relationship between styrene and butadiene?
Are you aware, or do you have any

opinion whether styrene plus butadiene would cause any type of cancer in humans?
A. I -- I -- the question is -- I'm -- I'm afraid I don't know quite how to answer your question.
Q. Well, have you
A. If you're asking me whether there are epidemiology studies on the relationship between potential exposure to styrene and human cancer, yes, there are. There are also studies, epidemiology studies on butadiene. The nature of those studies, they differ from one to the other, and the precise relationship between exposure to those agents and various human cancers, if any, is by no means clear at this time.
Q. In your opinion?
A. In my opinion.
Q. So, in your opinion, exposures to butadiene, singularly, or in combination with styrene, in your mind, does not have a causal relationship at all between any sort of cancer in people?
A. No, I did not say that. I said that the evidence in support of a causal relationship is

by no means clearly established, and it is impossible, at this time, to determine, in my mind, what, if any, human cancers are specifically associated in a causal relationship with those exposures.
The data is out. The -- I think a conclusion is not yet forthcoming from the data we currently have.
Q. Would you recognize that other experts may voice a different opinion with regard to a causal relationship between butadiene exposure, either singularly or in combination with styrene, and its causal relationship with cancers? Are you aware of that opinion being held in the epidemiological field and the toxicological field?
A. There's currently considerable discussion and controversy over the quality and the nature of studies that have been performed. Some of them contradict each other. Some individuals hold one opinion, some old hold another. The literature is by no means clear.
Q. And, again, that's the opinion you've gleaned from reading the epidemiological investigations and --

A. That's correct.
Q. -- studies?
Have you issued a report, whether it be
a preliminary or final report in this case, as
you've been retained as an expert by Marathon?
Have you issued a report?
A. No.
Q. Do you plan on issuing a report?
A. No.
Q. Do you have any plans, sir, to appear
live at trial of this case, to give testimony on
behalf of Marathon Oil Company?
A. If I am asked, I will do so.
Q. I'd like the jury to have a clear
understanding of what your expertise is, and what
I'd like to know is: Do you consider yourself
and hold yourself out as an expert in toxicology?
A. Yes, sir. 19 Q. Are there any other fields that you
consider yourself or hold yourself out to be an
expert?
A. Experimental hematology. And I do serve
as a member of the Department of Pathology at the
University of Colorado in the -- in the training
and differen -- providing expertise in terms of

differential diagnoses associated with the morphology and/or laboratory differential diagnostics of lesions involving hematopoietic and immune system.
Q. So if I can summarize this for the jury, you hold yourself out as an expert, consider yourself an expert in the fields of toxicology, experimental hematology, and some aspects of pathology?
A. That's correct.
Q. You don't hold yourself as an expert in epidemiology, do you?
A. I don't consider myself and epidemiologist, but I teach epidemiology, I'm called upon to review data in epidemiology, and to render opinions with respect to the quality of that data in a variety of settings.
Q. Are you here today, sir, to give us expert opinion in the field of epidemiology?
MR. SCOTT: I object to the form of the question. He's already referred to the epidemiologic literature in providing the opinions and bases for -- that he has provided.
A. As a toxicologist, I am frequently called upon to both teach and to evaluate the

epidemiology data -- data in the literature. So as a toxicologist, I feel competent to review epidemiology data.
If you're asking me whether I would go out and design, without collaborating with an epidemiologist, an epidemiology study, the answer is no. But I certainly am qualified to evaluate the experimental design and results that are obtained in epidemiology studies.
MR. BARRIE: Well, I object to the nonresponsiveness of the answer.
Q. (By Mr. Barrie) You've brought for us, here today, sir, some documents in this blue binder that's been marked as an exhibit. Are those the articles of which there are some, perhaps, in the field of industrial -- some of which contain epidemiological investigations on which you're relying in forming the basis of some of your opinions in this case?
A. Yes, sir. 21 Q. When were you first contacted in this case, sir?
A. I'm not sure exactly, but I believe it was in December.
Q. Of 1990?

A. Yes.
Q. And who contacted you?
A. I believe it was Mr. Scott.
Q. And I believe Mr. Scott represents Monsanto in this case; is that your understanding?
A. That's my understanding, yes.
Q. When Mr. Scott contacted you, what did he ask you to do?
A. He asked me to take a look at the medical records in this case and to review the literature and to render an opinion as to the issues that we've been discussing here today.
Q. Have you ever been contacted by Mr. Galbraith, who represents Marathon?
A. No.
Q. Aside from the medical records, Plaintiffs' First Amended Complaint, the lawsuit that was -- the papers that were filed in the lawsuit, some information on depositions, is there anything else that was provided to you for you to review and inspect, at all?
A. No, not to my knowledge.
Q. Now, you mentioned that summaries of the depositions of Mr. Chambers and Mrs. Chambers

were provided to you?
A. Yes.
Q. Did you actually read Mr. Chambers' entire deposition, or Mrs. Chambers' entire deposition, or did you really rely on the summaries that were provided to you?
A. I relied on the summaries to obtain an idea of the character of the allegations in the Complaint. I did not rely on the summaries for -- as a basis for any of the opinions that I've given.
Q. Did you read Mr. Chambers' or Mrs. Chambers' entire deposition?
A. No, sir, I did not.
Q. Who prepared the summaries of their testimony for you?
A. I don't know. They were given to me by Mr. Scott.
Q. You also mentioned that you reviewed the depositions of Dr. Savitz, who is an epidemiologist, and Dr. Fehir, who is a hematologist, oncologist, internist?
A. Yes. 24 Q. Can you tell me, sir, of what importance or reliance you've placed on those particular

depositions?
A. Well, I reviewed those depositions and the opinions of those two individuals and evaluated their -- both the information and the literature on which they base their opinions, along with their opinions, in arriving at my own.
Q. You are familiar, in general, with the field of hematology, as you've told us a moment ago, correct?
A. Yes, sir.
Q. Do hematologists look at diseases of the blood and the blood-forming organs, such as leukemias and lymphomas and other types of diseases or cancers?
A. Principally the leukemias.
Q. Are you suggesting that hematologists limit their investigation into leukemias or --
A. No. I'm -- I'm just saying that hematologists principally focus on diseases of the blood of which leukemias are an example. Occasionally, hematologists will deal with lymphomas. Oncologists deal with lymphomas, as well. The -- the disciplinary bounds are somewhat fuzzy.
Q. Part of a job of a hematologist is to

not only treat the patient, but to also look at what may be the cause of a particular disease of the blood-forming organs, correct?
A. On occasion that can be the case, yes.
Q. So they're not just trying to treat a patient. Part of their job, also, in taking a clinical history, is to also determine what is the etiological agent, or what caused their particular blood dyscrasia or problems in their blood-forming organs, correct?
A. I would say that that's correct, with the caveat that certainly most practicing clinicians are -- emphasize, in their daily activities, primarily the diagnosis and treatment, as opposed to the more research oriented activities, such as determining etiology, although they can participate in those activities, as well.
Q. Is there anything that you plan on doing in this case, sir, that you haven't done yet, that may affect, in any way, any of the opinions that you've already given to us today?
A. Not to my knowledge, no.
Q. Have you been asked to do something that you haven't done?

A. Not that I know of.
Q. And one of the reasons I ask that, sir, is I -- I just want to know if you're going to do something else, so if it affects your opinion in any way, I want to just have an opportunity to question on you on that, and that's why I asked that question.
A. Understood.
Q. Is chronic lymphocytic leukemia, "CLL," as it's called by initials, is that a disease of the blood and the blood-forming organs?
A. Yes, it is.
Q. Is the disease acute myelogenous leukemia, or "AML" by initials, also a disease of the blood and the blood-forming organs?
A. Yes.
Q. Is the disease chronic myelogenous leukemia, or by the initials, "CML," a disease of the blood and the blood-forming organs?
A. They're all diseases of the blood-forming organs, yes.
Q. Or in general, so we can make it a little bit simpler, diseases of the hematopoietic system?
A. Yes.

Q. Also, they can be called "blood dyscrasias" or "blood problems," am I correct?
A. In a general -- in a very general way, yes.
Q. The reason I use those terms, sir, is that the jury may hear those terms throughout the course of the trial, and I want them to understand that we're talking generally about the same problem, right?
MR. SCOTT: I object to the form of the question. What do you mean when you're talking about the same problem"?
Q. (By Mr. Barrie) We're all talking about diseases in the blood, the bone marrow, those types of diseases, are we not?
A. These are all different diseases that are associated with the blood and the blood-forming organs.
Q. But chronic myelogenous leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia, they're blood dyscrasias?
A. They are diseases of the blood. Blood dyscrasia is simply a fancy word for abnormalities of the blood, so, yes.
Q. And they're diseases of the blood and

the blood-forming organs, correct?
A. Yes. Q. Now, you've given us here today, sir,
two of the opinions that you've formed in this
case; am I correct?
A. Yes. Q. Are there any other opinions that you
have formed that you're going to tell the jury
about in this case, other than those two?
A. No, not that I know of.
Q. You mentioned in your first opinion
that, in your opinion, there is no -- and I think
this is a quote -- "reliable evidence," unquote,
that benzene or any other agent has a
relationship, a causal relationship, to the
disease chronic lymphocytic leukemia. Did I
understand that correctly?
A. That's correct.
Q. By that statement, sir, are you
suggesting to the jury that there is no evidence
at all of a causal relationship between benzene
exposure or products that contain benzene and
this type of leukemia, this CLL?
A. Well, as I mentioned earlier this
morning, in fact, I discussed, summarized the

work of McMichael, et al., that originally suggested there might be an association. So, obviously, I'm not saying that.
What I'm saying is that followup studies by the same group have changed their initial opinion with respect to the nature of benzene exposure and the findings in that study.
Q. So the study by McMichael identified, in that study, a causal relationship between benzene exposure or that cohort or group and the disease chronic lymphocytic leukemia?
A. No, sir. No, sir. A single epidemiology study can define an association. The chances that a single study would be so well-designed and the findings so clearcut that a causal relationship would be established is very remote.
What the McMichael study did was indicate a possible association or correlation between what was presumed to be benzene exposure, without looking at it closely, and lymphoid neoplasms, which included, within that group, CLL.
Q. Did they report, sir, workers who were exposed to benzene, and the workers that were

similarly exposed that had chronic lymphocytic leukemia? Did it identify cases such as that?
A. It did not deal with exposure, her se. Exposure to benzene was a point of departure for the study. They did not look at exposures, per se, in that study.
Q. Well, were they looking at workers who were working in areas where benzene exposure, more likely than not, could occur in some of those individuals having the diagnosis of chronic lymphocytic leukemia?
A. They examined individuals -- they examined workers who worked in situations where benzene was one of the possible exposures that they could have had.
Q. And some of those individuals had the diagnosis of chronic lymphocytic leukemia, correct?
A. Some of those individuals had lymphoid neoplasms and, within that group, there were some patients with CLL, as I recall.
Q. And I want the jury to understand when we're talking about epidemiological investigations, what we're talking about is studies that are done on large groups of people,

and we're looking at controlling everything except for, in this case, exposure to benzene, to see if there's an incidence among that exposed group relative to those that are not exposed, of whether there is a type of disease that they have to draw a causal inference among the group whether benzene may have a causal relationship to the disease. Am I correct?
A. That would be the ideal situation, yes, sir.
Q. I don't want the jury to understand that epidemiological investigations establish causation in a person. Am I correct in that?
A. That's correct.
Q. So when we talk about epidemiological studies and what findings they give us, we're not establishing causation in a person, but rather we're looking at groups of people and what an inference may be, correct?
A. That's correct.
Q. You mentioned that in the McMichael study, there were other solvents. Can you tell me, sir, what those other solvents were?
A. From the list -- certainly, from the followup studies, the potential exposures

involved a wide range of compounds. I can provide you with a list, if you'd like. The two particular agents that in the followup studies were much more markedly associated with lymphoid neoplasms than benzene were carbon tetrachloride and carbon disulfide. Now, I should add, to be complete, that that's the only association, or potential association with those two compounds and any lymphoid neoplasms that I'm aware of. And whether or not that proves to be a real causal related association would require a great deal more study.

MR BARRIE: I'll object to the nonresponsiveness of the answer.

Q. (By Mr. Barrie) Do you have an opinion, sir, whether carbon tetrachloride has any causal association with chronic lymphocytic leukemia?

A. Not to my knowledge, not in the study.

Q. What about -- what about carbon disulfide, do you have an opinion whether that has a causal relationship to the disease chronic lymphocytic leukemia?

A. Not to my knowledge.

Q. Is benzene a leukemogen?

A. In individuals chronically exposed to high concentrations of benzene, there is a clear and generally accepted relationship with acute myelogenous leukemia. So, by definition, benzene is a human leukemogen.
MR. BARRIE: I'll object to the nonresponsive portion of that answer.
Q. (By Mr. Barrie) When was it established, in your mind, sir, that benzene was a leukemogen, in the scientific community?
A. There was no point in history where everyone suddenly came to a consensus, but I would say, in general, we're talking about mid to late 1970's, where it became generally accepted within the scientific community that there was a relationship between benzene and AML.
Q. Are you saying that it was when there was an establishment that benzene had a causal relationship with a leukemia called acute myelogenous leukemia, that that's when the scientific community, in your opinion, said that benzene is a leukemogen?
A. In terms of a general consensus, yes.
Q. Do you have any opinion whether aplastic anemia is a necessary precursor to leukemia? In

other words, you get an association between benzene exposure and acute myelogenous -- and aplastic anemia, and that's necessary before you can go on to get a leukemia. Do you have any opinion on that regard?
A. Certainly, the clinical literature indicates a very, very strong association between those two processes, that one has to have some evidence of bone marrow suppression, of which aplastic anemia is an example, in order to create the situation that may, in fact, lead, in some individuals, to developing AML.
I personally think that it's much more likely that our understanding of that process is going to involve looking at damage at the level of the stem cells.
What I'm trying to say here is that I do think there has to be pre-existing damage associated with exposure, but not necessarily the evolution of aplastic anemia, although the clinical literature would suggest that, in fact, that is the case.
Q. To summarize, in your opinion, the literature seems to suggest, in your opinion, that aplastic anemia is a necessary precursor to

the development of leukemias, although there can be other types of problems prior to a leukemia, other than aplastic anemia?
MR. SCOTT: I object to the form of the question. He very clearly said to a specific type of leukemia, not to leukemias in general.
Q. (By Mr. Barrie) My question is very broad, and I want you to just focus on the breadth of it, if you will.
Is aplastic anemia a precursor to any leukemias? Is it a necessary precursor?
A. I really do not understand the question. I can describe, again, what I said before or, if you could, could you reframe it?
Q. I'll certainly do my best.
Does an individual with chronic lymphocytic leukemia, in your opinion, get the disease immediately, chronic lymphocytic leukemia, or is there some stage that precedes that, whereby he has, and one must have, a suppression, an aplas -- an aplastic anemia, or some other condition that's necessary prior to going on to get a CLL?
A. Chronic lymphocytic leukemia has not been assoc -- it is not a secondary leukemia.

It's isn't secondary to exposure to anything, be it benzene, radiation, or anything else. An individual who comes down with chronic lymphocytic leukemia does not present with previous symptoms associated with exposure because exposure does not play a role in the development of CLL.
MR. BARRIE: I'm going to object to the nonresponsive portion of the answer.
Q. (By Mr. Barrie) My question is: Does a person present himself with CLL, or does he present him something with a precursor to CML, which later becomes CLL?
A. I'm sorry. You said CML, then CLL.
Q. I'm sorry. But I'm dealing with chronic lymphocytic leukemia.
A. Patients present spontaneously with chronic lymphocytic leukemia. They are not associated with previous exposure or previous blood dyscrasias because they do not play a role in the evolution of the disease.
MR. BARRIE: I'll object to the nonresponsive portion of that answer.
Q. (By Mr. Barrie) Doctor, is benzene genotoxic, by that I mean affecting chromosomes,

the genes of an individual?
A. Benzene metabolites have been demonstrated to cause certain types of chromosomal abnormalities.
Q. By these metabolites, are we talking about phenolic and polyphenolic compounds, and others?
A. Yes.
Q. Is it your opinion that the affect of benzene on the blood and the blood-forming organs is caused by benzene itself or its metabolites?
A. Metabolites.
Q. Can you list for me, sir, the metabolites that, in your opinion, are responsible for causing the problems of the blood and blood-forming organs?
A. This is a very complicated area. It appears that the precise toxicity that's seen in the bone marrow associated with benzene exposure is a function of a combination of metabolites that are present. It's not necessarily a single metabolite that's responsible for what benzene does.
The principal metabolites that we focused on are the polyphenolics, primarily

hydroquinone and its terminal oxidation product, benzoquinone. There are also a variety of other polyphenolic compounds, such as hydroquinone, which are produced as a function of the metabolism of benzene. And these, in concert, are most likely responsible for the damage that's seen in bone marrow following benzene exposure.
Q. You're familiar with the term "initiator" and a "promoter," are you not?
A. Yes.
Q. An initiator is a compound or a chemical that initiates a process, and that may go to a full-blown problem or it may sit dormant and later require an agent caused -- called a "promoter," which will kind of kick it in, if you will, which later becomes a full-blown disease or problem, correct?
A. That's a model system in toxicology, an experimental system that has been used to describe carcinogenesis primarily in skin and liver models.
Q. Do you have an opinion whether benzene is an initiator or a promoter?
A. Well, first of all, there are no

initiation/promotion models that are relevant to any leukemias that I'm aware of, either in experimental animals or in man.
So the initiation/promotion paradigm or model, from a strictly a theoretical point of view, may or may not be important in the case of leukemias.
Benzene, in my opinion, and its metabolites, are very poor actors with DNA. The DNA is the molecules from which our genes are made. They do not react readily or directly with DNA and, therefore, in that system, they're less likely to play a classic role as an initiator than, say, other compounds that might interact or alkylate with DNA.
Benzene metabolites appear to act at different places much more effectively within the cell, in terms of interfering with cell replication and division. I would hesitate to use initiation and promotion as a classification or category because, again, as I said, benzene doesn't appear to follow that model in other systems, such as the skin or liver, and there are no initiation/promotion models that I'm aware of that are relevant to leukemogenesis.

Q. You're aware of no chemical, by itself, or compound that would potentiate the effects of benzene on the blood and the blood-forming organs?
A. No, not in particular. I mean, obviously, you can -- you can hypothesize or speculate on the combined exposure of, say, benzene and chemo -- a chemotherapeutic agent or other agents that show toxicity of the bone marrow, and you certainly would expect that if an individual was exposed to these agents all at the same time, he would experience much greater toxicity or effects than he might from just exposure to one. But I don't know of any agents that specifically synergize or exacerbate benzene toxicity, per se, other than what I've said.
THE VIDEOGRAPHER: Mr. Barrie, I'm sorry. We're pretty near down to a minute and a half of tape. Are you just wanting to stop now?
MR. BARRIE: Sure. This is a good time.
THE VIDEOGRAPHER: It's 12:25. This is the end of Tape No. 1. We're off the record.

(Whereupon, the proceedings continued on the stenographic record as follows:)

MR. SCOTT: Let's get something to eat.
MR. GALBRAITH: Let's just take thirty minutes for lunch.

(Whereupon, there was a luncheon recess, after which the video deposition continued as follows:)

THE VIDEOGRAPHER: It's now 1:07. This is the start of Tape No. 2, and we're back on the record.
Q. (By Mr. Barrie) I'd like to ask you, sir, have you ever talked to anybody about this case, or discussed this case with anybody, and have their conversations with you formed, either in whole or in part, any of the opinions that you've given us today?
A. No, actually.
Q. You haven't asked a colleague, either where you're located, or at some other university, or you haven't called anybody on the

phone and asked them to do any calculations for you or provide you with any information, or do anything to assist you in any way, however small, that may play some role, in whole or in part, in coming to any of your opinions?
A. I've had technical staff perform some of the arithmetic and data extraction from the records, but other than that, no.
Q. You've not had a chance to visit with any of the other experts that have been retained by the Defendants in this case?
A. No, sir.
Q. I want to ask you now, sir, about the toxicity of benzene and ask you, sir, if you have any opinions regarding the concentration of benzene that would be necessary, in your opinion, to cause or contribute to the leukemia that's been identified as acute myelogenous leukemia. The reason I ask that, sir, and to refresh the jury's memory, is that you had said "at some concentration," and so I'd like to know, sir, if you have an opinion about a specific concentration and a duration or length of time of exposure that you believe is necessary before somebody can develop the disease leukemia,

which is specifically acute myelogenous leukemia?
A. Well, I can only tell you the strength of the evidence associated with various concentrations of exposure. It's clear that benzene toxicity to the bone marrow, bone marrow toxicity, shows a dose-response relationship; that is, that as you increase the concentration to which an individual is exposed, you increase the likelihood that there will be bone marrow damage, and you increase the severity of that damage.
The most severe subacute or initial effect you'll see with repeated exposure to benzene would be aplastic anemia, which is a failure of the bone marrow to produce blood cells of all types, in very simple terms.
It's very clear from the literature that repeated exposure, continuous exposure to a hundred parts per million of benzene or greater for lengths of time -- certainly, six months or longer, and maybe less, is associated with the development of a variety of blood dyscrasias, including a loss of various types of blood cells, such as lymphocytopenia, which is a decrease in lymphocytes, or granulocytopenia, although that's

rarer for benzene. Certainly, thrombocytopenia, a decrease in the number of platelets, or aplastic anemia can result as a function of repeated exposure at those levels.
As we look at the data available to us on lower levels of exposure, it becomes more difficult to determine the relationship between exposure and an effect.
Certainly, I have concerns about exposures of 50 parts per million or greater. There is evidence that, in fact, some bone marrow abnormalities have occurred in patients exposed at that level.
As we get down to, say, 25 parts per million or lower, we don't have direct experimental and/or clinical evidence that allows us to make definitive statements about what concentration produces bone marrow toxicity.
So as we get lower in concentration, the data becomes much less reliable.
MR. BARRIE: I'll object to the nonresponsiveness of the answer.
Q. (By Mr. Barrie) Sir, my question was specific in that I wanted to know whether you had an opinion regarding whether there was a certain

concentration of exposure to benzene that was necessary for the development of a leukemia that is called acute myelogenous leukemia?
A. In my opinion, the types of damage that benzene causes to the bone marrow and the relationship of that damage to the ultimate development of acute myelogenous leukemia suggests what is known as a classic dose or concentration response, and one would -- that follows from that that, in fact, there is a threshold of exposure below which no serious side effects will be seen.
The nature of the controversy or the discussions, if you will, in the field, at this point in time, evolve around what that concentration is, what concentration of exposure is going to be associated with an increased chance of developing AML or not.
Q. My question, sir, is: Do you have an opinion with regard to this concentration?
A. As I said before, as one looks at progressively lower concentrations, the data becomes much less reliable. There's no evidence to directly determine an effect of benzene below, say, somewhere between -- below 25 parts per

million, there's virtually no direct evidence on which to base such an opinion.
I expect, that whatever that concentration is, it's below 25 parts per million. It may or may not be below 10 parts per million. There's no evidence directly to support or to refute that.
Q. So, are you able to give us a range which, in your opinion, is the concentration that's necessary to be exposed to benzene for a prescribed period of time prior to a risk for the development of acute myelogenous leukemia?
A. Can I ask you to rephrase that?
Q. Yes. And I'm sorry. Maybe it was inartfully asked.
I'm trying to ask if you can give me a range for exposure to benzene whereby an individual exposed to that concentration would more likely than not develop the leukemia called acute myelogenous leukemia? j
A. Well, actually, the way you phrased the question, even at exposures in excess of a hundred parts per million, an individual is not more likely than not to develop leukemia. A very small percentage of the individuals who go on to

develop frank bone marrow toxicity will ever go on to develop leukemia.
So even in populations or individuals who have been exposed to concentrations that are clearly associated with the development of leukemia, only a small percentage of those individuals will go on to actually develop the leukemia.
Q. And of those who go on to develop leukemia from exposures to benzene, do you have, sir, a range or a concentration of exposure that is necessary over some period of time to develop the disease?
A. Well, as I've said, clearly, above a hundred. I think that probably above fifty. And we really don't know, in terms of any measurable end point we currently have, that exposures below twenty-five parts per million have been or are associated with those effects, although I would think it's reasonable to expect that somewhere below twenty-five parts per million is going to be a threshold.
Q. And you've described for the jury as a threshold that, in your opinion, the concentration below which there would be no

causal relationship between the disease being established or identified?
A. There would be no relationship -- benzene basically would not produce the types of damage that is required or is a prerequisite for the eventual development of acute myelogenous leukemia.
Q. You mentioned, in your opinion, the carcinogenesis or the leukemogenesis of benzene, I believe you said, was dose-response related, correct? There was a dose-response relationship between the two, correct?
A. There is a dose-response relationship between benzene and bone marrow toxicity. And, in my opinion, that relationship is important with respect to the development of acute myelogenous leukemia.
Q. Let me ask you this, sir: Have you been able to draw the dose-response or dose-incidence curve for benzene and benzene leukemogenesis? Have you been able to establish that curve yourself?
A. I'm not sure what you mean by that. I don't know what you're talking about, per se.
Q. Let me ask you: In your opinion, is the

dose-response relationship between benzene and leukemia, is that a linear relationship, a straight-line relationship?
A. The -- certainly, from both human studies and animal studies, looking at toxicity and blood dyscrasias associated with benzene exposure, it's clear that the relationship between benzene and blood dyscrasias is a very complex product of dose and duration.
You have to have doses or concentrations of exposure that are, as I said, certainly, for the experimental models, between 25 and 300 parts per million, but the actual duration of exposure varies in a very complex fashion.
Repeated exposure appears to be a very important requisite or prerequisite. We're not talking about single exposure. We're talking about repeated exposure. And it is not yet clear what the exact relationship is between the product of dose and duration.
Q. Are you telling us, then, that you're unable to draw for us the dose-response curve, or relationship between the amount of dose that one would receive of benzene, the exposure, if you will, and the response that they may have at

increased dosages? Are you -i are -- are you saying we don't know for sure what that line or curve looks like?
A. Within -- within the range of concentrations and scenarios that I've described to you so far today, yes, we can. But, certainly, the exact shape of that curve is by no means established.
That's -- that -- that is the same thing as the questions with respect to threshold or a concentration that does not result in the development of leukemia. It's the same question from a technical standpoint. The characterization of that curve is what we're talking about.
Q. That's what I'd like to focus on. If we just focus our attention right now on what you believe to be about 50 parts per million over a prolonged exposure period leading to the development of leukemia, do we know the shape of the curve from, say, 50 parts per million, to greater amounts, with regard to the incidence of leukemia? In other words, is that a straight line?
A. We can certainly surmise or infer, if

you will, from both the human data and animal data on metabolism, as well as toxicity of benzene, that there is a peak concentration, if you will, above which probably you're not going to see any increased incidence.
And that concentration or saturation point is probably somewhere between -- in animals, it's between 100 and 300 parts per million. And, in man, I would expect that it's going to be somewhere above 100 parts per million.
Q. Would it be fair to say, then, that from approximately 50 parts per million up to approximately 100 parts per million, we have a linear relationship, in your opinion, between exposure, concentration and incidence of leukemia; and then, after that point, it pretty much goes straight -- straight up and down, in other words?
A. No. No, not by any means. There are two basic errors there.
First of all, it would flatten out, not go straight up and down, basically meaning we reach a point at which you're not going to increase the incidence of the disease, at some

point, theoretically. And there's no reason to believe that's not the case, because for one thing, toxicity to the bone marrow would become so blatant that you wouldn't have survival long enough to develop leukemia amongst -- among other possibilities.
And the other issue is that between fifty and a hundred parts per million, we simply do not have sufficient data to describe the nature of that relationship.
Q. So, basically, between fifty parts per million and a hundred parts per million exposure to benzene, we can't define the shape of the curve, if you will, on the dose-response axes, in terms of whether it's a linear relationship, whether it's curved or linear, we just don't know, in your opinion?
A. That's -- that's correct.
Q. And as we try and take the end point, 50 parts per million, and work backwards, are you able to say, with any degree of certainty, sir, whether we're able to continue that line, whether it's straight or curved to the origin point, in other words, zero parts per million?
A. There's no data on which to base those

characterizations.
Q. So it's your opinion that when we leave 50 parts per million and go backwards to0ards zero, regardless of duration of exposure, we're unable to characterize the dose-response curve or line with regard .to benzene exposure and leukemia?
A. Certainly, in terms of the human data, that's correct.
Q. Let's talk about animal data. Is there an animal model, sir, that you're aware of that can be used as a predictor for human leukemogenesis?
A. No.
Q. Is it your testimony that there-'s no animal model that can be used as a relatively accurate predictor for human leukemogenesis and benzene exposure?
A. We have animal models that allow us to look at -- called blood dyscrasias, and certainly, in the mouse, I've been successful in producing blood dyscrasias with very complex dose product type exposures to benzene. The dyscrasias in the mouse are not directly extraporable to specific clinical entities in

man.
I personally think that there -- they are very analogous to leukemia in general, but there are no clinically accepted animal models for the types of leukemia we see in man. So it's very difficult to extrapolate from the animal models to man, in terms of understanding what benzene is doing and at what concentrations you're going to see leukemia.
The controversies really -- really are with the mouse, with respect to the morphologic and clinical entities that we see, whether they are, in fact, frank leukemias or not.
Q. In your opinion, sir, does benzene cause mutational aberrations in any animal or bacterial system?
A. Benzene is not a classic mutagen, certainly, in bacterial systems, by itself. As I mentioned before, it does produce secondary changes in chromosomes. It does produce certain abnormalities associated with chromosomes that may be important with respect to its toxicity.
Q. In your opinion, sir, is benzene a clastogenic agent or an agent capable of causing

damages and breakages in chromosomes?
A. Well, by definition, if it causes chromosomal breaks and/or abnormalities, it is a clastogen in that sense.
I would classify benzene as a reasonably weak clastogen. It certainly causes nondisjunctional events. It cur -- it certainly causes breaks. These are typical of agents that interfere with DNA replication and/or cell replication.
And we've demonstrated that benzene metabolites very clearly have that effect.
Q. How long, in. your opinion, has that been recognized, that benzene can cause breakages in chromosomes?
A. I'd have to review the literature specifically, to give you a complete answer to that question, but my vague recollection is we're probably talking about the early to mid '70's, the first indications. I could be -- I could be off by a few years there.
Q. Let's talk about the capability of benzene to cause mutations in various model systems.
One of the model systems that has been

used is the Ames Assay. Are you familiar with
that assay?
A. Yes.
Q. Is benzene a mutagen under the Ames
Assay scenario and model?
A. No, not by itself. It's not --
actually, benzene is not a very potent mutagenic
agent in those systems at all.
Q. In your opinion, sir, is that true,
also, when there's an S-9 activation factor added
to that particular test?
A. If you metabolize benzene, you can
produce certain mutagenic events. But by the
same token, if you compare benzene with an S-9 to
more potent mutagenic agents, it -- it does
not -- it is certainly not a potent mutagenic
agent in those systems.
Q. In your opinion, sir, is benzene a
mutational causing agent, but it's just not, in
your opinion, a strong one?
A. In the presence an S-9 fraction, you
can -- you can produce mutational events in some
bacterial systems, using a -- a reverse mutation
assay, like the Ames Assay.
Q. And would you tell us, sir, when was it

recognized that benzene was an agent capable of causing mutations in various test scenes --
A. In bacteria?
Q. -- such as the Ames Assay?
A. In bacteria? Again, I don't recall exactly. It's probably late -- it's either going to be late '70's or early '80's, I believe. I don't remember exactly when the Ames Assay first came into use.
Q. Are you familiar, sir, with sister chromatid exchanges?
A. Yes.
Q. Have you had a chance to look at that?
A. Yes.
Q. In your opinion, sir, does benzene cause any sister chromatid exchanges?
A. Benzene metabolites certainly do. Benzene administration to whole animals does. It increases the rate of sister chromatid exchanges that is seen in the normal animal.
Q. And for the benefit of us all, could you tell us what it means to have a sister chromatid exchange induced by a chemical such as benzene?
A. I wish I could, in a complete sense. It's really not known what the ultimate

significance of the sister chromatid exchange process is.
Q. But are we talking about, sir, a damage, if you will?
A. No, sir, actually, we're not. There is -
Q. Okay. What are we talking about?
A. There's no -- when we talk about DNA, and we talk about DNA damage, we're talking about a loss or change in information. If we change the code, we've altered the DNA.
In the case of normal biologic systems, we know that DNA changes places, and the code gets altered as a function of normal development. This goes on in lymphocytes. This goes on in B cells we've been talking about. It goes on in T cells, these are lymphocytes, a variety of different cell systems, as a part of normal development.
Sister chromatid exchange involves the transposition or movement of DNA from a chromatid, which is part a chromosome, or half of one, they change places. We have complementary chromosome pairs for each chromosome we have. And these chromatids change places in the case of

sister chromatid exchange.
They don't -- there's no ostensible change in the information, loss of information, or change in the code. They basically, various portions switch places. This goes on -- to a certain extent, there is a background frequency of sister chromatid exchange that goes on in the absence of treatment.
Some agents, when the cells are exposed to those agents, will go on to increase the rate of sister chromatid exchange. It's been used frequently as a screening tool to determine whether or not a compound had any effect on DNA, because it's easy to do.
And in this -- in this context, benzene has been demonstrated to increase sister chromatid exchanges in a variety of different cell systems.
Q. When you see a pattern of sister chromatid exchanges, is that not a normal finding to see in a person? Is that an abnormal finding?
A. Well, in -- categorically, no, it's not an abnormal finding. As I said, if you take individual cells and you place them in culture in an artificial situation in a test tube, and you

stimulate them to divide, you're going to see a background frequency of sister chromatid exchange.
Now, if at the same time, you directly expose those cells to increasing concentrations of agents that are potentially toxic, some of those agents are going to produce an increased incidence or an increased number of sister chromatid changes. Benzene is one of those compounds.
Q. Do you have an opinion, sir, whether a low level chronic exposure to benzene places a person at greater risk for the development of a leukemia, as opposed to an acute transient exposure to the chemical benzene and its relationship to the development of the disease leukemia?
A. What do you mean by "low level"?
Q. We can define it any way that you would like. Would you like to limit your testimony in low level to 50 parts per million or less, or do you have a range that you would like to talk about?
A. As I said before, I cannot fix -- I do not have a divining rod, and I cannot say that I

know the concentration of benzene that is associated with chronic exposure, the minimum amount that's associated with the development of AML.
Obviously, since I have told you that I believe that there is a threshold, and that everything that I have seen in the literature that points to a mechanism suggests a mechanism that's compatible with the dose-response and the threshold, I believe that there are concentrations of benzene, that following chronic exposure, or with chronic exposure to those concentrations, are not going to increase an individual's chance, if you will, of developing AML. We can play with numbers all day.
Q. Let's not do that. Let's talk about peak exposures that individuals may have on a transient basis, versus individuals who may be chronically exposed to low concentrations or small amounts over long periods of time.
And my question in that regard, sir, is: Do you view a person who has transient peak exposures to benzene at greater risk to the development of diseases of blood and blood-forming organs over a person who has

long-term exposure to lower concentrations of benzene?
A. If the concentrations are low enough that they do not, in my opinion, constitute a potential source of toxicity in the marrow, the answer to your question would be "Yes."
I think that intermittent exposure to benzene at high concentrations, repeatedly, is associated with potential to cause bone marrow toxicity, and eventually could lead to the development of AML. But we're talking repeated exposure.
Q. Okay. So, in your opinion, benzene has a causal relationship with the leukemia, acute myelogenous leukemia, correct?
A. Yes, sir. 17 Q. And when, in your mind, has that been established?
A. I think we discussed it this morning. I would say somewhere between the mid 1970's -- somewhere between 1974 and 1977 or '8.
Q. Do you have an opinion, sir, whether benzene exposure has a causal relationship to multiple myeloma?
A. I think the whole question of multiple

myeloma is one that requires a lot more work before we can say anything definitive about it. There are some studies that would suggest that there may be a relationship, but they're relatively small and, again, one of the biggest problems with these epidemiology studies is defining the exposures.
If one were to rely only on the McMichael study, one could reach the conclusion that perhaps there was a relationship between benzene and the lymphoid neoplasms seen there. But the followup studies have basically negated that original supposition, when they looked at exposures. I think that we don't have enough information, at this point, to really say one way or the other whether multiple myeloma is associated with benzene exposure.
MR. BARRIE: I'll object to the nonresponsive -- nonresponsive portion of the answer.
Q. (By Mr. Barrie) Do you have an opinion, sir, whether benzene exposure has a causal relationship with lymphomas, whether they be Hodgkin's lymphomas or non-Hodgkin's lymphomas?
A. I think, again, the principal -- the

studies where benzene exposures have been high and where they've been relatively the only exposures, these diseases have not been seen. I would refer to Infante, in particular, and several others, Vigliani. Where we have exposures that are very complex and involve more than benzene, we begin to see a totally different pattern. That has been seen in the rubber industry. And as I've said before, if one looks at the sum total of that literature, one's left with the conclusion that benzene is not the actor in that particular situation. And in those studies, there is an indication that there may be an increased incidence of lymphoid neoplasms. The problem there, again, is depending upon how the cases have been categorized and how they've been lumped together the way epidemiologists lump them, it becomes difficult to make distinctions between one disease type and another. And that requires very careful experimental design and a study large enough to distinguish between the different biological types.
Q. So, basically, if the study design in an

epidemiological study is not, in your words, particular enough, you may or may not pick up a certain type of leukemia, such as chronic lymphocytic leukemia, it may or may not be reported?
A. No, no. That's -- that -- that's not really what I mean. What I mean is that -- that epidemiologists are usually striving to get enough of -- to get a large enough sample size to see something, if there's something there.
So the tendency is to lump different diseases together in terms of categorization. For example, if you classify neoplasms as lymphoid, you may lump lymphomas or lymphosarcomas or chronic lymphocytic leukemia in the same pot, and when you're through, what you have is an increase in lymphoid neoplasms.
What you cannot say from that is any particular neoplasm has been increased, but you've got a very broad category that's increased.
The difficulty with that is that biologically we know these diseases are different, we know their origins are different, their progression is different, the cell types

are different, the prognosis is different. And it requires further study to characterize, in fact, if there's a specific association with one or more of those diseases.
Q. And one of the opinions you've reached in this case is that benzene exposure has no relationship, causally, to the disease of chronic lymphocytic leukemia, correct?
A. That's correct. 10 Q. And that, in your opinion, is true regardless of the concentration exposure, correct?
A. That's correct.
Q. And the articles on which you base your opinion are those that are contained in Exhibit No. 2?
A. In particular, yes. There are obviously many other articles that have helped contribute to the basis of my opinion, but if I brought everything in my file, I would have filled the room. The literature, in general, and in particular, supports my opinion, and the specific papers I brought I thought were pertinent to this specific issue.
Q. So with regard to the articles you've

brought in Exhibit No. 2, these are the ones you place particular emphasis on to support your position that benzene exposure, regardless of concentrations, has no causal relationship to the disease chronic lymphocytic leukemia?
A. That's correct.
Q. I'd like to move on now, sir, to the second opinion that you've rendered. And that, I believe, is that, in your opinion, Mr. Chambers' chronic lymphocytic leukemia was something that either preceded his birth, or shortly thereafter, in your opinion, correct?
A. Yes.
Q. And in order to come to that conclusion, you've done some analysis based on his blood count, his lymphocyte count, and done some analysis to reach that conclusion, right?
A. Yes.
Q. Is the article that sets forth the model that you used to come to that conclusion contained within Exhibit No. 2?
A. Yes.
Q. Okay. And I think you told us originally that that model was used for prognosis of individuals with chronic lymphocytic leukemia,

correct?
A. Yes.
Q. And what you've done is you've based a technique of regression analysis to work backwards from that model, to come to your particular conclusion?
A. Yes, sir.
Q. And will you tell me, sir, all of the assumptions that you had to make in order to perform this multivariant regression analysis to ultimately come to your conclusion that Mr. Chambers had his disease prior to his birth,. or certainly sometime thereafter?
A. Well, I used the approach to calculating lymphocyte doubling time that is referred to in the papers that are in this binder that have been demonstrated by Montserrat and others to, in fact, be a very good prognostic indicator of the progression of the disease.
The -- once the line is established or the slope the line is established, the only other assumption with respect to using it in the regression analysis, is that, in fact -- the principal assumption is that chronic lymphocytic leukemia is a monoclonal disease being derived

from a single cell.
Q. The disease chronic lymphocytic leukemia coming from a single cell, what takes place within that cell that initiates it, if you will, or causes it to develop into a lymphocytic leukemia?
A. Well, leukemia we generally think of as a multifactorial process, and that requires a number of different changes to occur. If we had a very clear understanding of all those changes, we'd understand the cause of leukemia in general, and specifically for each leukemia.
So we're not at that stage yet, in terms of being able to -- to say exactly what happens.
But certainly in the case of a disease like chronic lymphocytic leukemia, there are changes that occur, ostensibly at the level of the DNA, or within the cell during its early development that leads to it becoming a malignant cell.
As a malignant cell, it no longer abides by the same rules, if you will, and/or is -- it's no longer affected by the normal regulatory mechanisms that control the behavior of these cells in the body.
Q. This DNA, this DNA is a part of

chromosomes, are they not?
A. That's correct. In fact, in CLL, it's well known in CLL patients that there are chromosomal abnormalities that are specifically associated with CLL, that are not normally seen in other types of leukemias.
The most prevailing type of chromosomal abnormality that's seen in CLL's is called trisomy 12, or you basically have an extra Chromosome No. 12.
There are also, in a subpopulation of patients, seen other abnormalities, such as a deletion of part of Chromosome 14,,called 14 Q minus. This does not appear to appear early in patients with the disease, but only after the disease has manifest itself, for the most part.
Q. If I can, I'd like to just kind of reduce that, if I can. That was an awful lot for, I'm sure, us all to gather. But, basically, it's a held opinion that benzene affects the DNA, and DNA is part of the chromosomes, and that is a thought as to how chronic lymphocytic leukemia is developed. Would that be a very simple way of reducing it?
A. No, that's misleading, in terms of our

knowledge and the conclusions that can be derived from it. If you look at leukemias that are associated with exposure to benzene, or chemotherapy with alkylating agents, you see, first of all, AML as the leukemia, not CLL. Secondly, the types of chromosomal abnormalities that are seen in the -- there's a striking incidence of specific types of chromosomal abnormalities that are seen in secondary AML. These are five -- deletion of Chromosome 5 or 7 -- 5Q minus, 7Q minus. We are talking about a different pattern of chromosomal aberration and abnormality that are seen in CLL.
Q. Let's talk a little bit about this graph that you've done and its relationship to-, in your opinion, Mr. Chambers having his disease prior to his birth, or shortly thereafter.
You used various lymphocyte counts that were taken from approximately nineteen sixty to nineteen -- '67, approximately, to 1989, correct?
A. Yes.
Q. And from that, you derived a line with a particular slope on what's been marked as Exhibit 4, correct?
A. That's correct.

Q. Let me ask you, sir, how you were able to draw that line from the 1967 point, backwards, when there was no particular information to fill in to make sure that the line was A, straight; B, going to the origin along one of the axes that you have. What assumptions did you have to make?
A. The basic assumption, the most important one is that the doubling time was constant. That is based -- that, in fact, is the reason that doubling time is a valuable prognostic indicator in C LL, because, in fact, for CLL, and CLL, alone, is it -- is there information that indicates that the doubling time and the kinetics of cell replication and cell loss are constant. For other leukemias, this type of analysis is of not very much prognostic value, because the kinetics of the disease, the kinetics of replication can change. The -- as I see it, the proof is in the pudding. The calculation of doubling time and its constancy for CLL is the cornerstone of why that type of analysis is useful for prognosis.
And, in reverse, that it is reasonable to extrapolate, as well, backwards, with respect to obtaining some indication of the rate of tumor

development and increased body burden.
Since we're dealing with a monoclonal
disease, it's reasonable, based on that to make
some -- arrive at some conclusions with respect
to the relationship between the time of the
initiation of the disease and its progression.
Q. What -- what I'm trying to -- to get at
here is you have this line on Exhibit No. 4
hitting a part on one of the axes that's
labeled "Cell Number" somewhere around 10 to the
6th, correct?
A. Yes.
Q. Is there a level below that which you
would opine that this gentleman did not, at birth
or shortly thereafter, have this disease?
A. Well, if -- if the line clearly
intersected the X axis at some time prior to
1930, or since 1930, excuse me, one would -- one
would surmise that within a certain margin of
error that that was the most likely point at
which the clonal expansion, certainly of his
tumor, began.
In this case, that's not the case. We
basically do not intersect that axis prior to
reaching his date of birth. The -- based on

other studies, looking at twins, looking at the familial predisposition of families and siblings to the development of CLL, it's reasonable to assume, in the absence of any other information, that the -- that the initial event that resulted in the creation of this population occurred at some point either prior to birth, or shortly thereafter.
Q. In Mr. Chambers' family, nobody has had any chronic lymphocytic leukemia, that you're aware of, in his family, are you?
A. Not to my knowledge.
Q. Is your reliance on this particular study that identifies the prognostic tool for looking at chronic lymphocytic leukemia,-is that article the article that you're going to rely on in coming to your opinion that this gentleman, Mr. Chambers, had his disease prior to birth, or shortly thereafter?
A. There's several articles in the literature, numerous articles which discuss the kinetics of lymphocyte replication and CLL and the use of doubling time as a prognostic indicator.
I have included the majority of those in

the documents I've provided. There are some others, however, that I have not included simply because these, I felt, were sufficient. There are one or two others, that if you search the literature, you will find and they, in my opinion, are entirely consistent with those that I have provided here.
Q. Is there going to be some other article that you're going to rely on, other than what you've provided here, that will support your opinion that Mr. Chambers had this disease prior to birth, or shortly thereafter, any other specific articles that you're going to rely on?
A. Not -- not to my knowledge at the present time. As I -- as I mentioned earlier, if I'm asked questions that specifically deal or require me to rely on articles I have not provided, I will do so, but it's not my intention to do so, unless I'm required to.
Q. But you've given us, today, the opinions you have in this case?
A. Yes, sir.
Q. And you have no other opinions?
A. No, sir.
MR. BARRIE: We'll just take five

minutes.
MR. SCOTT: That would be great. I was hoping somebody would say that.
THE VIDEOGRAPHER: It's 12:41, and we're off the record.

(Whereupon, after a brief recess, the video deposition continued as follows:)

THE VIDEOGRAPHER: It's nine till 1:00. We're back on the record.
Q. (By Mr. Barrie) Sir, you've given us an opinion of yours that -- regarding. Mr. Chambers' chronic lymphocytic leukemia. In your opinion, it's not caused by his benzene exposure,-and I'd like to ask you this question: Do you have an opinion of what did cause his chronic lymphocytic leukemia?
A. Well, as I think I've said, it's more probable than not that he was either born with it, or he developed it very shortly after birth. Chronic lymphocytic leukemia has not been associated with exposure to hazardous agents. It's one of the very few leukemias for which it's reasonably clear that radiation doesn't even

cause it. And radiation causes most.
Q. And I understand, sir, that's your opinion. And what I'd like to know now is: Other than his, in your opinion, having it prior to birth, or after the birth, is there any other etiological agent or cause that you can subscribe that may have caused or contributed to his disease?
A. No.
Q. Do you have a contract, sir, with any attorney that's hired you in this case, a written contract?
A. No.
Q. Who would you be directing your bill in this case to?
A. That's a good question. I'll probably send it to Mr. Scott.
MR. BARRIE: I'll pass the witness.

EXAMINATION
QUESTIONS BY MR. SCOTT:

Q. I'd like to, Dr. Irons, if we might, do a couple of things.

First, I want to talk a little bit about more about some of the educational experiences you've had and some of the work experiences you have had.
You mentioned earlier that you had - you were involved in a study of the effects on the hematopoi -- hematopoietic system of extended space flight. For whom are you doing that work?
A. The National Aeronautics Space Administration. The University of Colorado and the University of Rochester have a consortium research effort that has resulted in us being awarded a center grant from NASA to examine the potential adverse effects associated with the space flight environment, principally associated with exposure to toxic agents, although, because the space environment is so foreign compared to that which we experience on earth, we have to look at a variety of different phenomenon in terms of evaluating potential hazards in space. There is evidence that individuals who have spent an extensive amount of time in space, that upon returning to earth, they have had problems with anemia, with problems related to calcium in their bones, and a variety of

physiological difficulties that are apparently associated with extended time in space. And we are part of an effort to determine just what the factors are that impact and influence those problems and, hopefully, to develop strategies to eliminate those problems.
Q. What is a center grant?
A. A center grant is a grant to establish a center, an organization that has a -- a focus on dealing with a particular problem.
In this case, we're talking about the adverse effects associated with potential exposure to toxic agents in space, and/or the problems associated with other conditions in space, such as weightlessness, radiation, and this type of thing.
Q. And did your group -- do you know how your group was selected by NASA to -- to do this work?
A. It was a highly competitive process in which we submitted a grant proposal, and it was initially reviewed on the basis of the proposal. We then had a site visit, which is a meeting where an independent panel of scientists come and look at the site and talk to the

scientists, and evaluate what they propose to do in light of what the requirements are to determine which is the best possible site to establish this center.
There were, initially, I think, approximately thirty universities that responded to this request by NASA. There were at least four that were site-visited, and we won the award.
Q. You also mentioned a -- some work that you had done with the Chinese Government. Can you describe how you got involved in that and what your role was?
A. Well, I've known Dr. Yin, who is the head of the -- what could best be described as the Occupational Medicine Branch of the Chinese Institute of Occupational Medicine, similar to our NIH, or NIOSH, if you will, kind of a combination. And I've known him for many years, because he has an interest in benzene toxicity. And -- and I believe it was in nineteen -- the fall of 1988, I accepted an invitation to visit the People's Republic to lecture on primarily the moni -- biological monitoring of workers and to participate or

advise them in the design of a potential epidemiology study to look at the effects of chronic exposure to butadiene in Chinese` workers.
They have a population of workers who, compared to western standards, have been heavily exposed to butadiene for what is now almost two generations, and it represents an attractive group of individuals to study, from the standpoint of having an opportunity to look at people who have, unfortunately, had relatively high exposures.
Q. And you did make a visit, then, to China?
A. Yes. Yes.
Q. You also mentioned, that among your other duties at the University of Colorado, you teach in the graduate epidemiology program. And I think you said you teach epidemiology graduate student -- students and MD's. What group or department within the University of Colorado is that program?
A. That program is centered in the Department of Preventive Medicine and biometrics.
Q. That may lead to my next line of

questions, and that is, I'd Pike some of the terms that you've used today to be defined for us. "Biometrics" would be a good place 'to start.
A. Oh, that's a good question. I think -- the best way to describe biometrics is biostatistics, I guess. It's the mathematical process of evaluating biological populations. In this case, obviously, the principal focus is human populations.
Q. You also used the term "immunopathology." What does that mean?
A. That's a specialization within the field of pathology that deals with the diagnosis and examination of tissues of of the immune system, and abnormalities or diseases associated with the immune system.
Q. Similarly, you used the term "hematopathology." What does that mean?
A. The -- there are very -- the distinction between hematopathology and immunopathology is relatively fairly indistinct, because, as I said before, these systems are intimately related. But that simply, again, is pathology associated with diseases of the blood and

blood-forming organs.
Q. You used a term called "leukemogenesis." What does that mean?
A. The genesis of leukemia, the cause of leukemia, the start of leukemia.
Q. Is "pathogenesis" a similarly defined word?
A. Yes. It's the genesis, if you will, of pathology in general. The progression of disease, ;the natural history of the disease, and what happens to an individual, or tissues, or biochemical or biological parameters during the course of that disease.
Q. You used the term "neoplasms" and specifically "lymphoid neoplasms." Can you tell us what those terms mean?
A. Neoplasm is -- is basically from the Greek. It means neo or new growth. A neoplasm is a growth. It can be a benign growth, or it can be a malignant growth.
If it's a malignant growth, it's cancer. As far as the lymphoid neoplasms are concerned, within the lymphoid system, per se, there's no such thing as a benign neoplasm, so all lymphoid neoplasms are malignant diseases.

They are cancer.
Q. You also used a term called "kinetics."
What does kinetics mean? And "cell kinetics," I think, is the way you said it.
A. They're -- cell kinetics deals with the replication of cells, the rate at which they divide, and how the populations, if you will, of cells change, in terms of the total number of cells. It can also relate to cell cycle kinetics, which is the characterization of cell replication.
Q. Now, finally, you've used a term, "monoclonal" and also "clonality." Can you tell us what those terms mean?
A. "Monoclonal" means that a disease, such as a leukemia, and CLL as an example of one that does this, virtually all do, they are derived from single cells, "mono" being one. "Clonal" means that each group of cells are clones of an original cell. So they're all basically mirror images of the parent cell. They all are derived from the same cell.
Q. How does the clonality or monoclonality of leukemia cells and, in this instance, chronic lymphocytic leukemia cells, help in the analysis

which you have done in this case?
A. Because they are all descended from a single cell, and we know that the way cells replicate, or duplicate, is to divide. We -- we know that the -- there was an original cell that was malignant, or changed, abnormal, and it divided to produce two. Those, in turn, divided to produce two, and so on.
So we know, that in terms of the progression of the disease, it started as a single cell, and we can, therefore, extrapolate, with reasonable confidence, backwards with respect to gaining some idea as to when the process started.
Q. Is that the same thing as saying that when a leukemia develops, and in this instance, chronic lymphocytic leukemia, that the -- there is an original leukemic malignant or cancerous cell?
A. Yes.
Q. And that everytime that cell replicates or divides, it essentially makes carbon copies of itself that have the same malignancy or leukemic features?
A. That's correct.

Q. I have a document that I'd like for you to look at, if you will. And we might want to hold it to the camera first. Let me hand it to you.
MR. SCOTT: We may want to mark this as an exhibit before we put it on the camera.

(Whereupon, the instrument referred to by counsel was marked for identification as Irons Exhibit No. 6.)

Q. (By Mr. Scott) This will be Exhibit 6 to your deposition. Can you take a look at it and then allow our camera operator to try to zero in on it, if he can.
1? A. Can I stand up?
Q. Sure, if that will be helpful.
A. If I'm going to see it, it is.
THE COURT REPORTER: Your microphone, Doctor.
THE WITNESS: Whoops. 23 THE VIDEOGRAPHER: Would you hold that up again?
Thank you.

MR. SCOTT: Okay. Do you have it?
THE VIDEOGRAPHER: All right.
Q. (By Mr. Scott) Can you tell me what that -- what Exhibit 6 depicts?
A. Well, this is a schematic diagram of normal blood cell development. It -- it shows the general pathways and the cells of origin for the various cell lines within the blood, both the myeloid cells we talked about and the lymphoid cells.
Q. In a case of chronic lymphocytic leukemia, is the cell which is the original cancerous or malignant cell, depicted on Exhibit 6?
A. Not directly, but we certainly know where it resides on the -- on the -- the chart itself, in terms of pathway.
Q. Can you show me where that is?
A. Okay. These lines, incidentally, depict directions that cells mature in. It doesn't depict all the different representatives of the types of cells that we know are here. There are many different stages going through this compartment.
They -- it's very clear, with CLL,

certainly the type of CLL that we're talking about in terms of Mr. Chambers, that the cell type that's involved are the B lymphocytes. And based on the gene rearrangements that occur -- see, this -- this cell line is the cell line that produces antibodies. Every antibody-producing cell produces a different antibody molecule. The genes that are associated with making that molecule rearrange at the point that the cell becomes a mature lymphocyte and during the process of development.
In the case of CLL, from the gene rearrangements that occur in both -- there are two -- there are two genes involved, one that codes for the heavy chain of the immunoglobulin and one that codes for the light chain. And both the heavy chain rearrangements occur at this level. The light chain rearrangements occur right here at the point of commitment, or maturation, to the lymphocyte lineage.
And the cell that's responsible for CLL has both, and it falls right here. So we're talking a relatively mature to intermediate level of maturity B cell, at this stage.
THE VIDEOGRAPHER: Doctor, can you

hold the exhibit off your microphone. It scratches on it.
THE WITNESS: Sorry. 4 THE VIDEOGRAPHER: Thank you so much.
MR. SCOTT: I wonder, could you help him try to set that up and let you look around the side of it, rather than standing.
THE VIDEOGRAPHER: Can we go off, the record for just a second?
MR. SCOTT: Sure. I think that's a good idea.
THE VIDEOGRAPHER: It's 2:18, and we're off the record.

(Whereupon, after a brief recess, the video deposition continued as follows:)

THE VIDEOGRAPHER: It's now 2:19. We're back on the record.
Q. (By Mr. Scott) We have just -- we've made the arrangements a little more comfortable to look at this exhibit now, but we had just talked about the -- the target or original cancerous cell in chronic lymphocytic leukemia,

and I believe you told us that that is in the B lymphocyte line, and that it is a cell of some -- some level of maturation; is that fair?
A. 95 percent of CLL's arise in this line. There's a small percentage that are associated with T cells. However, the nature of the disease, its progression and the prognosis are different. They are much different than that which has been experienced by Mr. Chambers. And so it is reasonable to expect that this is, in fact, the cell line we're talking about.
Q. Based upon your review of the medical records of Mr. Chambers, is it your opinion that that is -- that line, the B lymphocyte line, and the point to which you have directed us, is the target or origin cell for his chronic lymphocytic leukemia?
A. Yes, sir.
Q. I'd like to try to talk about several of the other leukemias, some of which Mr. Barrie discussed with you earlier today.
Let's start with chronic myelogenous leukemia. What is the target or origin cell for those people who have chronic myelogenous leukemia?

A. Well, chronic myelogenous leukemia is clearly a disease of the pluripotential stem cell. It involves an abnormality that occurs at the -- in the cell that's responsible for the development of all blood cells prior to its differentiation or maturation into either of these major cell lines. So CML is clearly a disease of this cell.
Q. Maybe it will be helpful to have some background on the terms "differentiation," as opposed -- as that term, as opposed to "replication."
In her deposition last week, Dr. Fehir, the Plaintiffs' expert told us that the pluripotential stem cell had two characteristics that were important. One is that it could differentiate; the second is that it could replicate. Do you agree with that, first?
A. Yes.
Q. Now, the cell marked "pluripotential stem cell" to the far left on Exhibit 6, does that cell have those characteristics?
A. Yes. It is capable of giving rise to all the different cells that are found in the blood. And it does so by becoming either a

myeloid progenitor cell, or as it's indicated here, a myeloid stem cell, or a lymphoid stem cell. That's differentiation.
Differentiation is the process whereby a cell begins to take on more and more specialized characteristics that eventually are associated with functional end stage cells. This cell has very few characteristics that allow anyone to distinguish it by looking at it, or it also doesn't have any specialized functions like these cells.
It has two major capabilities. One is to divide and produce either one of these type of cells --
Q. For purposes of our written record, "these type" are the lymphoid stem cell or the myeloid stem cell.
A. Yes.
-- or it can reproduce itself. "Self-renewal" is the term that's used. This distinguishes it from virtually any other cell within the bone marrow. It has the capacity to reproduce itself without necessarily committing to a differentiation pathway.
Q. All right. And I notice you have, in

the far left compartment of Exhibit 6 that - that is marked, "Self-Renewing Stem Cell Compartment," correct?
A. Yes.
Q. In other words, the pluripotential stem cell may divide to become another pluripotential stem cell, or actually two of them, I suppose; or, alternatively, it may divide to become either a myeloid stem cell or a lymphoid stem cell?
A. That's correct.
Q. Once you get into what's marked as the "Committed Stem Cell Compartment" either on the lymphoid stem cell side, or the myeloid stem cell side, what characteristics do those stem cells have?
A. Well, to -- to describe these -- what these cells do, I should probably say one more thing about this cell, and that is, although it can divide, it has a tendency to just sit there. It very rarely divides. At any one time, we may only have a few, literally, only a few stem cells that are responsible for making our blood cells, that is -- that are actually dividing and producing these cells.

And you have to remember we're producing over 200 billion cells a day to replace the normal amount of blood cells that are destroyed in natural, everyday life.
These cells, the -- what I prefer to call the progenitor cells, rather than the stem cell, myeloid progenitor cell and the lymphoid progenitor cell, have an increased tendency to divide. They divide much more often than this cell, but they have very re -- they are restricted in terms of the types of cells they can become. They can't go backwards. They can't go back this way. They can only go forward.
That's part of one of the protective mechanisms that we have within the -- the bone marrow. But these cells have an increased tendency to divide, and they're capable of giving rise to the different committed lineages.
The red cell in the case -- in the case of the myeloid progenitor cell, the red cell platelets, granulocytes or macrophages. The lymphoid progenitor cell is -- is not as well characterized, but it's clear that this cell gives rise to T cells and to B cells.
Q. To -- to try to put it in terms that I

can understand, then, the -- the myeloid, what's called myeloid stem cell on Exhibit 6, which you prefer to call "myeloid progenitor cell," may differentiate, so that it replicates into cells eventually becoming what are called erythrocytes or red blood cells on the chart, correct?
A. Yes. Q. And those carry oxygen in the body, is that --
A. That's correct.
Q. -- what red cells do? They may differentiate into what you have called platelets, or what are called platelets on Exhibit 6. Is there a name for that cell?
A. The megakary -- megakaryocyte, or megakaryocytic lineage, if you will. Megakaryocytes are the -- are very large cells. You can see them on bone marrow sections as being the largest cells on the section. They are the cells that actually break up the cytoplasm, which is that -- the main part of the cell, not the nucleus, but the rest of it, actually fragments to form platelets.
Q. And the platelets are responsible for clotting, so that we don't bleed to death with a

little cut?
A. They are responsible for clotting, and it appears that they play a role in wound-healing and repair, as well.
Q. And then, finally, there is a cell coming from the myeloid progenitor cell which appears to differentiate into granulocytes and monocytes or macrophages. What are those cells?
A. Granulocytes are our first defense, first cellular defense against infection. They don't respond to specific `agents. They respond in general to anything they see as foreign. And when we get an infection, they're the very first cells that come to the attack.
The macrophage is a cell that -- that can play a similar role, but it also functions in helping to regulate the interplay between this system and lymphocytes in the immune response.
Q. Can the myeloid progenitor, or stem cell, as it's marked on Exhibit 6, father, if you will allow my inartful use of the term, lymphoid cells?
A. This cell here? Q. Yes. A. No.

Q. Going to the lymphocyte, or lymphoid progenitor cell on the upper part of the drawing, can that cell father, if you will, any of myeloid cell lineage?
A. No.
Q. I've asked you where the target cell for chronic myelogenous leukemia is, and you've indicated what's called the "pluripotential stem cell" on Exhibit 6. How do we know that?
A. We have, on occasion, the capability of using specific genetic markers, or cytogenetic markers, that allow us to follow the progeny, which is simply the children, of a given cell. In the case of CML, there are a couple of different types of markers that have been used. One is the Philadelphia chromosome, which is a specific chromosomal abnormality that is associated with CML in -- in a large majority of cases, vast majority of cases. And this particular chromosome can be seen in all the cells that are daughter cells of the abnormal stem cell. In addition, we have markers such as the gene for glucose 6-phosphate dehydrogenase, which is a sex-linked gene that in some patients -- and

again it's sex-linked, so that we can see this in female patients, associated with the woman, she may have two different X chromosomes, and carrying one gene and one the other.
In any cell, there will only be one of those expressed, so you have a 50 percent chance of having an A type or a B type.
In a disease that's monoclonal, all the cells that are produced from an abnormal stem cell will have only one type, so you won't see a random pattern, or equal A and B. You'll see all one type. So you can follow which types of cells are descended from the abnormal cell.
In the case of CML, one can find either the -- the Philadelphia chromosome or glucose 6-phosphate dehydrogenase homozygosity, or the same type, in all of these cells.
So it's clear, in CML, in the patients that have been followed, that we can follow, that that the lesion has to reside at the level of this cell.
Q. Is that, to try to -- to reduce it from the term you just used to something that may be a little easier words to understand, is that the same thing as saying that there are certain

markers that doctors can use that will show up in a CML case in every one of the blood cells, or mature blood cells that descended from the original cancerous cell?
A. That's correct. And when you see those abnormalities or markers in different types of cells, especially when you see them in both lymphocytes, and in either red cells or granulocytes, you have a means of -- of concluding that it had to be this cell that was responsible for all of them, because that's the only cell that can give rise to all the different types of blood cells.
THE VIDEOGRAPHER: Doctor, can you scoot your microphone up a little bit. It's dragging on the table.
THE WITNESS: Sorry.
THE VIDEOGRAPHER: Thank you.
Q. (By Mr. Scott) Now, are there similar markers that can be used to determine -- or have been used to determine where chronic lymphocytic leukemia originates, or the target cell for it?
A. Well, as I said, the one -- the characteristic genes that we look at for determining the origin or the site of maturation,

the maturation level for cells in the B cell lineage are the immunoglobulin genes. In this particular process, going from the pluripotential stem cell to the lymphoid stem cell, somewhere in here, we may see rearrangements in the gene that codes for the heavy chain of immunoglobulin. It could occur even in the cell that's going to go down this pathway, theoretically. And in my experience, that can happen. But it doesn't mean anything, unless you also see a light chain rearrangement, because then you have the both chains of the immunoglobulin molecule that can make a whole functional immunoglobulin molecule. That occurs here, and that's the point at which CLL's of B cell lineage, that's the type of cell we see. The rearrangements are consistent with that. And, in fact, they do produce small amounts, usually, of IGM, which is a type of antibody molecule, on their surface. Fortunately for the patient, in most cases of CLL, they don't actively produce a lot of this antibody, because that would be abnormal and could lead to some problems. But they tend to be fairly quiet cells that don't do a lot of

damage and aren't very aggressive as they begin to multiply.
Q. In a case of chronic lymphocytit leukemia, do you see these markers you have discussed in the myeloid line, or the blue cell lines on Exhibit 6?
A. No.
Q. I want to quickly talk about one other type of -- general type of leukemia, that is, acute myelogenous leukemia, which you and Mr. Barrie discussed at some length earlier. What is the target cell or origin cell for acute myelogenous leukemia?
A. Well, again, we're using the same general type of marker analysis to conclude what the origin might have -- or had to be. In the case of certainly greater than 90 percent, maybe 95 percent of the AML's that have been examined in this way, the cell of origin is either a committed cell down here, or it's this cell here. There is a small number of cases which we cannot say that of and, in fact, we cannot determine whether it's here, or possibly here. This cell is often referred to as a

"multipotential progenitor cell," because it is capable of giving rise to different lineages. These would be called "unipotential," because they're capable, certainly, these two, of giving rise to just single lineages.
Q. Let me, again, for purposes of the written record, which will not be quite as clear as the videoed record here, the cells you have described as unipotential cells, or progenitors, are the three cells on the blue lines directly downstream from what's marked as "Myeloid Stem Cells" on Exhibit 6, correct?
A. Yes. At the risk of insuring there's no semantic confusion, this one is obviously -- this cell here, which is the granulocyte macrophage precursor, is technically multipotential, in the sense that it can give rise to two different lineages. But we know this cell exists.
Q. The cell you referred to a moment ago as the multipotential progenitor is what we've marked as "Myeloid Stem Cell" on Exhibit 6, correct?
A. Yes.
Q. And it's multipotential because it can differentiate to the erythrocytic line,

megakaryocytic line or the granulocytic,
macrophage --
A. Yes.
Q. -- or monocytic line?
A. And, in fact, in AML, there are several
different variants of AML that in determ -- that
are determined by the predominance of the
abnormal cell types that are seen. And they can
fall into any of -- they call fall into any of
these lineages.
Q. Now, is the description you have just
made or described for us, the target cells for
various types of leukemia, a hypothesis of Rich
Irons, or is it something accepted in the -- in
science and medicine?
A. The literature is there to support these
concepts. They are not my concepts. They are
the concepts of others. The -- as I've -- as
I've indicated, the -- the relationship between
this cell and CML --
Q. This is the pluripotential stem cell.
A. -- is very clear. There is absolutely
no doubt about that. As I have mentioned in the
case of AML, the relationship with respect to
this cell for 95 percent, or greater than 95

percent of the cases is clear. There is some question about some of these cases.
Q. That's the myeloid stem cell.
A. That's right.
In the case of CLL, the rearrangements that are seen in the genes that lead to the development of the cell type with the functional capabilities of a mature B cell are known and clearly described, and that's been clearly documented in the literature. These are not controversial.
Q. Can you give us, just by way of example, text, or something like that, where we might confirm that this is not just the world according to Rich Irons but is accepted in the hematological community?
A. If you want to look at a hematology text, I would suggest Dr. Jandl's book, or the Wintrobe text.
In the case of the leukemias, I would direct you to the recent edition of "Leukemia" which I presented.
In the case of additional information on CLL, I direct you towards the book "Chronic Lymphocytic Leukemia" by Poliak and Catovsky,

which I believe was last published in about 1986. It might be slightly later. There are numerous articles in the literature that deal with these subjects. I could direct you to the work of Philip Fialkow, who did some of original work on characterizing this cell, the pluripotential stem cell in CML.
Q. Okay. Thank you.
I want to -- do you have -- we can put down Exhibit 6 now. I think that's all we need with that right now.
And do you have your blue notebook? I think we marked it as Exhibit 2.
Earlier today, you described -- in describing your opinions, you indicated that there was evidence that benzene has not been associated with chronic lymphocytic leukemia, and I want to explore that a little more and go to some specific references in the materials you have.
Are there general statements about the etiology or cause of chronic lymphocytic in any of the articles you have that might be helpful to us, just to know what people writing reviews and articles today say on that subject?

A. Well, as I think I indicated earlier in -- this morning to Mr. Galbraith, I've already summarized a statement in the Foon review article in which it's indicated that chronic lymphocytic leukemia is not increased by exposure to alkylating drugs, radiation or chemicals. I've also included a number of other reviews that say similar -- make similar statements. Here's one exampled I included from a 1990 pathology text. And I included this simply to indicate that this is -- this level of understanding and consensus is one that is appreciated at the level of a general text that would be used to teach medical students, and, in fact, we use to teach medical students today.
Q. Would you read the title and editors of that text and the page -- and the entry that is relevant, and the page numbers?
A. It's "Pathology" by Emanuel Rubin and John L. Farber. Dr. Rubin is Professor and Chairman of Pathology at Jefferson Medical College, and John Farber is a professor in that department, as well. It's published by J. B. Lippincott Company in Philadelphia. I believe the publication date is 1990, although it may not

be on this particular page.
What I was citing was a page several pages from Chapter 20, which is by Dr. Hugh Bonner, and Chapter 20 deals with blood and lymphoid organs. And the statement I refer to is on Page 1083. And in reference to chronic lymphocytic leukemia, it reads: "The cause is unknown, and there is no known association with ionizing radiation or with myelotoxic agents."
Q. Is benzene one of the myelotoxic agents?
A. Yes, sir, by definition.
Q. Let's then -- I notice on that page Dr. Bonner goes on to say, "Genetic influences may be important."
A. Yes.
Q. On down in that paragraph, he also indicates that chronic lymphocytic leukemia is the most common type of leukemia in this country. Is that the case?
A. That's correct.
Q. And do people who have never been in chemical plants, or around them, get chronic lymphocytic leukemia?
A. Oh, yes.
Q. I think you've already read from

Dr. Foon's article. I want to be sure.
I'd like to go back to Dr. Foon's
article for just a moment, if you have it there.
A. Sure. Q. And, again, trying to focus on the most
recent articles and reviews, can you tell us when
Dr. Foon's article was written and where it
appeared?
A. It was published in October of 1990, in
the "Annals of Internal Medicine."
Q. I noticed, also, that one of the
coauthors with Dr. Foon is a doctor named Kanti,
K-a-n-t-i, R. Rai, R-a-i. Who is Dr. Rai?
A. Dr. Rai is a well-known hematologist
who, along with Dr. Eugene Cronkite, was-
instrumental in developing a staging system for
use in the prognosis, in determining the
prognosis of patients with CLL.
They developed this system at Brookhaven
National Laboratory in 1968, and published it,
eventually, in 1975.
Q. Is that a system routinely used by
hematologists in staging chronic lymphocytic
leukemia patients?
A. Yes, that as well another system that is

more recent, the Binet system', has seen considerable use. The Rai System is still -- certainly, the modified Rai system, which was modified in 1988, is still in use.
Q. I also noticed in the first -- on the first page of the Foon article, Page 525, that the authors -- and it's the right-hand column, it looks to be the third paragraph. The authors indicate, that in preparing this article, they say, "In our review, we emphasize recent insights into the biology and treatment of chronic lymphocytic leukemia. An English-language literature search was done using MEDLINE and CANCERLIT (1980 to 1990), abstracts and reviews from meetings, and extensive manual searches of bibliographies of identified articles."
What are "MEDLINE" and "CANCERLIT?"
Q. These are computerized databases that are supported by the National Library of Medicine and that all clinicians and medical scientists in the country access or use in searching the literature for articles that relate to subjects that they're interested in.
Q. Are those computer tools that one -- that you would expect one, in your field of

expertise to -- to utilize, ifs trying to
determine what articles had been written on the
etiology or causation of chronic lymphocptic
leukemia?
A. Oh, yeah, every day. These are -- these
are extremely -- these are the major computerized
sources for current published information in the
field.
Q. Going over to Page 526 in the very first
paragraph in the left-hand column on the page, I
believe you read it earlier, but I have a
question about -- about it. That paragraph
indicates: "The cause of chronic lymphocytic
leukemia is unknown. Unlike other forms of
leukemia, the incidence of chronic lymphocytic
leukemia is not increased by exposure to
alkylating drugs, radiation or chemicals."
What are "alkylating drugs"?
A. Alkylating drugs are chemotherapeutic
agents, primarily, immunosuppressive and
chemotherapeutic agents that alkylate, which
implies that they bind to, in this case, DNA, and
alter DNA.
Q. Earlier, when Mr. Barrie was asking
questions about the mutagenicity of benzene, I

believe -- and I don't want to misstate what you said, but I believe you said that it was - benzene was not as powerful a mutagen as some of these alkylating agents. Is that a fair statement?
A. That's a very fair statement.
Q. Can you give me some examples of these alkylating agents?
A. Cyclophosphamide is an alkylating agent. Nitrogen mustard is an alkylating agent. A large number of chemotherapeutic agents that are routinely used in treating leukemias and other cancers are, in fact, alkylating agents.
Q. Now, if I understand the way alkylating drugs or agents are used in chemotherapy, it is that there are certain patients who have -- that present with some type of cancer, that is, generally not leukemia, and that in treating those cancers, the doctors give them these alkylating drugs or agents to treat the underlying cancer; is that fair?
A. That's correct.
Q. And that in some percentage of those patients who have received these alkylating drugs, the -- a leukemia later develops. Is that

true?
A. In a small proportion of the patients receiving these types of chemotherapeutic agents, that can happen, yes.
Q. Does the literature show what type of leukemia arises, when it does, from the administration of these alkylating drugs?
A. Yes, it does. That literature is very well developed because, unlike the situation that we often have in an occupational setting, with respect to characterizing exposure to chemicals, in this case, the patients are basically a captive audience. They have been administered these drugs, which are very potent and are designed to attack their cancer cells. We know the doses they've received, we know when they've received them, and they're followed throughout their lifetime to see what effects result from that.
So here we have a literature that's well developed. The -- the individuals are well defined. They're known, their exposure is well-defined and known and quantitated, and the outcome is also well-defined. And that literature, which is considerable over the last

20 years or so, indicates quite clearly that
exposure to alkylting myelotoxic drugs results in
an increased incidence of acute myelogenous
leukemia in those populations.
It also indicates that they are not
associated with lymphoid neoplasms, per se. And,
in fact, I recall one reference in the leukemia
text that specifically addresses that -- that
statement, in terms of a review of the literature
and the conclusion that's been reached.
Q. That is, the author in the leukemia text
we have up here on the table specifically noted
that the lymphoid neoplasms, which I take it
includes chronic lymphocytic leukemia, don't show
up with this sort of administration of alkylating
agents?
A. That's correct. Would you like me to
find it?
Q. It might helpful if you could locate
it.
MR. BARRIE: How much longer do you
have?
MR. SCOTT: Five minutes, maybe
ten.
A. This is Chapter 14 in the "Leukemia"

text by Henderson and Lister, and it's -- it's written by Dr. Rosner and Dr. Grunwald, who I believe are at Roswell Park in Buffalo. Although I'm not certain, I think that's where they are. And the title is "Chemicals and Leukemia." And the last paragraph of the article, the book chapter, reads: "This review is limited to acute myeloblastic leukemia, or one of its variants, developing in patients treated with cytotoxic chemotherapy for neoplastic and nonneoplastic diseases. Other types of leukemia, such as acute lymphocytic leukemia, acute myelofibrosis, and chronic myelocytic leukemia has sporadically been reported following chemotherapy for a variety of neoplasms,-.but without a trend or pattern, thus suggesting a purely coincidental occurrence."
And if you'll note, they don't even recognize or mention chronic lymphocytic leukemia.
Q. Mr. Barrie had asked you earlier about benzene affecting the DNA and, again, you indicated that it was not a particular -- not particularly powerful in that regard, certainly as related to something like these alkylating

drugs; is that true?
A. Yes.
Q. And what the reference you have read to us indicates is, that even with the use of these much more powerful alkylating agents, these agents that have that propensity, more so than a chemical like benzene, CLL's don't show up?
A. That's correct.
Q. Are you familiar with references that indicate that radiation has not been associated with the development of chronic lymphocytic leukemia?
A. Yes, sir.
Q. Does that fact assist you in any way in reaching the conclusions you have reached concerning chronic lymphocytic leukemia in this case?
A. I think the the debate over the potential relationship between chronic lymphocytic leukemia and any -- and any causative agent is really clarified or aided by knowledge that even radiation, which we know can cause virtually all types of leukemia except CLL, is not associated with an increased incidence of CLL. There's just no definitive, reliable body

of information anywhere that would lead one to draw a conclusion that CLL is caused by exposure to cytotoxic agents or radiation.
Q. I want to turn to the second opinion that you have provided today, and I want to look at a little bit of the literature that I -- I think you've got in your notebook there related to the lymphocyte doubling time analysis.
Again, I want to determine whether this is -- the use of a lymphocyte doubling time analysis or the accuracy of that type of analysis is a hypothesis of yours or something that's been recognized in science -- in the scientific and medical literature.
Can you point to some articles that discuss that analysis, how it's done, and the prognostic uses of it?
A. Yes. I can do it in two ways. One, I can refer to the original papers, to begin with, and then, if you like, I can refer to the same reviews that we've been talking about and others that I have that, in discussing the biology of disease, comment on the utility of lymphocyte doubling time as a reliable factor for prognostic purposes.

Q. I'd appreciate it if you would do it in that order, then.
A. Okay. The -- there are a great many papers that have been written that deal with the kinetics of lymphocyte replication in CLL. These are papers by Sweet, et al., February 1977, "Clinics in Haematology;" Zimmerman, et al., 1968 in "Blood;" Theml, et al., from 1973, dealing with the kinetics of the tumor cells in chronic lymphocytic leukemia; the lymphocyte doubling time, the -- the -- probably the most important paper with respect to characterizing its use as a prognostic indicator ~s that of Montserrat, M-o-n-t-s-e-r-r-a-t, which was published in 1986, in the "British Journal of Haematology."
And it -- it -- it demonstrates rather impressively in a group of a hundred untreated patients that the lymphocyte doubling time distinguishes two populations, those that have a doubling time of less than 12 months, and those that have a doubling time of greater than 12 months.
The -- as I indicated earlier today, the prognosis, or the outlook for those with a

doubling time of greater than 12 months is much better than that for those that have a more rapid turn-over.
The estimation of body burden that I used is based on an article by Stryckmans, which appeared in February of 1977 on the kinetics of chronic lymphocytic leukemia.
Now, I've use technique because, as I mentioned before, as a function of variations in weight, it's a more reliable indicator than the absolute lymphocyte counts in the blood.
By the same token, the slope of the line that's created by using either the absolute lymphocyte count or an estimation of body burden is going to very similar, so that, in fact, in this particular case, there would be no appreciable or significant differences between the slope generated using either. method. I chose this one because it's the most conservative.
Q. "Conservative" in what sense?
A. It's considered to be a more reliable indicator of body burden than the lymphocyte count, which can fluctuate widely.
By the same the token, it should be kept in mind that the absolute cell numbers that are

projected here are not necessarily that accurate in terms of body burden. They could vary considerably, but they're all going to vary the same way, and it's not going to affect the slope of the line.
That's the real value of this technique. You're not using an individual blood level or a blood value for an estimate on which to base a -- an analysis. You're looking at the total progression of the disease and the development of an increased tumor load with time.
Q. I'd like to turn to Exhibit 4, which is the graph that you discussed earlier with Mr. Galbraith. And we might, again, put up our document stand and see if we can have the camera look at it and let you talk about it a little bit.
THE VIDEOGRAPHER: Can you kind of move that toward the Doctor, Mr. Galbraith?
THE WITNESS: I'm tangled up in my --
THE VIDEOGRAPHER: In your umbilical?
THE WITNESS: Yeah. 25 MR. GALBRAITH: Like that? Can you

see that, Doctor?
THE WITNESS: (Witness nods')
THE VIDEOGRAPHER: Go ahead.
Q. (By Mr. Scott) Now, there are a number of black dots on Exhibit 4. Can you tell me what each one of those black dots represents and where it came from?
A. Well, as I mentioned earlier, I took the individual blood data from Mr. Chambers' chart, each time that I could find blood data, and determined, using his weight, the estimated body burden for total lymphocytes, according to the Stryckmans nomogram.
I then averaged that for every year, because there were some years in which he had multiple measurements, and they vary somewhat, which is reasonable, given both the variability of the peripheral blood -count, in cases of CLL, as well as any laboratory variation or error.
So I averaged them for every year and then plotted them on this graph as a function of time.
Q. How do we know that your Exhibit 4 is accurate? For instance, if one of the blood counts that Mr. Chambers had, as a result of lab

error or something like that, was way off?
A. Well, as you can see from the chart, not every point on that line, every point on the graph is on the line.
So there, in fact, are variations from, or deviations that you see here that are well within experimental and/or clinical error. And, in fact, I'm impressed with the tightness of the fit. I mean, the -- for any given point, one could arguably say that it's not necessarily representative of what's going on in that patient with time. But all the points define a line.
As I said before, the -- the actual cell number that's defined by the line may not be accurate. It could be, within plus or minus, maybe even an order of magnitude of that point. But the points themselves depict a line or a slope that isn't going to change.
Q. In other words, assuming that the actual number of lymphocytes measured is incorrect and is off -- let's say the actual number was actually one order of magnitude less than what is depicted by Exhibit 4, would that have any bearing on the opinions you have reached in this case?

A. No.
Q. And why not?
A. Because the slope of the line is very clearly defined by those points and is not going to change as a function of the estimate, because the estimate, which is based on, again, the Stryckmans study, is constant, so, therefore, whatever that estimate is pertains to every point on the line. So the asbolute number, in reality, might differ, but the slope won't.
Q. And Exhibit 4, the -- the line that was drawn was done using a technique that is set out in Dr. Stryckmans' paper which is in your blue book, "Cell Kinetics in Chronic Lymphocytic Leukemia."
A. The estimate of the body burden was according to Dr. Stryckmans' paper. The use of it to calculate doubling time was based on the Montserrat paper.
Q. I understand. What -- on the Y axis, the "Cell Number" axis on the left-hand side of the page, what is it that you are measuring? What is the datapoint on the left-hand side, under "Cell Number"?
A. That's the estimated body burden of

lymphocytes, which in the case of a patient with CLL will progressively, with time, become more and more associated with the tumor. So, eventually, you're dealing with a majority of cells that are abnormal.
Early on, you're dealing with very few and, in fact, you can't tell they're there.
Q. Is it abnormal cells that are listd -- that are described by this graph on the Y axis on left-hand side, as opposed to all lymphocytes?
A. It's all lymphocytes. And as we go out in time, that becomes progressively, again, a representative of the tumor cells. And the -- that's characterized quite well in the Stryckmans article.
Q. Does the fact that the line that is drawn through these various datapoints on Exhibit 4, related to Mr. Chambers, tell you anything about the constancy of the doubling time of chronic lymphocytic leukemia.
A. You betcha. It illustrates that once the -- the very well-known and appreciated characteristic of CLL is that the kinetics are very constant. The other thing it demonstrates, in this case, is -- again, the fact that those

points depict a line so -- so well is characteristic of a very reproducible dodbling time.
Q. Are the opinions which you have provided in this case to Mr. Galbraith, in response to the questions posed by Mr. Galbraith, Mr. Barrie and myself, based upon reasonable scientific probability, after a review of the medical records of Mr. Chambers and the various scientific and medical articles you have referred to, as well as your background, which you've described for us?
A. Yes, sir.
Q. Have you -- during your career, have you authored or edited any books in the -- on the subjects of hematology, toxicology, molecular toxicology, those sorts of subjects?
A. Yes, sir.
Q. Can you tell us the names of the books which you've either authored -- authored chapters in or edited, or are they listed on your CV?
A. They're -- they're listed in my CV.
Several times throughout your deposition today you have said things like, "I've been successful in demonstrating," or "We've been successful in

demonstrating" in referring to certain
investigations. What were you talking about?
A. I was referring to studies that I've
been involved in, or have been done in my
laboratory. Basically, we have -- "we" again,
meaning in my laboratory, either at CIIT or since
then, have been involved in a variety of studies
to characterize the effects of benzene, benzene
metabolites, on toxicity to the bone marrow, to
the stem cells in the bone marrow, to lymphocytes
and to the blood-forming organs and the immune
system.
And at various times today, we've
touched on subjects for which my own work was
relevant to the discussion and, in that context,
I've said, "I" or "We."
Q. One thing I want to be sure we
understand, when you talked about demonstrating
something in your lab, you're not talking about
just reviewing articles that someone else has
written; is that fair?
A. That's correct.
Q. You have actually been involved directly
in animal studies; is that true?
A. Yes, sir.

Q. Have you been involved in -- and I hesitate to use the term, and I'll hope you'll tell us what it means, but in human studies?
A. Yes, sir. 5 Q. Obviously, we can't use, and wouldn't want to use humans to study the effects of drugs, chemicals, and that sort of thing, the way we can with animals. How do you do human studies? What are you talking about?
A. Well, we basically -- there are two major types of research that one can do with -- and that can be called human studies. We're -- we're -- we're engaged in both. The first is to compare human bone marrow cells and stem cells and their behavior and their susceptibility to toxic -- toxic compounds in culture. And we can compare those to animal cells such as the mouse. And we can, doing that, obtain a -- an understanding as to the relative differences and the susceptibility of the individual cell types. And since we can expose mice to toxic compounds, we can then begin to extrapolate from the mouse to man based on what we know about the relative susceptibilities and effects of the different cells in culture.

The other arena in which we can begin to get a handle on the -- the nature of how-blood cells work, and their susceptibility to toxic agents is in the arena of therapy, where patients are being treated for diseases, such as leukemia or other solid tissue, tumor types, and may - and the therapy may, in fact, require an examination of their bone marrow, or it may involve a bone marrow transplantation, which is now a very rapidly progressing and developing area of research in terms of approach to therapy for tumor types, as well as leukemia.
And one of the areas we're interested in is understanding how one can go about taking a patient's own stem cells, purifying them, treating him for whatever his particular cancer is, in such a way that we don't have to worry about the damage it's going to cause to his bone marrow, because we can then reinstall his own bone marrow cells back into him, to allow him to survive and recover.
This is a new treatment, modality, if you will, that is being investigated at a number of centers across the country and in various types of protocols.

Our own particular bone marrow transplantation center at the University of Colorado is focusing on what's called -- it's a big word, but it's very simple -- autologous bone marrow transplantation, which is reinfusing the patient's own marrow back after treatment for cancer.
Q. Mr. Barrie mentioned earlier a test known as the "Ames Test." What types of cells does the Ames Test use in determining mutagenicity?
A. Particular strains of E. coli, which are bacteria that's normally found in the gut and the intestines.
Q. These aren't human tissue cells; then, that are being used, but rather bacteria cells; is that fair?
A. That's correct.
Q. And that would be as opposed to the types of human tissue, marrow tissue investigations you described for us a few minutes ago.
A. Well, certainly, we're using human cells, bone marrow cells. We're not using bacteria.

Q. Mr. Barrie also asked some questions about the -- what's called clastogenecity of benzene. I know I've had four or five cups of coffee during this deposition today. Is coffee or caffeine a clastogenic agent?
A. Yes, sir, it is.
Q. Are there lots of clastogenic agents that each of us ingests each day of our lives?
A. Lots of clatogenic agents and lots of carcinogenic agents.
MR. SCOTT: I believe that's all I have. Thank you, Doctor.
MR. GALBRAITH: Let's take a little break.
THE VIDEOGRAPHER: It's now 3:13. We're off the record.

(Whereupon, after a brief recess, the video deposition continued as follows:)

THE VIDEOGRAPHER: It's now 3:28, and we're back on the record.

(Whereupon, there was a discussion held off the record, after which the proceedings continued

as follows:)

(Whereupon, Irons Exhibit Nos. I and 8 were marked for identification.)

MR GALBRAITH: Dr. Irons, after reviewing my notes, I have no further questions for you. Thank you, sir.

RE-EXAMINATION
QUESTIONS BY MR. BARRIE:

Q. Sir, let me just show you what's been marked as Exhibit No. 7 and ask you, sir, if you can identify that document?
A. Yes. This is the letter that I received, the cover letter I received with the medical records of Mr. Chambers, when they came.
Q. Is that the engagement letter, if you will, with Mr. Scott --
A. Yes.
Q. -- retaining your services as an expert in this case?
A. Yes.
Q. Let me also show you, sir, what's been

marked as Exhibit No. 8, and it's the last page of three documents, and ask you if you can tell me what that is, sir?
A. These are the notes of my technical assistant, who I had go through Mr. Chambers' medical records to determine his weight history in those records and to associate his weight at the time that the various blood tests were performed.
Q. Those three pages, which is marked as Exhibit 8 on the last of the page, were those the documents that you used to come up with your printout which is marked as Exhibit No. 5 in this case?
A. These were used simply to correlate his weight with the blood data, which was then used to construct that chart. And that, in turn, was used in providing the averages that are used on the computerized sheet.
For most of those, the weight corresponds to the actual day or admission when the blood test was taken. When, in fact, there was no weight data available, we used the nearest weight we could find in the chart. Since his weight doesn't vary that much, it didn't seem, to

me, to be particularly important.
Q. These three documents marked as Exhibit No. 8 on the last of the third page, these report weight in pounds at a specific time period?
A. Yes.
Q. And does that correlate with Exhibit No. 7 to give us the weight in kilograms during the same time period?
A. We simply translated pounds into kilograms so that we could use the nomogram as published by Dr. Stryckmans.
Q. I understand that, but I just want to make sure that Exhibit No. 8 relates to number - Exhibit No. 7, insofar as we're transposing weight in pounds to weight in kilograms, correct?
A Yes, sir.
Q. I want to just ask you some general questions of Exhibit No. 7. I understand what the column under "Date" means, and I'm fairly sure I understand what the WBC, or the white blood cell count is.
The next column is "Percent."
A. It should be "Percent Lymphocytes."
Q. Okay. And where did that number come from?

A. From the differential smear -- differential examination of the blood smear in each of those particular blood tests.
Q. And that was reported in the medical literature you reviewed?
A. In -- in his medical history, yes, sir.
Q. The next column is "Absolute" -- "Absolute Count Lymphocytes."
A. Yes.
Q. Can you tell me where that number came from?
A. That is simply the product of the fraction of total cells that the lymphocytes represent times the total blood count, so it gives you the -- the quantitative number of lymphocytes per cubic millimeter.
Q. As we move over, there's a column called "Weight" in kilograms, and we've established what that is.
The next column is the "Body Burden."
A. Yes.
Q. And there's something written on the top of that I just can't read. Would you just tell me what that is.
A. "Stryckmans." That's --

Q. So that's the calculation from the Stryckmans' work --
A. That's the
Q. -- that you talked about?
A. Yes. I'm extrapolating from his -- from his chart.
Q. And then there's another column with a star over -- over the top, giving some numbers. And the first one, corresponding to the date December 20th, 1989, 8.7 times 10 to the 11th. And what number is that, sir, and how was it derived?
A. That's the estimated body burden, which would be the product of his weight in kilograms times the Stryckmans' nomogram number.
Q. And what significance does that series of numbers under that column play?
A. That is the estimated body burden using that technique.
I then averaged that on a yearly basis to come up with the numbers that are on the computerized sheet that was then used to -- as the basis for the graph.
Q. You're referring, of course, to Exhibit No. 5?

A. Yes. And there's also a doubling time analysis on that.
Q. And the way Exhibit No. 7 and Exhibit 5 and Exhibit 4 relate together is that you take these numbers on Exhibit No. 7, as modified by Exhibit No. 5, and you plot it on Exhibit No. 4?
A. Yes.
Q. Although you have the numbers under Exhibit No. 4, that work around this line that you've drawn through them, would it be fair to say that the line, as it goes towards the axis which is labeled "Cell Number" is frankly an assumption on your part, based on the analysis contained within the works that you've cited?
A. This is an extrapolation, which-by definition assumes that the -- the literature that I -- that has formed the basis of my opinion and this analysis is, in fact, correct, yes.
Q. Have you understood my questions today, sir?
A. I believe so, yes.
MR. BARRIE: I pass the witness.
MR. SCOTT: Let me grab this microphone. I have just a couple of questions.

RE-EXAMINATION
QUESTIONS BY MR. SCOTT:

Q. Dr. Irons, Mr. Barrie asked you same questions earlier about -- asking whether you had been in either a Marathon -- Marathon Oil or a Monsanto Company chemical plant or refinery. Have you been in chemical plants and refineries in your career?
A. Yes, sir, I have.
Q. And I understand not for either of these Defendants, but for other companies, you have visited and seen the types of operations that those companies have in chemical plants and refineries?
A. Yes, I have.
Q. He also asked you some questions concerning 55-gallon drums of benzene, and you indicated that the use of 55-gallon drums -- well, I don't remember -- was outrageous or outlandish, something along those lines.
MR. BARRIE: Let me just object to the form of question. I've not asked this gentleman one question about 55-gallon drums of benzene.

MR. SCOTT: Okay.
Q. (By Mr. Scott) I'm sorry. Mr. Barrie --
Mr. Galbraith may have asked you those questions
earlier today. I want to be sure I understand
what you were saying.
First, do you have any reason to believe
that there were 55-gallon drums of benzene at any
Monsanto or Marathon facility in which
Mr. Chambers worked?
A. No. I have no information on that.
Q. Based upon your knowledge of the
processes that are involved in chemical plants
and refineries, do you have reason to question
whether there are -- there were 55-gallon drums
of benzene at those types of plants and
refineries?
A. Based on my knowledge of the chemical
industry, and only that, I would find it
extremely unlikely and, in fact, I can't think of
any reason why any company would leave 55-gallon
drums of benzene sitting around for any length of
time.
Benzene is flammable. It's extremely
flammable. It represents a fire hazard, amongst
other things. And keeping large amounts of

benzene around for use as a cleaning solvent seems, to me, incredulous. It's hard to believe.
MR. SCOTT: I believe that's all I have. Thank you.

RE-EXAMINATION
QUESTIONS BY MR. BARRIE:

Q. You have no personal knowledge, sir, of what the standard operating procedures were of the Marathon plant, or for the contractors, subcontractor personnel working in that plant, or of any other facility here in Texas, do you?
A. No, sir.
Q. And you mentioned it would be incredulous to have barrels of benzene used for cleaning solvents, from a probability standpoint. Did I understand that correctly?
A. Yes, sir.
Q. Would it not also, sir, be incredulous, from a health standpoint, to have barrels of benzene used in a refinery for the cleaning of hands and tools?
A. For that purpose, yes, sir.
MR. BARRIE: I pass the witness.

MR. SCOTT: I think that's all I have. Thank you.
THE VIDEOGRAPHER: It's now 3:37. This is the end of Tape No. 3. We're off the record.

(Whereupon, after a brief discussion off the record, the stenographic record continued as follows:)

MR. BARRIE: I just need to put a statement on the record.
MR. SCOTT: Okay.
MR. BARRIE: Plaintiffs are going to object to the use of this testimony in the trial of the matter of this case insofar as it concerns the Defendant Monsanto. The Judge has ruled on several occasions that the Defendants are not able to use Dr. Irons as a testifying expert, and I'll object to all questions being directed by Mr. Scott to this gentleman. And I'll further object to its being used by Mr. Scott, Ms. Lewis or Mr. Goforth in the trial of the matter, pursuant to the Judge's Order.

MR. SCOTT: Monsanto would obviously comply with all orders of the Court, and any reconsiderations of those.

RICHARD D. IRONS

SUBSCRIBED AND SWORN to before me, the undersigned authority, on this the day of 1991.

Notary Public

1 THE STATE OF TEXAS
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5 I, Emanuel A. Fontana, Jr., Certified
6 Shorthand Reporter in and for the State of Texas,
7 hereby certify that at the time and place stated
8 the witness, Richard D. Irons, personally
9 appeared before me, and after being by me first
10 duly sworn to tell the truth, was examined by
11 counsel for the respective parties hereto; that
12 the testimony of said witness was taken in
13 shorthand by me, later reduced to typewriting
14 under my direction, and the foregoing 203 pages
15 are a true and correct transcript of said
16 testimony.
17 GIVEN under my hand and seal of office
18 on this 5th day of February, 1991.
19
20
21
Emanuel A. Fonta a, Jr. -
22 Certified Shorthand Reporter in and for the State of Texas 23 Reporter Certification
'Nb. 1232 Expires December 31, 1992 24 25