IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF PENNSYLVANIA

THOMAS J. McCONNELL and DIANE McCONNELL, his wife, individually and on their own behalf and as parents and natural guardians of KRISTINE McCONNELLL, a minor,	:	CIVIL ACTION
vs.	:	
CIBA-GEIGY CORPORATION	:	
and	:	
ORKIN EXTERMINATING COMPANY, INC.	:	NO.80-1692

Philadelphia, Pennsylvania

December 9, 10, 1982

BEFORE: HON. ALFRED L. LUONGO, CHIEF JUDGE
(And a Jury)

TESTIMONY OF DR. SAMUEL EPSTEIN

APPEARANCES:

STEPHEN R. BOLDEN, ESQ.,
WILLIAM W. SPALDING, ESQ.,
RICHARD C. FERRONI, ESQ.,
Attorneys for the Plaintiffs

F. HASTINGS GRIFFIN, JR., ESQ.,
FRANK J. EISENHART, JR., ESQ.,
Attorneys for Ciba-Geigy

EDWARD L. McCANDLESS, ESQ.,
Attorney for Orkin

REPORTED BY: DAVID S. EHRLICH, CSR, RPR, CP, CM
OFFICIAL COURT REPORTERS
Room 2722
U.S. Courthouse
Philadelphia, Pa. 19106

DR. SAMUEL EPSTEIN, Sworn.

THE COURT REPORTER: State your full name, please.

THE WITNESS: Samuel Epstein, E-p-s-t-e-i-n

DIRECT EXAMINATION

BY MR. BOLDEN:

Q What is your profession, Doctor?

A I am a toxicologist, pathologist, M.D..

Q Do you specialize in any areas of medicine?

A I specialize in the effects of toxic chemicals in the environment, in air, water, food and the workplace.

Q Would you give us your educational background.

A My educational background, as spelled out in the curriculum which I gave you, is basically that of, I qualified in physiology in London University, England, I took a degree in medicine in 1950 in Gy's Hospital in London University; in 1952 I took a degree in tropical medicine and hygiene; in 1954 I took a degree in pathology; in 1958 I took an advanced degree in medicine; in 1963 I was awarded a Diplomate in public health and medical laboratory microbiology; in 1971 I was a Fellow of the World Society of Health, in England.

Q By whom are you employed at the present time?

A University of Illinois Medical Center.

Q And, in what position are you employed by them?

A I am Professor of Occupational and Environmental Medicine.

Q What does that mean?

A That means basically that I have the responsibilities in the areas of occupational health and environmental health, with particular reference to considering, discussing, researching problems of toxic chemicals, either in the workplace or in the general environment, and in consumer products too.

Q How long have you been associated with the University?

A Since about 1976.

Q Have you ever acted as a consultant to any federal or state agencies in the areas in which you specialize?

A Oh, very, very, very much so.

Q Would you please list them for us, what you have done.

A First of all, I was a consultant -- I have been a consultant to Congress for many years. From '69 onwards, I was a consultant to the Senate Committee on Public Works, and assisted them in their analysis of problems of adverse health effects from air pollution and from water pollution, with particular reference to toxic chemicals.

I have consulted to other congressional

committees on and off since then, most recently to Veterans' committees on problems of Vietnam Veterans and Agent Orange.

Additionally, I have acted as an expert witness in the Environmental Protection Agency in a variety of its Cancellation-Suspension proceedings against pesticides, with particular reference to aldrin, dieldrin and chlordane, and heptachlor.

I have consulted to the Occupational Safety and Health Administration extensively, and in fact was in 1973, one, a member of a small committee that set up the first guidelines for regulation of occupational carcinogens, cancer-causing chemicals in the workplace.

Additionally, I have been a consultant I have been a member of expert committees for the Environmental Protection Agency, particularly the Environmental Health Advisory Committee, and pesticide subcommittees which had specific reference and expertise in areas of pesticide regulation, and have helped to develop guidelines for methods of testing for pesticides, and also for problems of pesticide exposures.

Additionally, I was the Chairman of the Teratology Committee, the Teratological Panel -- that is the birth defects panel -- of a major government

commission in 1969.

Secretary Finch, in 1969, who was HEW's Secretary, convened a panel, a commission, known as the MRAK Commission, specifically to investigate problems of pesticides and their relationship to environmental health. And, I sat on the Carcinogen Committee, that is the cancer -- problems of cancer from pesticides. I was the Chairman of the Mutagenicity Committee -- that is the committee on genetic effects, adverse genetic effects of pesticides; and, Chairman of the Teratology Panel or Committee.

Additionally, I have acted as consultant to various state boards. I was consultant to the Massachusetts Pesticide Board from 1970 to 1971; and additionally, I have consulted to Governor Brown in California on various aspects of toxic chemicals, including pesticides.

That is, I think, as far as I can recall, those are the major areas of my involvement with government in problems of pesticides.

Q Are you a member of any professional organization which deal in your area?

A Yes. The professional organizations which I have been involved in, on page 3 -- and, there are about thirteen professional societies and organizations,

ranging from New York Academy of Sciences, Society of Occupational Environmental Health, which was the society composed of government, management, academia and labor, and I was the president of that society;

The American Association for the Advancement of Science; The Environmental Mutagen Society, of which I was a co-founder and executive secretary;

The Society of Toxicology; largely an industry oriented society of professional toxicologists, although with membership from academia and government; and this society gave me the Honors Achievement Award in about 1970;

American Board of Microbiology, American Association for Cancer Research, American Society for Experimental Pathology, Air Pollution Control Administration, Society of Protozoologists, Society for General Microbiology, and Society for Pathology and Bacteriology.

Q Doctor --

THE COURT: Excuse me.

Do you wish to question on qualifications?

Had you concluded on qualifications?

MR. BOLDEN: I was going to get into some of the articles he was involved in, if I might, your Honor.

THE COURT: Sorry. Go ahead.

BY MR. BOLDEN:

Q Have you published articles or texts in your field, and specifically any in the area of teratology?

A My publications amount to about 260 scientific articles and about six or seven books, specifically with relation to -- I wonder if I may break down your question into more manageable elements.

I have about 30 publications on pesticides, and as far as publications on reproductive toxicity, including teratology, about 20 publications, including chapters in books on teratology, and also publications in the official journal of teratologists known as, "Teratology." So, I have reasonable publications in the area of reproductive toxicity.

Q One final question. Have you ever donated any of your services in an unpaid capacity in your area?

A I would say I donate a very substantial amount of my time for what is called pro bono work, doing things for nothing.

For instance, hardly a week goes by in which I don't either respond to requests by radio, press, TV, for information either on a consulting basis or making statements. I donate my expertise freely to citizen groups, public interest groups all over the country.

I am the President of the Rachel Carson Trust, for which I -- for several years I have never been paid a penny, and lucky ever to get travel expenses.

For instance, I am talking about media, this week I have three TV -- two TV appearances, I think -- one of them on pesticides in fact, and so on and so forth.

Additionally, I have donated my services pro bono for the last two years or so to litigation on behalf of Vietnam Veterans, the Agent Orange Litigation.

So, I spend a great deal of time on a pro bono basis.

MR. BOLDEN: Your Honor, that would conclude the questioning on qualifications.

MR. GRIFFIN: I do have a few questions, your Honor.

THE COURT: You may.

VOIR DIRE EXAMINATION

BY MR. GRIFFIN:

Q Bottom line, Doctor, are you attempting in this case to qualify yourself as an expert teratologist?

A No.

MR. GRIFFIN: In that case, your Honor, I have no further questions.

MR. McCANDLESS: I have one or two.

VOIR DIRE EXAMINATION

BY MR. McCANDLESS:

Q Doctor, in what states are you licensed to practice medicine?

A None.

Q You have an M.D. degree, right?

A I do.

Q You talked about a number of appointments you have had in consulting work. I haven't heard any date since 1971. Are you currently serving in any governmental consulting capacity now?

A No. The last governmental work I did was, I think I stopped in 1979. That was the Environmental Protection Agency, the Environmental Advisory Committee. Since then I have also been doing some government work on a state level, particularly in California.

Q Just to make it clear, is your appearance here today one of your pro bono activities?

A No.

Q This you will be paid for?

A Certainly.

Q Okay.

MR. McCANDLESS: I have nothing else.

THE COURT: You may proceed.

MR. GRIFFIN: Your Honor, I object to

this Doctor who is not licensed to practice and who says he is not an expert in this field that we are dealing with.

THE COURT: I will see counsel at side bar, because I have no idea what is intended to be presented.

(Side bar discussion on the record as follows:)

THE COURT: What is going to be presented?

MR. BOLDEN: For the purpose of establishing the teratogenicity of Diazinon, and his conclusions as to whether or not it was a factor in causing the birth defect of Khristine McConnell.

THE COURT: What was your --

MR. GRIFFIN: My objection, sir, is that the science of teratology, whether certain substances cause teratological effects --

THE COURT: I must confess I am thoroughly confused. He doesn't purport himself to be an expert in this field. I don't know what he is an expert in. I am trying to figure it out based on listening to all he has done.

MR. BOLDEN: I believe, your Honor, the gist of what I heard, he is a toxicologist who has a great deal of expertise in the area of teratology and

pesticides --

THE COURT: But, he doesn't even say that he is. He doesn't say that he is an expert teratologist. That is what confused me. I was expecting him to answer Mr. Griffin's question, yes, I do. He says, no, I am not.

MR. GRIFFIN: He has sworn too often in other cases not to be able to answer that question other than no.

THE COURT: Well, what is it you are proposing to establish through him?

MR. BOLDEN: To establish that the teratogenicity of this substance, and it is a factor in causing birth defect. I think the argument --

THE COURT: His testimony creates a serious problem for me. I am supposed to determine initially whether a person is an expert in a particular field. If the person himself disclaims expertise, then how can I tell the jury that I consider him an expert even though he doesn't?

MR. BOLDEN: Your Honor, I think -- I am not sure there even is, and I don't believe there is, any such thing as a Board Certified teratologist.

THE COURT: No, I don't think that is the question at all. The question is whether this

witness in response to a question that was posed to him, is at least obligated to say, yes, I do believe that I am an expert, and then he can explain there is no Board certification in this sort of thing, but I am qualified. He says, no. That is my problem.

If he himself does not purport to be an expert, how can I say to the jury, "You may consider him as expert in this field"?

Now, you may, at least assess his qualifications. It creates a very serious problem.

Now, I see an argument can be made that notwithstanding he doesn't claim to be, this jury can nevertheless determine that he is. That is difficult, because we are in an area, a very scientific area, and if the witness himself doesn't even claim to be, how can I let the lay persons in the jury come to the conclusion that in fact he is? This is my problem, and it is created by his own answer.

MR. BOLDEN: Well, perhaps if your Honor will let me explore with him a little further the degree of expert -- the degree of --

THE COURT: I will tell you what we will do. He apparently -- and, I don't know, he has not been asked the question yet -- he says he is a toxicologist. If he is going to testify simply to toxicity, I

think as long as he will at least answer that question that he considers himself an expert in toxicity, then maybe we will hear some testimony as to the toxicity of the material. But, before you get into an area as to the teratogenic effect, then we will have to consider again, because at the moment I can't permit him to testify in that area.

MR. BOLDEN: Your Honor --

MR. FERRONI: Can we question him as to his dealings in the area of toxicology so as to establish a foundation or a basis for the jury --

THE COURT: I have just said that -- if he will simply answer that he considers himself an expert in toxicology, I will permit him to testify as to the qualities of these various materials. But, I will not as this moment authorize any questions as to the teratogenic effect. That's all.

MR. GRIFFIN: If your Honor please, isn't that putting the cart before the horse? Even if we spend a lot of time, and we will take a lot of time with him --

THE COURT: Wait a minute. Two people are talking at once. That is no good.

MR. GRIFFIN: And, it will take a lot of time with him because he is, in my view, as bad as

Todd, or worse, we end up --

MR. SPALDING: I object.

MR. BOLDEN: He made remarks all week --

MR. GRIFFIN: We end up with the ball nowhere, unless they will follow it up with an opinion from someone who is qualified that this particular substance is teratogenic.

THE COURT: And, if they don't, it won't get to the jury.

MR. GRIFFIN: I think I am entitled to an offer as to whether they are going to prove that.

MR. BOLDEN: Let me shorten this. If the Court will not accept Dr. Epstein as a person who it will permit to testify with respect to teratogenicity of this substance, and its causal relationship to the issue in this case, we have no other witness to present.

The only other thing I can ask the Court to grant me leeway to do is to further explore with him the amount of time -- because, he covered it, but we covered it hurriedly -- the amount of time he has devoted to teratology and determining teratogenicity of substances, and perhaps it is a question of weight, rather than the --

THE COURT: I have devoted a great deal of my time to watching football games, that doesn't make

me an expert football player.

Now, this man, if he had simply said yes, I consider myself an expert, I would have permitted this to proceed. But, when he himself disclaims expertise, then I can't permit the jury to hear what this man has to say; not in this area. And, this is very critical in this case.

MR. BOLDEN: Well then, we have no --

MR. SPALDING: I think you indicated --

MR. FERRONI: Is there any question the witness understood the question that was asked of him?

THE COURT: I doubt there was any question about it. He seems to be a very, very capable person and would not have answered a question if he had not understood it.

MR. McCANDLESS: It was a three-word question. I think it was very clear.

I join in Mr. Griffin's objection to this.

MR. BOLDEN: He has used the word to me, bench teratologist; I am not a bench teratologist.

I don't know what he means by that. He may have been answering Mr. Griffin's question in a context which is not the same as whether he considers himself to have expertise in the area.

MR. GRIFFIN: Mr. Bolden, I have sworn testimony from him in another case in which he says, I am not a teratologist, I cannot give a professional opinion in that area, I do not consider myself qualified in this area.

THE COURT: We will cut this short. Mr. Griffin has raised the question after his cross-examination. You have not yet undertaken your redirect examination. Do you want to ask him that direct question: Do you consider yourself an expert teratologist in any sense; then we will find out where we go from there. Then, of course, Mr. Griffin will still have an opportunity to cross-examine, recross after that, if he should change his answer. Just so there is no question that he understood what he was being asked.

MR. BOLDEN: All right.

THE COURT: But, I caution you that if that is what we end up with, that he disclaims expertise, if that is the end of the case, that is the end of the case.

MR. BOLDEN: All right.

(End of side bar discussion.)

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consider yourself an expert in any aspect of that field?

THE WITNESS: Yes, sir. In the evaluation of teratological data.

If the Court permits, I would like to clarify my previous answer to Mr. Griffin, being, no.

When I was asked if I was a professional teratologist, that implied did I constantly --

THE COURT: Excuse me, Dr. Epstein. I don't recall hearing such a question.

THE WITNESS: I beg your pardon, sir, I thought I was asked a question if I was professional or expert.

THE COURT: Mr. Ehrlich, would you go back to the question posed by Mr. Griffin and repeat it.

THE COURT REPORTER: "Question: Bottom line, Doctor, are you attempting in this case to qualify yourself as an expert teratologist?

"Answer: No."

THE WITNESS: If the Court permits, I would like to qualify that answer by saying I am not an expert teratologist in the sense that I perform experimental teratology on a routine basis. However, I am expert in the area of evaluation of teratological

data in general, and in particular with problems of risks to humans from exposure to teratogens in the environment.

Apart from my publications in the area, this is attested by my various governmental appointments in areas including those in teratology, such as Chairman of Important Blue Ribbon Commissions, which dealt with the -- the panel which dealt with teratological effects of pesticides.

THE COURT: Do you wish to cross-examine further?

MR. GRIFFIN: Yes, sir.

VOIR DIRE EXAMINATION(Continued)

BY MR. GRIFFIN:

Q. If I hear what you are saying, you are saying although you are not an expert teratologist, you are going to take some literature and you are going to look at it and tell us what you think the literature means as a teratologist would view it, is that fair?

A. I repeat what I said, that I have expertise in the evaluation of teratological data, but I do not practice teratology on a routine basis.

Q. The same as any other doctor, you can read a medical report on teratology and interpret it.

A. No, sir, not the same as any other doctor in the

sense that I am a person who has published extensively in the areas of toxic chemicals in the environment, I have advised government committees on this, I have set up standards for government, and have very substantial expertise in the evaluation of risks to pregnant women from exposure to toxic chemicals in the environment.

Q Let me ask you this, Doctor: In the chemical exposure cases in California Superior Court, in San Francisco, where you gave a deposition in September of 1982, did you testify, in answer to a question as to your qualifications:

> "First of all, the literature on this is pretty modest in comparison with the overwhelming literature on teratology, and before answering it I should also point out that I don't hold myself out as an expert in teratology, so the answers I will give you will be -- I won't say poorly informed, but not expert, not that of a professional."

A Certainly. As I repeat again, I am not a professional teratologist in the sense that I do experimental teratology on a routine basis. I have made that clear, I think.

Q I think we need to define teratology. What is the science of teratology?

A Well, if we accept it as a science, teratology is the study of birth defects caused by exposure to agents in the environment, or in some instances simply just the study of birth defects with no known exposure.

Q And you, yourself, I gather, when you say you are not expert in the field, means you have never conducted such studies.

A No, sir, that is not what I said. What I said is, I don't conduct such studies on a routine basis. I have conducted such studies.

In fact, let me be very specific. I have specifically studied the fetotoxic and teratogenic effects of N nitroso compounds in guinea pigs, and I have several publications in this area. But, I don't do this on a routine basis.

Q And, you do not consider yourself an expert teratologist, you have said so over and over again, haven't you?

A With due respect, the possibility exists that we may be indulging in a semantic argument.

When I said I did not consider myself an expert teratologist, that definition relates to the routine practice of experimental or clinical teratology. That answer to that is no.

With respect to the evaluation of human

risks from exposure to teratogenic agents, and with respect to the evaluation of experimental data, I do most certainly consider myself an expert, and in fact I am so considered by a wide-range of government and non-government bodies.

Q Now, as far as this case is concerned, what you propose to do is simply review literature and draw some conslusions from it, correct?

A No, that is not entirely the case.

Q What is entirely the case?

A I propose to produce to the Court statements from the literature from which the Court can draw its own inferences.

In addition, I will be drawing inferences from those data which may or may not be consistent with the statements in the literature. In other words, I will be --

Q Thank you.

A Excuse me, sir.

Q Excuse me.

A In other words I will be confining myself to my area of expertise, which is the evaluation of data and also the evaluation of human risk, which is my professional area.

Q But, your professional area is not that of a

teratologist, and what we are concerned with in this case is the evaluation of teratological data, aren't we?

A You are forcing me to be repetitive, sir. I am experiment professional teratologist in the sense that I do not perform experimental teratology on a routine basis.

Q That is --

A But, as far as the evaluation of data is concerned, I am indeed expert in this area.

Q And, in that area, you say you are not -- poorly informed, but not expert -- you don't have the views of a -- your views are not that of a professional.

A Precisely. I am not an experimental teratologist.

Q How, Doctor, if you are not expert in that field, if you don't keep yourself up, as it were, with everything that goes on in the field, can you properly evaluate literature in the field? That is what you are doing.

A Because, my expertise is in the area of evaluation of toxicological data.

Toxicology is the study of the toxic or adverse effects of chemicals, which includes carcinogenesis, cancer; mutagenesis; teratogenesis, birth defects; acute toxicity; subacute toxicity; chronic

toxicity. It is a wide-range of adverse effects in which I have substantial expertise.

Now, it is humanly impossible to be performing all of these individual subareas of toxicology on a routine basis. My profession is in the evaluation of data on toxic effect, be it teratogenic or carcinogenic, together with a formulation of opinions as to human risk.

MR. GRIFFIN: Well, your Honor, I have no further questions.

THE COURT: I will permit the witness to testify, and the jury of course will accept the testimony from this witness in light of the answers that he has given in which has expressed the reservations that the jury will evaluate.

You may present your case, Mr. Bolden.

DIRECT EXAMINATION(Continued)

BY MR. BOLDEN:

Q Doctor, at my request, did you conduct an investigation into the pesticide Diazinon for the purpose of determining its teratogenicity?

A I did, sir.

Q And, as a result of that investigation did you arrive at an opinion on its teratogenic properties or potential?

A. Yes, sir.
Q. Would you please state what your conclusion is.
A. My conclusion is that there is a substantial probability that Diazinon is teratogenic and represents a teratogenic hazard to humans exposed to it.
Q. Would you please state how you arrived at your conclusion and what underlying data you reviewed for the purpose of forming your conclusion.
A. With the permission of the Court, I would like to use one or two simple charts to explain the basis for my opinion.

THE COURT: I haven't any idea what you are going to do here, Mr. Bolden. I can't rule on the admissibility of a chart without an idea of what it is all about.

THE WITNESS: May I respond, or do you wish Mr. Bolden to respond to that?

THE COURT: I think Mr. Bolden should respond to that initially.

MR. BOLDEN: Your Honor, as I understand it from talking to Dr. Epstein last night and this morning, he has prepared certain charts, actually three charts, one of which summarizes the findings from various studies of various kinds of animals as to whether they were negative or positive for showing teratogenic

effects, and has listed them as summarized chart, and another --

THE COURT: Excuse me. Let's just clarify one thing. Are these Dr. Epstein's studies?

MR. BOLDEN: No. These are studies from other --

THE COURT: Are these from certain publications?

MR. BOLDEN: Certain publications.

THE COURT: And those publications will be here to support those.

THE WITNESS: Yes, sir.

MR. BOLDEN: Yes, sir.

Do you have all of them here with you?

THE WITNESS: I think so.

THE COURT: All right. We will proceed. We will deal with them on an individual basis.

A This first chart, which I hope is visible is listed as "Quotations From Literature on Teratogenicity of Diazinon," and the chart contains two columns.

The column on the left is the author, and the date of the statement. And on the right the quotation is actually using the author's words.

If I may, I will proceed.

MR. GRIFFIN: If your Honor please, I

object to this procedure. This seems to me, is nothing more than picking words out of some study that is done somewhere and trying to give those words probative force, and they obviously can't have that. And, if there is an exception to the Hearsay Rule, I think your Honor should look at this whole picture to figure out whether there is. It certainly has to be introduction of an article, not words from it, and that this is just an attempt to build an argument based on what is in the literature, not an expose of the actual probative effect of what it may be.

THE COURT: I will give you the full opportunity in your cross-examination to probe all of that. We will at this time proceed in this fashion.

THE WITNESS: Thank you.

A (Continuing) The first article is by Khera, in 1968. Dr. Khera is a member of the Canadian Food and Drug Administration, and Dr. Khera states that Diazinon induced -- and, I quote, "congenital foot deformities," in duck and chick eggs.

The next article by Kimbrough and Gaines in 1968, Kimbrough and Gaines were government scientists working at the Center for Disease Control in Atlanta, states, and I quote: "Diazinon produced some mal-formations."

"The spontaneous incidence of malformations' -- well, no. That is fine. "Diazinon produced some malformations."

The next is Green, 1969. "Diazinon produced teratogenic activity in all chicks."

The next is Earle, 1973, United States Food and Drug Administration. "Teratogenic abnormalities have been observed in dogs given Diazinon. Teratogenic abnormalities have been seen in sows given Diazinon." That is pigs, miniature pigs.

Nishimura, a Japanese scientist, in 1973, "The following chemicals were proved to have a teratogenic effect: Diazinon."

NIOSH, National Institute for Occupational Safety and Health, 1978: "Based on the available evidence, Diazinon can be considered possibly teratogenic and should be handled with caution by women of child-bearing age."

Sax, 1979, a standard textbook on toxic chemicals: "Diazinon is 'an experimental teratogen.'"

NIOSH, National Institute for Occupational Safety and Health, RTECS, which stands for Registry of Toxic Effects of Chemical Substances, in 1977, in 1978, in 1979 and in 1980, states that Diazinon is a

teratogen.

That, sir, is the first chart I wish to draw to the attention of the Court.

The next chart relates to the actual summary of the experimental findings on teratogencity of Diazinon.

The chart is headed, "Teratogenicity of Diazinon." And, I have attempted here to summarize all the literature in which I am familiar, all the studies done on Diazinon from the point of view of its birth defect potential.

And, there are three columns here. The column on the extreme left is the species, the animal in which it was tested. The middle column is on the author, including the date, and the right column is on the results.

I would like to stress at this stage that this chart represents my most recent evaluation of the literature.

I had in fact considered the literature prior to a deposition last year, but since then I have have the opportunity of going into the literature more thoroughly, evaluating studies which I had evaluated before, and also evaluating all evidence which has become available to me. And, this is my evaluation of

the data, and in many instances such evaluation actually reflects the author's own statements.

The first --

MR. GRIFFIN: Excuse me, your Honor, I don't like to interrupt, but here again I have an objection based on what the Doctor has now said.

Your Honor ruled in an Order that we were to be able to take this Doctor's deposition since he was held out as an expert. And, at the time of the deposition he should be fully informed to testify about everything that he was going to testify to in Court, that we could have advance notice.

We took his deposition and got such advance notice. Already he has come up with on the prior chart there, with studies for books that I haven't had a chance to even look at. And now he says in his testimony, I have since my deposition, I have gone and done other work. And --

THE COURT: I will --

MR. GRIFFIN: Your Honor, I think he shouldn't be permitted to do it.

THE COURT: I will have to limit him to what he disclosed at the time of the deposition, Mr. Bolden. He will have to -- whatever way he has to tailor his testimony, he has to go back to what it was

at the time of the deposition.

We had a serious problem in this case and we tried to resolve it as best we could by the ruling that was made. He will have to conform to that ruling.

BY MR. BOLDEN:

Q Do you understand that, Dr. Epstein?

A Am I permitted to make a comment, sir?

THE COURT: No. I think the best you can do is give us the testimony that you gave at the time of deposition, or that which is consistent with what you gave at the time of deposition.

If what you have learned since makes a substantial change in your opinions or testimony, you will simply have to ignore it.

THE WITNESS: All right, sir.

THE COURT: We must conduct litigation by certain rules, Doctor, and the rule that I made earlier was that whatever was disclosed at deposition is what would be the subject matter disclosed at trial.

A At the time of -- with further reference to this chart, at the time of my deposition I stated specifically that I had not yet completed my evaluation of the literature and, therefore, the statements which I made at my deposition reflect such incomplete evaluation.

To be specific, I stated, "I don't think I have really completed the work yet." Therefore, statements at my deposition reflect such incomplete evaluation, but I will proceed on that basis.

MR. McCANDLESS: Your Honor, I object to the voluntary statement of the witness in response to no question, and apparently in contempt of your order in directions to him to try to limit himself to whatever it was --

THE COURT: No. I think he was explaining that at the time of deposition he made the statement that he was giving testimony based on incomplete data, and I have simply ruled that whatever it was, that is what he will be limited to.

MR. GRIFFIN: Your Honor, I don't think your Honor perhaps has actually looked at your Order. Your Order stated that he is to be fully informed when his deposition is taken.

THE COURT: And, all that I am ruling now is that fully informed means that he will now confine himself to what he had at the time of the deposition.

The jury will ignore everything else. We do operate according to rules here.

A. It is clear from the literature that a variety of

studies have been done --

MR. GRIFFIN: Excuse me.

If your Honor please, could I get the Doctor to strike from the chart the post-deposition literature he is referring to?

THE COURT: Was all of that that you testified to earlier post-deposition?

THE WITNESS: Some of these data, sir, are based on material which I hadn't examined at the time, but which I have examined, but which are in the published literature.

THE COURT: I will have to sustain the objection. We will have to strike the references to literature that was not referred to at the time of deposition.

That deposition was taken when?

MR. BOLDEN: --

THE WITNESS: August of 1981.

THE COURT: All right. Not '81.

THE WITNESS: Yes, sir --

MR. BOLDEN: August 26 of '81.

THE WITNESS: Yes, sir, of '81.

THE COURT: Nothing further was done before trial?

MR. BOLDEN: Your Honor, I might add

that -- of course -- maybe I should do it at side bar.

THE COURT: Come to side bar.

(Side bar discussion on the record, as follows:)

THE COURT: How can you permit the case to come to trial without updating the expert material?

MR. BOLDEN: Your Honor, the literature --

THE COURT: I was surprised when he said August '81. I thought he meant '82.

MR. BOLDEN: All the literature we are talking about is literature which came from Ciba-Geigy's files which was made -- if I am not mistaken -- all of the literature are their published works, all of it was in Ciba-Geigy's files.

We may have had some of it ourselves, but it was all turned over to us as part of the studies -- not studies, part of the documents which Ciba-Geigy produced.

MR. EISENHART: All that was made available to them well prior to the deposition.

MR. SPALDING: That is not true.

MR. BOLDEN: That particular statement is not true.

MR. SPALDING: Your Honor, you will

remember the controversy arising over my trip down to Greensboro when they refused to produce the documents here in Philadelphia. Then we had the controversy over the copying of the documents, whether they would be brought up to Philadelphia to be copied, or copied down there at our expense and transported up.

Thereafter, the copying did occur and was sent to us.

In addition to that, there was also a study that was done by Ciba-Geigy, which I don't believe was completed until August of 1981 --

THE COURT: Let me just --

MR. SPALDING: -- which could not be turned over to the Doctor.

THE COURT: Why was not an updated report given to opposing counsel long before now?

MR. SPALDING: The doctor never prepared --

THE COURT: If the expert was going to rely on additional materials, why was it not disclosed before trial?

MR. SPALDING: The only materials that he is relying on in addition to those which he himself obtained, are the material which Ciba-Geigy has in its own files.

MR. BOLDEN: That is not his question.

THE COURT: The question is, why was it not disclosed that this expert was going to rely on material that was in Ciba-Geigy's files, material that was included in other publications, whatever, so that they could be prepared in the expert area where required.

You are required to -- there is not much sense in my talking.

MR. SPALDING: It is somewhat implicit that the published material --

THE COURT: I was simply noting that I stopped speaking because you distracted Mr. Bolden's attention. Whatever it was, I lost my train of thought. You may proceed.

MR. BOLDEN: Your Honor, your Honor of course is right. The only thing I can say is that in the interests of fairness, that because the literature we are now talking about comes from Ciba's files and is published literature, that it is difficult to see how any substantial prejudice would result to them from permitting this witness to testify, not only to what he previously testified to, but simply supplement or -- and add to whatever conclusions he had arrived at at the time of his deposition.

I might say, for instance, that one of the things I believe he intends to say is that he made -- he made a mistake on the Ciba report which would be favorable to Ciba which he intends to point out. But, under your -- if your Honor forbids him from even stating what he has been able to review since the time of the deposition, it places us in a very awkward position.

THE COURT: Did he state an opinion at the time of this deposition?

MR. BOLDEN: Yes. Yes.

THE COURT: All right. You will confine your direct examination to what he presented at that deposition. I suspect that cross-examination will open the door to what he has learned since, and I will rule upon it at that time.

MR. BOLDEN: Thank you, your Honor.

THE COURT: But, at this time, since this was all -- the deposition was given in August of '81?

MR. BOLDEN: Yes, your Honor.

THE COURT: We are now in December of '82, and no update was given. I'm going to confine him to what he gave.

MR. BOLDEN: Okay.

THE COURT: And, if it becomes pertinent I will allow the door to open.

MR. BOLDEN: May I explain that to him at side bar so he understands it very clearly?

THE COURT: Yes.

MR. GRIFFIN: As a practical matter, your Honor, if I am going to cross-examine the Doctor, and that is the whole purpose of your Honor's ruling, to give me a fair chance to do that, he is going to be able to use literature and things I have never seen that I will not have time to look at before I go into cross-examination, that I will not have time to go over it with my expert. He has just a plain unfair advantage, and that is the purpose of the ruling, and, when your Honor said, well, as soon as Griffin opens his mouth, we will let him spew all this at you --

THE COURT: I didn't say that. I think I anticipate that your questioning is precisely going to open the door, and it may well. I have not ruled that it will. I am simply saying we will consider at that time whether I will relax the rule and allow him to testify concerning this.

MR. GRIFFIN: All right, sir.

THE COURT: You will have to try to guide yourself accordingly.

MR. GRIFFIN: My objection -- it seems to me the whole purpose of this is to avoid that kind of thing for the poor attorney who is trying to get himself ready to try a case. We are dealing in the field we know not ourselves. All we can do is take advice from others, and if we don't have the time to get the advice ahead of time, we are unduly strapped.

THE COURT: Yes, I understand.

MR. BOLDEN: Your Honor, in his direct examination will he be permitted to correct an error he made? Now, this is not a question of supplementing new literature. It is a question of clearing up an area --

MR. GRIFFIN: He is just anticipating cross-examination.

THE COURT: Well, I think he has a right to.

MR. GRIFFIN: He can if he wants to.

THE COURT: Yes, and I think he should.

MR. EISENHART: He was reading this chart backwards at deposition, Mr. Bolden.

(End of side bar discussion.)

THE COURT: Members of the jury, we have had a long discussion here at side bar, and it requires Mr. Bolden to make a statement out of your

hearing to his witness in order that he may conform to the ruling I made at side bar.

(Off-the-record discussion between Mr. Bolden and the witness.)

A. In further response to the questioning, let me just summarize the previous chart where the quotations from the literature on the teratogenicity of Diazinon.

There were at least eight statements in the literature going back to 1968 that Diazinon is teratogenic, produces birth defects. Four of these statements come from actual people who have conducted the experiments. So, the actual people who conducted the experiments in four instances -- let me return to the previous chart, if I may, the previous one which I have just completed.

(The chart is made available for the witness.)

A. Thank you.

The people who did the experiments in this list include the first one, Khera, 1968; Kimbrough and Gaines, 1968; Green in 1969; and Earle, 1973.

Now, to come back to the summary of the teratogenicity of Diazinon, if I can trouble you again, sir.

(Another chart is made available for

the witness.)

It is clear that there have been somewhere in the region of 13 studies on the teratogenicity of Diazinon. These studies have involved eight species. And, I think it is necessary to emphasize to the Court that these studies have not produced uniform results. They are a mixed bag.

In some of the experiments Diazinon was shown to be teratogenic and in some of the experiments it was shown not to be teratogenic. Some of the experiments are better than others, some of the experiments are worse than others. In other words, it is difficult to place equal weight on all the experiments whether positive or negative.

But, it is necessary for me to explain the difference between positive and negative data from a toxicological standpoint.

In toxicology, in the study of --

MR. GRIFFIN: Your Honor, what question is being answered now?

THE WITNESS: I am --

THE COURT: I think he is outlining and summarizing certain information from studies. He may proceed.

THE WITNESS: Thank you, sir.

A In the chart which you see in front of you, you will see some pluses and some minues in the extreme right-hand column. And, before getting into any specifics, I would like to explain the difference, the difference in toxicological significance between a positive study and a negative study in toxicology.

In general, a positive study -- finding a result in a toxicological test, be it study of birth defects or cancer, supersedes a negative study. In other words, if you have a positive finding of an adverse effect in any one system, this result is much more important than a study in which you failed to find an effect. And the reason for this is very very clearcut. The reason for this is, toxicology is a very insensitive subject. It is a very very insensitive discipline and it is terribly important to get this point across before we get into the specifics of any positive and negative studies. And, with the permission of the Court, I would like to explain why toxicology is an insensitive subject.

t3 Let us say we introduce into the environment an agent which induces 1 in 10,000 cancers, or 1 or 10,000 birth defects, okay? Therefore, in the United States alone, that one agent would be responsible for 20,000, or 20,000 cancers a year, which would be

a national calamity.

Now, what are our chances of picking up such an effect in experimental systems?

Now, let us assume that the sensitivity of a rat, or mouse, or guinea pig to a particular agent is the same as that of a human being. Therefore, if you were to test in animals at the same levels as you test in humans, you need 10,000 rats, or 10,000 mice in an experiment to get one adverse effect, one cancer or what have you, and for statistical significance you may need 20,000 rats or 20,000 mice.

In an attempt to reduce this insensitivity of animal tests compared to large human populations, we tend in animal tests to test at levels higher than those of human exposure.

But, the fact is this: When you are dealing in an animal test with 20 or 30 or 10 animals, this is very insensitive, and your chances of picking up an agent which induces birth defects or cancer, in one in a thousand, is virtually nil; in one in a hundred can be virtually nil. Therefore, you have got to understand, toxicology per se is a grossly insensitive subject. It is grossly insensitive because we test for very small numbers of animals compared to massive human populations at presumptive risk. And, this is an

axium in teratology, and in toxicology in general, that a positive result, unless in a study of course that has controls, and doesn't -- and in which other advers effects have not been introduced, that a positive result is very much more important than a negative result.

Q Doctor, can I stop you in your explanation to ask you one question with respect to that.

Is there anything from recent history of the last 30 years that demontrates a point that a negative study is superseded by a positive study?

A Let me tell you about thalidomide.

Q Is the answer yes?

A The answer is yes. And, thalidomide is a most excellent example of this.

Rats and mice are somewhere in the region -- mice are somewhere about 700 times more resistent to thalidomide than humans --

MR. GRIFFIN: Do I have to try a thalidomide case? I have enough trouble with the Diazinon case.

MR. BOLDEN: Your Honor, he doesn't have to try a thalidomide case, but I believe this witness is entitled to explain why a positive and a negative study have different implications. And, if he has to do it by illustration, I believe that is an

appropriate way of receiving it.

THE COURT: All right. But, he should be careful not to intrude in an area where an objection has been made and until it has been clarified.

THE WITNESS: Yes, sir.

THE COURT: I will permit it, but I will caution Dr. Epstein once, and I hope I won't have to caution him again: When you hear an objection, Doctor, be very circumspect and very careful about what you say until we get a clear ruling.

You may proceed along that line.

A My point about thalidomide is not wishing to get into any aspect of this, but merely to talk about problems of insensitivity of animal tests.

There are many occasions in which you can demonstrate that animal tests are very very insensitive and, therefore, when you get a positive in an animal test, this is a lighted beacon, and ignore this at the peril of society.

Now, to come back to the --

Q Just one second, Doctor. With respect to that statement, as it related to the experience that actually happened in the thalidomide situation, how does that relate to the positive-negative aspect of what you were talking about? What was demonstrated there?

A Well, to the best of my recollection, thalidomide is -- the teratogenic effects of thalidomide in mice are 700 -- mice are 700 times more resistent. Therefore, testing -- 700 times more resistent to thalidomide than humans. And, therefore, one could easily have missed the teratogenic effects of thalidomide using rodent species. And, therefore, this is the principle in toxicology in general, not only in teratology, but in carcinogenesis, and the full area of toxic chemicals in the environment, the insensitivity --

THE COURT: Just a moment, Dr. Epstein. You offered thalidomide as an example. Were tests conducted and did it in fact fail to reveal something? Is that what you are trying to get across?

THE WITNESS: Essentially, the only point I am making is that you have major variations in sensitivity from animal species to humans --

THE COURT: No. Would you just answer the question. Were some tests conducted?

THE WITNESS: Yes, sir.

THE COURT: Well, this is the only significance, it seems to me, that your earlier comment could have. And, if you would address yourself to that

BY MR. BOLDEN:

Q Were there differences in animal speci[redacted] that were

tested with respect to thalidomide that produced different results?

A Yes, there are.

Q Explain that.

A But I must stress we are dealing with two factors here, both of which I would just like to segregate because there may be ambiguity.

One is the insensitivity of animal tests in general. Animal tests, irrespective of whether they are mice, rats, guinae pigs, monkeys, what have you, are insensitive because you only test a very small number of animals compared to very large human population. That is one problem.

The second problem is differences in sensitivity from species to species. Some species are much more sensitive than others and others are much less sensitive than others, and you don't have any way in advance of knowing whether humans are more sensitive or less sensitive.

Humans could be very much more sensitive to a particular cancer-causing agent, or birth defect cancer-causing agent. And, the importance of thalidomide lies in relation to this -- that thalidomide -- humans were much more sensitive to thalidomide than animal tests, particularly mouse and rat tests.

Now, to get back to -- I must apologize for that long explanatory note. But, to get back to the summary of teratogenicity of Diazinon, here you see about 13 studies done on teratogenicity of Diazinon, mixed results: some positive, some negative.

The previous chart had statements from four of the people who conducted these studies who clearly concluded that they are -- they were positive.

Now, my interpretation of the data, therefore, is weighed in the favor of -- there is a frank bias in the direction of positive data. I am biased in the direction of positive results for the reasons which I have explained. That is number one bias.

The second is that I don't believe that any one of these studies -- that -- I am not proposing that the inferences that I draw on teratogenicity of Diazinon rests exclusively on any one of these positive studies. They rest on the aggregate of the data.

In toxicology, you examine individual studies and you draw inferences from them, whether they be positive or negative, but you also examine all the positive studies together an you look at all the negative studies together. And, it is possible that in some instances you may say, well, I'm not terribly

happy about that one positive study alone, but that one positive study together with other positive studies creates a more persuasive position, and that is basically my feeling in the matter.

I subscribe to the position in the literature that Diazinon is teratogenic, and the basis for this rests on some of these studies here.

Now, I should point out, and I gather that I have the Court's permission to explain this, that there are some discrepancies between my listings of positive results here and negative results here, and those at the time of my deposition, because, as I indicated before, I had not completed my evaluation of the literature. And, I will be very specific as to these.

For instance, the first three studies -- the first two studies I call positive here, and at the time of my deposition I said they were negative. That is because I did not have access to a paper which I have in court which states -- the paper -- another paper by the authors which states that the duck egg and the chick egg study were both positive, and I did not have that paper with me at the time. And, therefore --

MR. GRIFFIN: It seems to me this is

precisely just the opposite what your Honor ruled.

THE COURT: No, no. We said that there would be a clarification of a mistake. Now, is this --

MR. GRIFFIN: This is not it, sir. He is simply using articles that you told him not to use and he is now saying, now look, I am only going to use three. Here are the three results. Now, one of those he didn't have before. Here are the three results and I want you all to know I am taking those out, but he is just repeating them and left them on the chart.

I don't know these cases that he is bringing up now. I never heard of them before.

THE COURT: I am not sure I understand exactly what it is everyone is saying here.

Members of the jury, I ruled at side bar it was brought to my attention that Dr. Epstein had made a mistake at the time of his deposition, and that he has since learned that it was a mistake, and I did allow him, or gave permission that he could clarify that he did in fact make a mistake, even though it was based upon information that he obtained later.

Now, let's not go beyond that. And, Dr. Epstein, don't you go beyond that.

BY MR. BOLDEN:

Q Dr. Epstein, specifically as it relates to the

mistake, confine yourself to the Ciba in-house study.

A. I beg your pardon. I was under the impression I was allowed to correct mistakes.

Q. Not at at this point. Just the mistake -- that specific mistake.

A. I understand. I understand. Therefore, as far as the first two studies are concerned, the authors themselves, the Khera and Lyons, and Green, all have stated that those results are positive. I will not be discussing those further at the moment.

MR. GRIFFIN: Are those ones you did not tell me about in the deposition?

THE WITNESS: In the previous chart, I listed Khera and Green as stating that they induced congenital abnormalities. I am not discussing this now. I had this up on the previous chart. On the previous chart I had a quote from Khera that it induced congenital deformities. I have already discussed that and I have already discussed Green's statement that Diazinon was teratogenic and, therefore, I was referring just then exclusively to statements in the literature in the previous chart.

MR. GRIFFIN: I just wanted to make sure that we were doing that, Doctor.

THE WITNESS: Oh, yes.

MR. GRIFFIN: We are not dealing with any literature subsequent to your deposition, right, and you are not calling any such literature to the attention of the jury, right?

THE WITNESS: In the previous chart I have made statements in the literature on the teratogenicity of the Diazinon. I am now discussing my analysis of the experimental data which is different from making quotations from the literature.

THE COURT: Did you understand that my ruling comprehended the chart as well?

THE WITNESS: This chart as well, I understand that, sir.

THE COURT: Not this chart, the chart you earlier referred to. Is that the chart that you earlier referred to?

THE WITNESS: No. The previous chart on quotations from the literature was a different one to this.

THE COURT: All right.

THE WITNESS: This is an analysis --

THE COURT: With respect to the previous chart on quotations from the literature, the restriction applies there as well.

THE WITNESS: I understand.

A. In the time of the deposition there was one particular study, a Ciba-Geigy study in 1974 which I took the position that it was positive. On further evaluation of those data in the sense that I evaluated all the data too, not only that, I have discovered that I misread one particular table and I am changing that positive result to a negative result.

Therefore, this is in accordance with the Judge's ruling. I will restrict my comments exclusively to that particular change, although there have been changes in the other direction which I am precluded from discussing.

Therefore, let us come back to the totality of this chart. The totality of the chart demonstrates there are negative studies and positive studies.

THE COURT: Dr. Epstein, you do understand English, don't you?

THE WITNESS: I will not make any further reference --

THE COURT: Not again. You have done it twice so you feel it won't be necessary to do it again, is that right? Now, Doctor, don't play games with me. I have told you, you have been told by counsel, to refer to nothing after the deposition,

except to correct that one mistake. Don't do it again.

A. Ignore the last column on results. Let me simply say that these studies are --

MR. GRIFFIN: Excuse me, your Honor, if we are going to ignore the last comment, can we just take it off? If part of it is supposed to be ignored, let's not play with it.

THE COURT: Is that the chart we are talking about?

MR. GRIFFIN: Yes, sir.

THE COURT: Yes.

MR. GRIFFIN: He says they are not appropriate and there are things he says to ignore. Let's not use it.

THE WITNESS: May I just make the changes in the chart to reflect the statement at the time of the deposition?

THE COURT: You may make a change to reflect what was included at the time of the deposition and we will block out the rest.

THE WITNESS: Thank you, sir.

Could I borrow your red pen, sir?

THE COURT: Counsel have in mind, of course, the time limit we put on for this morning.

MR. GRIFFIN: I would like to suggest,

why don't we take a little recess and redo the chart? He still has the same old chart right in front of us with all the old things on it.

THE COURT: We will get it out at a recess. At the moment the jury, I am sure, is not going to keep looking at that chart.

THE WITNESS: Thank you.

A I have crossed out the previous results.

MR. GRIFFIN: I would --

THE COURT: Any more than the jury is going to keep listening to Dr. Epstein's comments that I told him not to make.

Now, let's move along. We do have some time problems this morning.

THE WITNESS: With apologies to the Court, I will try and be as precise and clear as possible.

A The new figures which I put in, the new signs, are the statements of positive and negatives which I made at the time of the deposition, and again as I mentioned before -- these are a mixed bag: some are positive, some are negative. That in fact represents a brief summary of the teratogenicity of Diazinon.

BY MR. BOLDEN:

Q One further question before we leave this topic.

Is there any particular significance in any specific study to the fact that a low dose, or low number of animals are used in the study?

A. Yes. If in the study you use a low number of animals, you make that set -- that test more insensitive. You reduce the sensitivity of the test. Therefore, any negative inference or any negative conclusion based on a study with a small number of animals, I would not accept and I don't think any professional toxicologist or expert in the area would accept a study based on very small numbers of animals.

However, a positive finding in a study based on a small number of animals is entirely different. A positive study means that you are really dealing with a very, very marked effect, especially if this effect is seen in the test animals and not in the control animals.

Therefore, for this reason when I and others have sat on government committees drawing up guidelines for testing numbers of animals, for testing numbers of animals in a toxicology test, we have been very very careful to insist that in an attempt to reduce the insensitivity of tests, in an attempt not to have what we call a false negative -- and, a false negative is, you test a compound which induces cancer or birth

defects, and you miss it in animals, which is the worst possible thing that can happen -- in an attempt to prevent this, you like to have a reasonable number of animals.

Now, the definition of reasonable varies from time to time. However, a positive result, when you have a small number of animals, is very significant because it means even with this insensitive test, even with a small number of animals, you are getting adverse effects, you are getting your cancer or your birth defects.

So, therefore, the answer basically is that you would like to have a reasonably well defined study with a reasonable number of animals, that a negative inference from a study of small animals is just not acceptable whereas a positive inference may well be acceptable.

Q Doctor, have you formed an opinion as to whether or not the spraying of Diazinon at the Amtrak facility at Cornwells Heights by Orkin Exterminating Company, was or was not a substantial factor in causing the complete unilateral cleft palate and cleft lip which the infant Khristine McConnell was born with?

A Yes.

Q What is your opinion?

A My opinion is that there is a substantial probability that the exposure of Mrs. McConnell to the Diazinon was the contributory factor or the cause of her birth defect.

Q Can you explain why you arrived at that opinion?

A The conclusion is based on two major sets of considerations. The first is that she was exposed to a teratogenic pesticide, a pesticide causing birth defects, in her first trimester of pregnancy; that is, in the first three months of pregnancy. That is the particularly sensitive time when birth defects can occur.

And, as I indicated before, the reasons for my statements on the teratogenicity of Diazinon come from my evaluation of the literature and also statements in the literature. So, that is one set of considerations.

The second set of considerations relate to the fact that there were no other known predisposing factors. There was no family history, no -- the first child was normal, she took no teratogenic drugs; there were no other recognized causes of birth defects to which she was exposed in her first trimester. So, it rests basically on positive data, the exposure to a teratogenic pesticide in the first trimester, and the negative

data, the absence of exposure to other known teratogens, or the absence of other known predisposing factors.

MR. BOLDEN: May I have a minute with counsel?

(Pause)

Q Did you consider any specific records or spraying records in arriving at your conclusion?

A I examined the records, but have not used the records as a basis for quantitative determination of exposure, but for qualitative determination of exposure.

Q How many exposures would be needed to produce the result that we have been talking about?

A I can't, with due respect, answer that question simply.

The induction of an adverse effect such as teratogenic birth defects or carcinogenic, follows what we refer to as a dose response situation. The more the material you are exposed to the greater is the chances, the greater are the chances of an adverse effect.

Now, when I say the more of the material I am exposed to, that is a function of two factors: one, the actual level of the material or the dose of the material at any one time; and, two, the duration of the time. So, you have two factors: one, the duration

of exposure to the material itself, and, two, the actual concentrations at any one time.

So, the more you are exposed to and the longer you are exposed to it, clearly the greater are the risks. The lesser you are exposed to it, the shorter period of time, the lesser are the risks. But, there isn't a stage at which you can eliminate any possibility of a risk. You just say the risks are lower with lower exposures and with shorter periods of time.

t5 Q With respect to Diane McConnell, what time period and what exposure were you using in arriving at your opinion?

A The basic period of time which clearly one has maximal interest in is the sixth to the ninth week of pregnancy. That is the most sensitive time for the formation of the palates.

Now, therefore, the month of December is clearly more significant than the month of October. However, I am not prepared to exclude the possibility that there are residues from the month of October, and I can elaborate on that if you so wish me to. But, it is the month of December which clearly is the most critical time from the point of view of exposure.

For instance, on the 7th of December,

when he was seven weeks pregnant, I understand that she was only present at work for a short period of time that day, probably three-quarters of an hour or an hour. I don't have full details on that. My informatio on that is somewhat derivative. But, she did return to work eleven days later when she was about eight-and-a-half weeks pregnant then. Therefore, during the time of the single exposure on the 7th of December, and subsequent exposure on the -- when she returned to work on the 18th, that is clearly a time for which one has concern, and also time subsequent to that time after the 18th of December during which time she was exposed to, presumably, to residues in the environment. So, that is one set of exposures.

Therefore, let me go over this, if I may, a little more clearly. There was the exposures on the 7th of December for a short period of time, and from the 18th of December onwards. There was a transient -- that is one thing. And then in addition, there was a residue from the exposure on the 5th of October of the Diazinon, and we can discuss this in a moment; and, also, perhaps of significance, although I can't be too certain of this, an impurity, a very stable impurity in the Diazinon called sulfotep, which is highly toxic and highly stable.

So, essentially, we are discussing basically the December episode but possibly residues from the October spraying.

There is also one other possibility, which has to be considered, and that is that there were breakdown products in her body, persistent breakdown products in her body following the October spraying.

We do know that for one-to-two months after exposure to Diazinon there can be breakdown products of the Diazinon which can be recovered from the body. And, we don't know, therefore, what significance these have in terms of teratogenic effects.

Therefore, because of these areas of ignorance I would prefer to concentrate on the December spraying, particularly the December spraying on the period of time on the 7th and after the 18th, but I am not prepared to exclude residues from the 5th of October and -- residues in the environment from the 5th of October -- residues in the environment from the 5th of October, especially as the literature is very clear that residues can persist for a long period of time, and I am also not prepared to exclude the possibility that there are some metabolic or degradation products in her body which may also have played a role in the teratogenic effects.

MR. BOLDEN: Your Honor, that concludes my direct examination of Dr. Epstein. But, what I would like to request the Court's indulgence for, because it would only take until 11:30, I believe, is that if counsel would permit me to examine Dr. Hulnick, who is here, I am reasonably confident that his examination should only take five or ten minutes.

THE COURT: Do you have any objection? That way we can start the cross-examination and not interrupt it. We are only going to have a few minutes anyway.

MR. GRIFFIN: No, I have no objection, sir.

THE COURT: Thank you.

Would you step down, Dr. Epstein?

THE WITNESS: Yes, sir.

(Witness withdrew from the witness stand.)

(The jury entered the courtroom at 2:35 p.m.)

THE COURT: Good afternoon, members of the jury. I was happy to hear that you were all so jolly out there.

You may commence your cross-examination, Mr. Griffin.

(Dr. Samuel Epstein resumed the witness stand.)

CROSS-EXAMINATION

BY MR. GRIFFIN:

Q Doctor, this is not the first case in which you have been engaged as a witness, is it?

A No.

Q Maybe 12 other litigations you could recall quickly?

A Yes, by all means.

Q And, you have testified with respect to a number of different substances, right?

A May I take your questions one at a time?

Q I thought you answered it.

A I was going to answer that the --

THE COURT: Just a moment. Would you give me the question and let's see if the question was completely answered.

THE COURT REPORTER: "Question: Doctor, this is not the first case in which you have been engaged as a witness, is it?

"Answer: No.

"Question: Maybe 12 other litigations you could recall quickly?

"Answer: Yes, by all means."

THE WITNESS: I am sorry. I didn't hear "twelve."

THE COURT: Did you say twelve?

MR. GRIFFIN: I was not asking him to list them.

THE COURT: No, no. Did you say twelve?

MR. GRIFFIN: I said twelve.

THE WITNESS: I am happy to accept that.

A I haven't testified that number of times.

Q The various cases required many different substances

A That is correct.

Q Am I not correct that in everyone of those cases other than this one, you were really testifying about carcinogenicity?

A No, that is not true.

Q Have you testified about teratogenic effects cause and relationship in any of those cases?

A No. Teratogenesis was not the issue, but carcinogenesis also was not the only issue. For instance, there was a case in 1974 or '75 --

Q Well --

A -- in which workers were exposed to a chemical that produced, in a plant in Columbus, Ohio, and this

chemical produced paralysis in workers, and I testified on behalf of that. So, there have been areas other than questions of cancer.

Q. Well, for my purposes, to put it the other way around, you have not testified in a case before claiming that there was a cause-and-effect relationship between a chemical and a birth defect.

A. Correct, sir.

Q. When you were engaged in this case, did you consider whether you should tell the plaintiffs' lawyers they should get themselves a teratologist?

A. I made it very clear to the counsel for plaintiff what my areas of expertise are and have been, and what in what areas I could be helpful to them. I made it clear to them that I wasn't a bench teratologist in the sense of doing experimental work on teratogenicity, but I also pointed out that I had had extensive experience in the evaluating of teratogenic hazards, teratogenic data, and in the formulation of opinions on risks of birth defects from people exposed to teratogens. That I made explicitly clear to Mr. Bolden at the time when he first approached me.

Q. Doctor, my question was, did you consider referring him to a teratologist?

A. I said to them that I was not a bench teratologist--

Q I am not asking you what you said to them. I am asking, did you consider referring them to a teratologist?

A Yes, I did.

Q All right. In the course of that consideration, did you come up with the name of a teratologist who you thought would give the kind of testimony you have given in this case?

A Well, I -- that would be presumption on my part to predict what testimony another expert would give.

Q You know men all over your toxic field, don't you, or throughout the country, you have been on panels and you have worked on governmental things, you know men in this area, don't you?

A But I do not predict or would not be so presumptuous to predict the nature and the type of testimony that another expert would give, especially prior to their evaluation of the data.

Q Let's just put it this way, Doctor: If somebody comes to me with a question, with a legal question, and I say to myself, I understand that question, but that is not really in my field. I would know people around the country to whom I could refer who do know the answer to that question and who are specialists in it.

Now, my question to you was, you considered that because you told me you considered it.

Now, secondly, my question was, did you come up with the name of anybody in all this mass of people you know who you knew was a teratologist who you could expect to give the kind of testimony you are giving here?

A I repeat again, I would not presume to predict the nature of a testimony of another expert witness. I am perfectly happy to give names of people who they could go to get the data evaluated, but I reject the implication in the question that one can simply address a list of experts and say, ah, yes, they will testify favorably on unfavorably. I reject that most emphatically, sir.

Q That may be unfair, Doctor. Let me put it this way: Knowing the case as you knew it, did you make any references to any teratologists whom they should go and consult?

A That is your question?

Q That is my question, yes.

A The answer is yes.

Q And to whom did you refer them?

A I referred them to a teratologist, a Dr. Manson, in the University of Cincinnati.

Q Anybody else?
A No.
Q All right, sir.
You have been in court enough to know that a witness is supposed to be sworn before he testifies, right?
A Correct.
Q And, you weren't here.
A I beg your pardon?
Q Were you?
A Most certainly, sir.
Q My recollection was that you were not, people around me said that their recollection, when I asked at lunchtime, their recollection was you were not. Were you?
A Indeed, sir, I was.
Q Were you in the witness stand when it happened?
A I was not on the witness stand. I was facing the court reporter.
MR. GRIFFIN: Did you?
THE COURT REPORTER: Yes, sir, I did.
MR. GRIFFIN: I am sorry, that is a misunderstanding.
THE COURT: Mr. Griffin, if it did not happen it would be the first time in my courtroom.

MR. GRIFFIN: I am sure of it, Judge. That is the reason I thought it was very unusual, but that was our recollection. We probably were working on something else.

THE COURT: As a matter of fact, a witness does not even reach the witness stand without having been sworn. That is our practice.

MR.GRIFFIN: All right, sir.

BY MR. GRIFFIN:

Q Now, Doctor, let's get to the substance of the opinion.

As a scientist, can I -- is it fair to say that if you are trying to prove or give a scientific opinion that there is a cause-and-effect relationship between exposure to a substance and an end result in man, you have to go through at least some steps of the reasoning process.

A Certainly.

Q Is it fair to say that you should say to yourself, I have a substance which in my best judgment is teratogenic in man; that is one step, because if the substance was not teratogenic in man that would be the end of your search right then, wouldn't it?

A With due respect, sir, I have to disagree. The first question you ask yourself is, is there any

evidence that the agent is teratogenic, not necessarily in man.

Q No. That was part of the process I was going to go through.

A I beg your pardon.

Q You have to find in course, in your own judgment that the substance is teratogenic in man.

A No, sir.

Q Well, you have to get there soon or later, don't you?

A No, sir. May I attempt, with due respect, to explain the process.

The process is essentially to analyze the experimental data on the teratogenicity and see whether indeed this supports the inference that there was a substantial probability that the material is teratogenic in animals, or if the material is teratogenic in animals. That is point one.

On the basis of that, one makes the reasoned presumption on the basis of which all toxicolog is based, that one can extrapolate from the animal to to the human. So, the point of fact relates to the findings of teratogenicity in animals. From that, one makes the reasoned presumption of a likely teratogenic hazard in humans. That is the process.

Q I was really going to go through that process in arriving at the fact that before you can complete your chain of reasoning you have to have established that the substance is teratogenic in man.

A No, sir. There was a strong probability that it is teratogenic.

Q Well, that's --

A I have not made the statement it is teratogenic in man. I have made the statement, I believe this morning, that there was a strong probability that it is teratogenic, which, sir, with due respect, is different than what you quoted me on.

Q That is different from saying it is.

A Precisely.

Q You are saying in the scientific world that's different.

A I am stating in any world it is. I do not wish to be misquoted.

Q Suppose I say that as far as we lay people are converned, if there is a strong probability that it is we would accept that as saying well, if there is a strong probability, it probably is; fair enough?

A That is your inference, sir.

Q Well, you -- you nevertheless -- I will put it on the negative. If your scientific knowledge convinced

you that a certain substance was not teratogenic in man, you would cease your search right then, wouldn't you?

A That is -- I am afraid I can't -- I would like to answer the question simply, and please don't think I am being evasive if I don't answer the question simply, but I am just unable to do so.

To say that a substance is not teratogeni in man would imply the following: That it had been extensively tested in a wide-range of animal tests, and that in none of these tests was there any evidence of teratogenicity. That is point one.

Point two would be that there had been major human epidemiological studies covering hundreds of thousands of women, many many thousands of women who had been exposed to the agent for very prolonged periods of time, in different doses under different conditions, bearing in mind the possibility of a wide-range of confounding variables in the absence of effect. And then, all one would say is that there was no evidence that it is teratogenic. One would not say it is not teratogenic. Science has offered too many examples to the contrary of people assuming that the absence of data can be equated with safety.

Q Now, if you were a student of mine I would give you

a zero on that answer.

A Fortunately, I am not.

Q My question was, if you were convinced as a scientist that a subject was not teratogenic in man, at that point your search would cease; that is what I asked you.

A I have already answered that I cannot give a simple yes or no for the reasons I would be willing --

Q All you are doing --

A I would be willing to say that there was no evidence that it is teratogenic. I would not say that it is not teratogenic.

Q But, that isn't what I said, Doctor. Listen to my question. Just listen to it.

If as a scientist you are convinced that a subject -- that a substance is not teratogenic in man, you would cease your further search of trying to prove a cause-and-effect relationship.

A I would not presume that the absence of data would allow me to say that it is not teratogenic. I would say there is no evidence that it is teratogenic, which is an important scientific distinction, which I keep on coming to.

There was a major difference between saying that a material does not produce birth defects

and saying there is no evidence that it produces birth defects. This is a fundamental issue in toxicology.

Q I was not saying whether it does or doesn't. I was just saying, if you were convinced as a scientist that it didn't. If the best of your scientific knowledge and the best of your scientific judgment, and the best of all the tests that you did week after week convinced you -- you, not the scientific world -- but, convinced you, that this is substance was not teratogenic in man, once you got to that point you wouldn't go any further in your attempt to prove a cause-and-effect relationship, would you?

A I don't how --

THE COURT: May I interrupt, please?

THE WITNESS: I beg your pardon.

THE COURT: Dr. Epstein, is there any substance of which you are aware that you can say positively is not teratogenic?

THE WITNESS: (Pause) I think the overwhelming majority of substances are probably non-teratogenic. The vast, vast majority of agents are probably non-teratogenic. But, that does not allow me to say that a substance is non-teratogenic until and in fact there is an overabundant extensive evidence,

teratological evidence in animals, and epidemiological evidence in humans.

THE COURT: Mr. Griffin, what I understand him to be saying is that even the freshest of what we know as fresh air he would not state positively is not teratogenic. That being the case, then I think we can no longer pursue your line of questioning. He refuses to accept the major premise.

BY MR. GRIFFIN:

Q All right, sir. If you are going to -- if you are going to prove a cause-and-effect relationship, you are going to have to satisfy yourself as a scientist that there at least was enough of an exposure to this substance to have caused a teratogenic effect.

A Correct, sir.

Q And that means you have to know or at least have a reasonable scientific basis for knowing what level of exposure is necessary in order to create such an effect.

A The information which I personally would need would be the qualitative evidence of exposure; the fact that she was exposed.

The quantitative aspects of the exposure I did not consider myself competent to calculate, and

for this reason, at a very early stage I recommended that an industrial hygienist be brought in to produce estimations of the likely levels of exposure.

I should point out also that when it comes to areas of teratogenesis and carcinogenesis, there is a consensus in the informed independent scientific community that there is no way of setting safe levels or thresholds. So, any exposure to a teratogen is hazardous, can produce birth defects; the greater the exposure and the more prolonged exposure, the greater the risk.

Therefore, the two points are: One, I was satisfied qualitatively about the exposure; there was exposure. But, B, I felt as indeed you felt, sir, that it would be helpful to have the opinion of a qualified expert in this area on the levels and persistence over and above what I have read myself. And, that was, I believe, -- that was the area which I believe Mr. Todd had discussed with you and your colleagues in the court.

Q Well, are you telling me, Doctor, that as a doctor and as someone somewhat interested in teratology, you can't go the other way? In other words, you can't say, I won't have an opinion that any substance can cause a thing of this sort unless you show me a

reasonable exposure; I've got to see a reasonable exposure first?

A Well, sir, you have to understand what reasonable exposure means. Let me, if I may, give you an example.

You would have probably imagined that a part per million in air is very low, or part per billion is very low, or part per trillion is very low. One would probably say, well, ah hah, that is not reasonable exposure .

Let me point out to you that we have data on teratogenicity and fetotoxicity of agents at the parts per trillion level. The dioxin agent, the dioxin contaminant in 245T can produce defects at the part per trillion level. Therefore, I do not know what reasonable exposure is.

All I subscribe to is the opinion that there is no way of setting safe levels of exposure to agents causing birth defects.

Therefore, for that reason, I was interested in this from the -- in this exposure, from a qualitative standpoint. Was she or was she not exposed to Diazinon?

If she was exposed, fine. Then the problem begins.

The question statistically in a large

group of people, let us say you have 10,000 people exposed to Diazinon, the frequency of birth defects in that population, if they were all pregnant, would be influenced by the amount of exposure and by the duration. So, the longer the exposure the higher the exposure, the greater would be the frequency of birth defects in that population.

But, when it comes to any one individual you can't say. You can't really give an answer. And, for this reason I limited my interest in this to the qualitative aspects knowing full well that the quantitative aspects of the precise levels would be dealt with by those who are more qualified.

Q Do I understand you to say that if there is a molecule, a molecule somewhere which is breathed by a person, that is enough for you?

A No, sir, that is not what I said.

Q Well, then, you have to have some --

A Let me explain again what I said.

What I said, it is the consensus of opinion in the informed scientific community that we know of no way of setting safe levels or thresholds for agents to induce cancer, birth defects, or genetic abnormalities.

As you talk about one molecule, let me

explain what one part per trillion of dioxin is. One part per trillion of dioxin --

Q Doctor, I am not --

A Excuse me. I would like to explain this, if I may.

THE COURT: Dr. Epstein, he is asking you about Diazinon. Are you willing to make the statement, the same statement for Diazinon: One part per trillion of Diazinon would be sufficient? That is what Mr. Griffin was asking you a moment ago.

THE WITNESS: I understand, sir.

I am unwilling -- I share the opinion that we don't know of any way of setting safe levels or thresholds for Diazinon for exposure to any teratogen including --

THE COURT: Therefore, that would include one molecule.

THE WITNESS: I think the chance is that would be extraordinarily remote. But, we are dealing with billions and quadrillions and trillions of molecules. A part per trillion of Diazinon is probably somewhere in the region of quadrillions; not millions, not billions, not trillions, but quadrillions of molecules. So, a part per trillion of Diazinon -- and, if you want the paper calculations,

these can be done for you -- one part per trillion of Diazinon is not one molecule, it is not a million molecules, it is not a billion molecules, it is not a trillion. It is more than a quadrillion molecules, and that is the ball park, if you like, we can frame this discussion.

BY MR. GRIFFIN:

Q Well, let me go back to your deposition when you were being deposed upon the levels you were talking about in order to give your opinion at that time.

A Yes.

Q Now, you say here, among other things, on page 69, "So, we are dealing with exposures that were not trivial, and if you want to follow my line of reasoning that the dosage required to produce minimum symptoms is in the region of 50 to 80 milligram."

And, that is over -- "And, there are references to support that. There is documentation to support that. That's equivalent, say, to a milligram per kg body dose."

Now, when you are talking about a milligram per kg body dose, you are talking about one milligram per what?

A A kilogram of what he weighed.

Q Right. And, translated into something like the

TLV, the Threshold Limit Values, what does that mean?

A I really couldn't do an off-the-cuff translation, but it is very much in excess of that.

Q "This was going on repeatedly. It is not just one occasion an element like Diazinon, although it isn't very stable and persistent material. We do enough of it staying around after a spraying to make people sick when they returned." You knew that, didn't you?

A What is your question?

Q That was a premise for your opinion in those days, wasn't it, that there was an exposure of such an extent that it caused people to get sick when they came back the next day?

A Well, certainly. What you have read is several things, and I am not certain if you want a yes or no from me or you want me to comment on any part.

Q Well, that is what you testified to before, isn't it?

A Yes, I certainly did testify to that.

Q All right.

Then, "Well, is your basis for believing that there were incidents like that earlier in her pregnancy?" And you said, "Well, I am told again that there were multiple exposures to Diazinon in the first trimester. The dates, I have a couple of them."

Now, by multiple exposures, did you mean exposures of the kind that made people sick when they came back the next day?

A. By multiple exposures I meant exposures which wwere more than one.

Q. And, by exposure you mean exposure to more than one molecule?

A. Well, we didn't discuss the number of molecules there, but I have already indicated to you that we are dealing, if you want to translate this into molecules, you are dealing in the very, very high orders of magnitude in terms of more than quadrillions.

Q. Just dealing in terms of human experience, what is the experience to your knowledge of people coming in contact with molecules of Diazinon day in and day out, everywhere they go?

A. I am not clear what the question is. Is it relatin to birth defects, what is it relating to?

Q. I am just talking about people's exposure to that particular chemical. Are people exposed to it a lot or aren't they?

A. Well, certainly people who formulate and manufactur the material do have fairly constant exposure and people --

Q. Have you ever heard --

A Excuse me.

Q One at a time. If you will just tell me the people who are exposed, I will ask you after each one.

A Please let me finish.

Q Have you ever --

THE COURT: Mr. Griffin, let him finish his answer.

You do pretty well asking questions. Give him a chance to answer.

A What I was going to say was that people who tend to have sustained exposure would fall into several categories. First of all, manufacturers and then formulators and then applicators; in other words, people who actually manufacture the material, people who take the material once it is manufactured, make it up into solutions or preparations which pesticide applicators cna then use; and then the third are pesticide applicators, people who actually apply the material in homes or buildings or for agricultural purposes. Those are really the three major categories of people that have sustained exposure.

I am unaware of the likelihood that pregnant women would fall -- would be occupied or employed in those three categories, but I can't exclude

that possibility.

Q Well, you would assume, don't you, that there are some pregnant women who do gardening.

A There is nothing I have said which would lead you to a contrary assumption.

Q And would you think that some of them would use Diazinon? It is a very common insecticide, isn't it?

A I would not be willing to exclude that possibility.

Q And, in using Diazinon they become exposed to it in one degree or another.

A Possibly. Certainly.

Q As far as experience is concerned, do you know of any case in the entire world where somebody, because of being exposed to Diazinon had a teratogenic effect?

A I have no idea of this. Largely, because the vast majority of birth defects -- and, I can tell you that the incidence of birth defects is not trivial. In the vast majority of incidences of birth defects there have been neither investigation nor inquiry into possible causes. And, in fact, to produce an answer to your question, one would have to have a very long -- large-scale epidemiological study with a large number of women exposed to be able to develop such inferences of the kind you are inquiring about.

Q There seems to me that there is a fundamental

difference here between us.

In the courtroom, you know, what we are trying to prove is the fact, right; the fact, not the question of what might be or what could be, and, to the extent, as I see it, to the extent that science has not yet given us an answer, to the extent that we are still in the realm of that's the world and that's God, and that all those things we don't have answers for, we say they are not provable. Do you think differently from that?

A Yes, sir, sir, I think I understand what you are driving at. The situation here is, we know that this lady, during her pregnancy was exposed to a pesticide for which the substantial preponderant evidence in the literature demonstrates that it is teratogenic, period. Therefore --

Q Wait a minute. Teratogenic in where?

A Would you please not interrupt my answers and then I think we can proceed more expeditiously.

-- was teratogenic in a series of experimental animal systems. And, on the basis of this, this offers, this presumes a potential human teratogenic hazard because of the preponderance of evidence in the literature there is a presumption this agent is also teratogenic in women.

We also have some evidence of persistence of these materials, we also have evidence that there was an exposure roundabout the time of the critical time of the formation of the palate and lip. In addition to this, there was no other known -- she was exposed to no other known teratogens and there were no other known predisposing factors.

If you want to talk about the science, that is the science.

Q Now, let me go back. I was talking to you about exposure, and whether you knew of any cases of exposure in the world, and you said the answer is, you do not know. And so, it leaves, as far as the epidemiological world, as far as science knows it, they know of no connection, epidemiologically -- for the jury, you better tell the jury what epidemiologically means.

A Let me attempt to answer. The answer is no, I know of no evidence. Now, let me point out something.

Q First tell the jury --

A I have already given my answer. The answer is no, but let me explain what epidemiology is, and then let me explain --

THE COURT: Excuse me, Doctor. You did receive what amounted to an invitation from Mr. Griffin to deliver a lecture.

I think really what it called for though was a short definition of epidemiology. And, I would request that you answer the questions that are posed to you. There is a danger in delivering lectures.

THE WITNESS: All right, sir.

Epidemiology is basically the study of adverse effects in human populations. In other words, what evidence is there in human beings of cancer or birth defects. Are these related to ethnic factors, to race, to religion, sex, exposure to various chemicals in the environment. And, one of the problems about epidemiology is, like toxicology, it is very insensitive And let me explain this.

To develop inferences --

Q Doctor --

THE COURT: I think we passed the definition sometime ago. All right.

Mr. Griffin, please, please avoid the lecture soliciting-type of questions. Now, make them precise.

MR. GRIFFIN: It is difficult.

Q Am I not correct that as far as epidemiology is concerned, there is no demonstrated connection between Diazinon and human experience?

A. The absence of data in no way implies safety.

You have to do very extensive studies with large numbers of people over long periods of time before you can develop such evidence. For tobacco alone, where millions of people were exposed to tobacco, and smoked for years, for several decades it took four decades of research before relationships of tobacco and lung cancer could be established. Nowadays, the relationship between tobacco and lung cancer is clearly accepted, but it took millions of people. How many millions of pregnant women are being exposed to Diazinon at differe doses on a routine basis so we can develop information of of the kind you seek? The answer is --

THE COURT: Excuse me. Dr. Epstein, perhaps that would have been an answer to the question, is there positive proof that there is no connection. Perhaps that would have been the answer to the question

I think Mr. Griffin asked you, and I will ask the reporter to check this, is whether there is any epidemiological study that does connect the two; not whether there is anything that does not connect or proves that there is --

THE WITNESS: Thank you, sir.

I am unaware of any published epidemiological data in the literature of the teratogenicity of Diazinon and therefore you can't answer yea or nay.

BY MR. GRIFFIN:

Q In other words, as far as you know, no scientist had ever tried to study a cause-and-effect relationship between those two things?

A Ciba has not funded such a study or published the results of such a study, that is correct.

Q You don't know of any such study, do you?

A Ciba has not published --

MR. GRIFFIN: Judge --

THE COURT: Excuse me. No, no, no. Dr. Epstein, this is not a question of whether Ciba did anything. He is asking you whether any scientist --

A No, sir, there is no published data to my knowledge. There may well be data in Ciba's unpublished files, but there is no published data in the literature to the best of my knowledge, with two exceptions.

Now, these two exceptions are interesting.

Do I have permission to refer to them, sir, as I have not referred to them at the time of my deposition?

THE COURT: I am not sure which are the questions anymore and which are the answers.

Now, Mr. Griffin, if you will ask a question so that we can proceed.

Q. I will go back to exposure.

On page 72 of your deposition, did you not testify: "If she wasn't exposed at all, clearly my professional interest in the case would cease immediately. The calculation which I offer was simply illustrative of the kind of ball park dose level, the very high ball park dose level which she could have gotten."

A. Correct, sir.

Q. Do you still consider a level of, say, 1/4 to 1/8th of the TLV a very high dose level?

A. Well, you will have to explain what you mean by that.. For what period of time, what period of gestation?

Q. Well, I am talking, less than an hour of exposure.

A. You are absolutely right, that certainly the shorter the duration of the exposure and the lower the level of the exposure, the lower the risk. The longer the level of the exposure and the higher the amount to which you are exposed, the greater the risk. But, with TLV's, with due respect, are totally irrelevant in this connection. TLV's are standards based largely on acute and subacute short-term toxicity. TLV's don't reflect teratogenicity.

Q. Well, Doctor, the best you can do is the best you have. What, instead -- suppose I was a fellow who is

trying to set a level. Suppose I had the problem, I am in a business and I have a problem with women who work in my business and I don't want to exposre them to anything that is dangerous and I want to know the level for the pregnant women in my business. Now, where do I find it? Do I find it in charts somewhere that tells me?

A Good question. Good question. Now, let me try to respond.

Let me first of all make it clear what a TLV is. A TLV is a Threshold Limit Value which was set non-governmental groups originally known as the American Conference of Governmental, Industrial Hygienist -- actually they were governmental, but they were acting independently -- who reviewed the toxicity data on compounds and produced standards allowing -- governing allowable exposure in relation to acute and subacute toxicity. In other words, if somebody would drop down dead either today or would be -- within two or three weeks. None of these reflected long-term effects like cancer or birth defects. So, TLV's, again with due respect, are totally an absolutely irrelevant to the question of teratogenesis, with one exception, and this is an exception in which again I was involved in the formulation of these standards in the workplace:

namely, with lead. When it came to lead, we attempted to introduce --

Q (Mr. Griffin whistling.)

A -- introduce the area of birth defects --

Q Doctor --

A -- into the TLV. With the exception of that, TLV's are irrelevant.

THE COURT: Dr. Epstein, the question started out, Mr. Griffin wanted to know if he were in this particular business and he wanted to know what would be a safe level for pregnant women who worked in his business, could you give him an answer?

THE WITNESS: Yes, sir.

THE COURT: And, he didn't ask you about TLV. He is asking you the Epstein safe level for work. Can you give it to him?

THE WITNESS: The safe level for work in which I would ascribe, and all of the members of the independent and informed scientific community and government regulations is that we don't know of any way of setting safe levels for agents that induce cancer birth defects or genetic abnormalities. Therefore, you do not employ pregnant women under conditions under which they can be exposed to teratogenic agents, period.

We -- for instance, we now have data

that even a few glasses of alcohol in an early stage of pregnancy can produce fetal alcohol syndrome. Now, how much is enough? We don't know the answers to this.

For this reason, as the NIOSH document states, do not -- handle with caution by women of childbearing age. You do not take women who are pregnant or who are presumed to be pregnant and allow them to be exposed to agents which cause birth defects, period. That is the answer. There is no Epstein figure there is no National Cancer Institute figure, there is no government figure except we don't know of any way of getting safe levels for exposures to agents producing birth defects.

Q All right. I suppose it is fair to say you don't have any governmental agency that agrees with that one, do you?

A Most certainly. This is the position on inability to establish safe levels for carcinogens, mutagens and teratogens is a commonplace position. A very commonplace position.

Q Where does it appear? Where is there any governmental regulation which says, if there is -- when you used the word teratogen, incidentally, you are talking about a substance which has been shown to be teratogenic in a species, in an animal. You are not using it in

man, are you, because you don't know whether it is teratogenic in man or not.

A That's correct. We are talking about a presumed teratogenic hazard.

Q As I gather from what you say, your guide would be, if there is ever a demonstration of a teratogenic effect in an animal, then you don't hire pregnant peopl

A Yes. Let me respond to that.

The first time in which this was enunciated and enunciated very clearly in relation to exposure of pregnant women, was in perhaps in the leadi government report on this matter, namely, the MRAC Commission of 1969. That is Secretary Finch's commissi on pesticides and their relationship to environmental health, which clearly and explicitly and unambiguously stated that the use of pesticides to which -- which had been shown to be teratogenic, that use should be restricted to prevent exposure of pregnant women. This is a clear and unequivocal statement to HEW Secretary by an expert panel.

Q And was it adopted?

A There has been, certainly --

Q Does the government agree with it, that's what I want to know.

A Let me just point out that until very recently

it is only in the last two or three years that the question of reproductive hazards in the workplace, sterility in men, birth defects in women, it it only very recently that this has become a subject for concern.

There are, to my knowledge, no OSHA regulations as yet, governing the specifics of teratogenic exposure.

What I was discussing was the opinion in the scientific community that we don't know of any way of setting safe levels.

And, furthermore, you asked me what my recommendation would be, and my recommendation would be the same basically as that of the NIOSH, thatyou don't expose pregnant women to materials that can produce birth defects.

Q Now, listen to this question. I don't want Dr. Epstein's opinion. I simply want a volume somewhere that has a standard in it. Is there one?

A When I offer you data in the literature, you say I can't quote this because I didn't discuss it with you at the time of the deposition. I have given you repeated statements from the literature, Government scientists and others on the teratogenicity of Diazinon. You have sought to exclude this on the ground that I

did not discuss this at that time of the deposition. Now you are putting me in a difficult position now because if I refer to this again I risk being in contempt of court.

THE COURT: You are relieved from that if you can point out anything in the literature that sets forth the standards in answer to Mr. Griffin's question.

A I am unaware of any governmental standards on birth defects. These were under consideration at the time of the Carter Administration but have not been promulgated in this present Administration.

Q Now --

A That is in relation to occupational exposure.

THE COURT: Mr. Griffin, let me interrupt for a moment.

Counsel at counsel table are cautioned to make no facial expressions whatsoever.

A I beg your pardon. In relation, say, to consumer products in drugs, the FDA, I think, takes very clear and unequivocal action on this. And, let me just very briefly state what this was.

Subsequent to the thalidomide episode.

MR. GRIFFIN: Your Honor, please.

A You asked me --

MR. GRIFFIN: Your Honor, drugs and the FDA, I think we are just getting beyond our ken.

THE COURT: We are dealing here with the question of the effects of Diazinon. Let's move on.

The next question, Mr. Griffin.

Q Now, is it correct, Doctor, that in 65 to 70 percer of all cases of developmental defects in man, that the cause is unknown, flat out unknown?

A I think that is fair to say that, yes.

Q Talking again about man, what substances are there that have been shown of all the different substances we have, what substances are there that have been shown to be teratogenic in man as differentiated as being teratogenic in animals?

A Do you mean -- when you say, as opposed to, do you mean when the animal data are negative?

Q No. I mean -- forget all animal studies. I am just asking about what has been shown to the extent of present day knowledge of the scientific community, what substances are teratogenic in man.

A Okay. Well, the causes of birth defects --

Q What substances are teratogenic in man?

A Okay, fine.

Well, substances fall into various categories. First of all, infectious, like German

measles. Is that responsive to your question?

Q. It is ambiguous. I wouldn't have thought of it as a substance, but if you do --

A. May I simply answer your question in relation to the risk factors or predisposing factors of birth defects which would allow me to make reference to infectious agents which aren't in your understanding substances, okay?

Q. Okay.

A. Fine. So -- well, the first is, I suppose, genetic and familial predisposition, which is one factor. That is important. There is a genetic and familial predisposition.

There are ethnic factors. For instance, Orientals have a higher incidence of birth defects, particularly in cleft lip and cleft palate than non-Orientals.

The maternal x-rays, radiation, which isn't a substance, but is an influence, an adverse influence, and maternal radiation is an important cause; infectious agents, like rubella, German measles; drugs, a series of drugs have been shown to induce birth defects, such as thalidomide, which we have repeated, meclizine, a drug used in the treatment of morning sickness; Aminopterin, a folic acid antimetabolite;

anticonvulsant drugs, drugs used in the treatment of maternal epilepsy; then a series of toxic chemicals, particularly methyl chemicals like methylmercury, and then this may not be totally responsive, but there is an interplay of these factors, what we call multi-factorial influence; that is, the interaction of exogenous factors, such as infection, or chemicals, or what have you; and, genetic susceptibility.

In other words, it is possible that some people have a built-in genetic susceptibility. That coupled with the environmental exposure, whether it be a drug or pesticide, or what have you, the two of them are important.

So, I think we have to bear in mind, in addition to the exclusive external factors, and interplay with internal factors or genetic predisposi-tions. That is just an off-the-cuff listing.

Q But still, if you have a birth defect, and if you take into account all the things you know which may cause it, you still end up with 65 to 70 percent of them that you just can't attribute anything to.

A It is not you can't, sir. I wish that was the case. Unfortunately, the overwhelming majority of birth defects haven't been studied. We don't even, in this country, have a birth defect registry.

I am consultant on birth defects, on cause of birth defects to the March of Dimes. One of the things we are trying to do is set up a national registry. Sweden has a national registry. We don't have one in this country.

So, we don't have the baseline data on human birth defects. But, -- even, for instance --

Q But --

A Excuse me, just one second. The occupation, maternal and paternal occupation is not listed on birth certificates in this country. One of the things we have been trying to do just to answer your kind of question as to what maternal influences possibly could have had an effect on the birth defect, we don't have the information. But, it doesn't mean to say the influences, the environmental influences aren't there. You must not equate the absence of data with the absence of a causal association.

Q But, it doesn't mean that they are there either.

A I couldn't agree with you more.

Q It doesn't mean one way or the other. You just don't know.

A That's right.

Q And, in 65 percent to 70 percent of the cases, based on the present scientific knowledge, you don't

know what it is.

A Not based on the scientific knowledge, because nobody has really looked. It is an absence of data.

Q Then, based on our knowledge as human beings, we don't know.

A Based on the absence of data.

Mr. Griffin, if you will simply revise your question, based upon lack of knowledg then. Perhaps you will accept that.

Q There is not adequate knowledge.

A There is a lack of knowledge. There's almost an absence of it.

Q Now, for the purposes of our discussion from here on in, would you take the words "lack of knowledge," and "no", as the same thing?

A No, I most certainly would not be prepared to do that, sir, with due respect.

Q If, as a scientist, you don't know the answer to something, for the purposes of proof, can't you accept the proposition that it can't be proved?

A Most certainly not, and let me explain why.

In the majority of instances of consumer product safety, pesticides, there is a massive lack of information in the published scientific literature. However, there is a great deal of information in indust

files which industry has resisted making available for scientific inquiry and exposure.

Now, is one to say that because there is no data in the open published scientific literature there is no hazard, when knowing full well that there may be very extensive data in industry files. And, I have had extensive experience as a government witness looking into industry files for data which have never been published in the open scientific literature.

So, are you putting me in a position of saying, because an article is not published in the scientific literature I am to assume that it doesn't represent a hazard from cancer or birth defects when a firm, or industry, may have data stacked to the ceiling on the ability of this material, but this information has never been made available to the public.

Q I don't recall asking you anything about literature.

A Yes, you most certainly did. You talked about the absence of information. The absence of information cannot be equated with safety, sir.

Q Doctor, the absence of information to me means absence of information. If we have the information, wherever you say it may be, if we have it, then you are going to know.

A You are asking me to equate this with no effect.

That is the hangup, sir.

Q If we don't know, if it doesn't come into this courtroom today, as far as this courtroom is concerned, we are not going to know, correct?

A No. For instance, if you have information in your files which you refuse to make available, or if you refuse to allow me to refer to information which I have in my files, that is not the same as saying there is not effect.

Q Well, I think you have to accept for the purposes of our procedures, Doctor, that it is the same effect, and you have to --

A Not in my book, sir.

THE COURT: Doctor, you will have to operate according to our book.

Q You have to understand our process, Doctor, or we never can get anywhere. And, our process is to simply take the evidence that is before the Court and to weigh the evidence that is before the Court.

You aren't the weigher. You are here to give us some evidence that is helpful if you've got it, and I am trying to find out what there is in the way of evidence on a question really where is the evidence; not are there suppositions, not are there possibilities. Finding out what it is.

MR. BOLDEN: Your Honor, I have an objection. The objection is this: What Mr. Griffin has asked Dr. Epstein to do is accept the proposition that from here on in -- and we don't know what from here on in is going to be -- that lack of knowledge means no knowledge. I think that what he ought to do is ask his questions one at a time and then perhaps Dr. Epstein can answer each specific question. But, to ask him to give a broad-premised statement and agree to it, I think is unfair.

THE COURT: Well, I think the question started with what appeared to be a very simple proposition; that if there is no knowledge on a particular subject, one must answer, I don't know what the answer is. And, it was in the refusal of the witness to accept that apparently simple position that we got into this by-play, and it is a great deal of by-play and I would request Mr. Griffin to cut it as short as possible and move on to a more fruitful area of inquiry.

MR. GRIFFIN: I will cut it right there, your Honor.

BY MR. GRIFFIN:

Q Doctor, in this area -- if we are trying to solve the question is a substance teratogenic to man, we don't have any epidemiological evidence on it, we go to

the animal studies, correct?

A. We try to look for humans first. We do look at the animal data, certainly.

Q. Once we looked at the humans to the extent that we are able to and we don't have data there, or what we see doesn't give us any proof, we then go to the animal studies.

A. Fine.

Q. And, that is what the subject of teratology is all about, isn't it?

A. Well, it is one aspect of teratology, certainly.

Q. The man who is a teratologist is a man who spends his life doing that process, correct?

A. No, not necessarily. A teratologist can be a bench teratologist and do experimental work; he can be a clinical teratologist, he can be an epidemiological teratologist, he can be a teratologist who studies basic mechanisms.

Q. But, they are all in the process of trying to use the best judgment they can in developing data from animals and then extrapolating that in humans.

A. Not in the slightest. A lot of teratologists work on basic mechanisms trying to understand what are the basic mechanisms involved in teratology. The whole area of risk assessment is an important part of

teratology, but please, sir, don't equate the two. They are just not equatable.

Q Believe me, Doctor, I may give an oversimplified question to you because I don't understand the subject. And, if I don't understand --

A Well, I am trying to be helpful to you.

Q Then, I will put it: In this process of doing animal experimentation, there are teratologists who do that, right?

A Certainly.

Q And then there are people who draw conclusions from the experiments, and the process of trying to get experimental data, and to work from the experimental data as best you can, extrapolating that and saying to what effect does that show it's likely the substance might have on man.

A Fine. Okay.

Q And, in that area, you looked at these studies, correct?

A Correct.

Q And, in any study that you looked at, to start off with don't you have to evaluate whether the study is a good scientific study?

A Oh, certainly.

Q And so, if we were discussing whether these various

studies really meant anything in this overall area --
A With due respect, you are looking at the wrong chart.
Q Okay. -- whether these studies are meaningful in this overall area and whether they really prove anything if you go study by study, you are going to ask was the study correctly conducted according to standards that are not accepted in the world of teratology; that is the experts who say what kind of a study ought to be conducted; that is the field you are not an expert in, is it?
A Well, I have been involved in helping set up guidelines, but as I said before, I am not a professional teratologist.
Q If somebody was going to set up all the parameters of a study, you haven't really don't that yourself, have you?
A Oh, indeed I have. I have been involved --
Q On teratology --
A Excuse me, would you allow me to finish?
Q Yes.
A Most certainly in the MRAC Commission I and my panel created guidelines and set up and helped formulate guidelines for teratogenicity testing in animals.
Now, as I said before -- I don't wish to

be difficult or confuse you. I am not a bench teratologist in the sense that I don't spend my time everyday exposing pregnant animals. But, I have been massively involved in the interpretation and validation of data and also in developing guidelines for how to handle toxicologic experiments in general, also teratological data -- teratological experiments.

Q Before you take an esperiment and would be willing to rely on the results, you have to convince yourself that the experiment is a sound one, is that fair enough

A Yes, there is a question of judgment, I agree with you.

Q And, --

A Yes, there is a question of judgment involved here clearly.

Q And, why is it that an experiment must be a sound one?

A Well, let me explain. If, for instance, you have a very small number of animals and you inject or administer a material to it, and you get no effect, you can't, on the basis of that, say this agent is not teratogenic. Therefore, if you are dealing with a very insensitive test, you can't develop negative inference from it.

However, you don't have the same set of

equally strict concerns when you are dealing with a positive effect.

As I explained this morning, there is a great difference between a negative and a positive effect. One is less concerned about a small number of animals when it comes to a positive effect, especially if you have reasonable overall design, you have multiple doses, and especially if the results of that experiment are replicated or reproduced in other experiments. So, it is a question of judgment. But, you are absolutely right, with a small number of animals you don't allow negative inferences, you don't allow somebody to say it is not teratogenic.

With a small number of animals, however, you can make inferences on positive effects on teratogenicity, especially if the results are replicated in other experiments, especially if there are multiple doses, and factors of this kind. So, it is a question of judgment.

Q I assume, Doctor, that what you are trying to do when you say you take animals, we are going to try to eliminate by the animals we have all the chance things that may occur.

A Well, could you be just a little bit more precise in your question?

Q Well, maybe it is not a good question.
A I think I know what you are getting at, but --
Q Well, what I am getting at is, animals are subject to birth problems and they are subject to birth problems the same as other people are.
A Sure.
Q And they are subject to birth problems from all sorts of potential causes, and you are not sure exactly what they are. And, if you just take some animals and just study the animals, you are not sure if you administer a substance whether it is the substance that is causing the change or one of these many many other extraneous factors.
A Right on. Absolutely.
Q And, you have to make sure that your animals are such to the extent that science is able to do that.
A You are absolutely right.
Q And, so, part of this art in making sure you have got the right strain of animals, right?
A Well --
Q That you have them protected and all that.
A Well, when you say the right strain of animals, I wish one was gifted with design instincts for prophesy. Unfortunately, we never know what the right strain of animals is. All one can say is that there were

suggestions from the literature that in 1967 and 1968, the two strains of rats got birth defects when Diazinon was administered. Now, when the Ciba-Geigy 1974 study was done, they selected another strain of rates.

Now, the question, what is the right strain of rats, I don't know. But, I would suggest that one way of defining the right strain of rats would be to try to look at that strain of rats from which you had positive data already, or suspicious data already.

Now, having said that, let me admit that there was an argument in the literature as to whether or not you should concentrate just on rodents, or have mammals or have mammals other than rodents. And there are some people who would suggest that over and above mice and rats or rabbits, what have you, you should have one or two nonrodent species, like a pig or a dog. And here, this is what we have.

In addition to the rodent species of two strains of rodents, you have mammalian species other than rodents. You have a pig and a dog.

So, I don't really know what you -- the answer is select the right strain. The right strain is the strain in which you find positive findings, and that is somewhat circular but --

Q What was the question?

A You asked me how to select the right strain.
Q I didn't ask you that. I said, part of the art of this business is the process of selecting the right strain, isn't it, Doctor?
A Well, I just told you it is difficult to select the right strain. It is customary to use a couple of rodent species, not necessarily to finding what the strain is. Strain is different. And, also in the view of some, you should use a nonrodent species.
Q The scientist is trying to get a species which, if there is a substance applied, and if that substance is teratogenic in that species it will show up, right?
A Fine.
Q That is one judgment you have to make. You have to decide that to start with.
A You are really dignifying this and suggesting it is more scientific than it really is. We don't really know of any way.

Most people do teratological testing on a couple of species, on a rat and a mouse, and what have you, and they select very often the strain that happens tobe available.

Your suggestion dignifies the process to a higher scientific level than it generally really is.

Q It is a judgment call whether you are doing --
A Well, it is often convenience, what you happen to have around in the lab.
Q It may be convenience and it may be a judgment call, right?
A Fine. Fine.
Q And, then, after you have made your selection, you have to try to the best that you are able to isolate that animal from anything else happening to it.
A Yes. Certainly. Essentially what you try to do is to prevent your test animals from being exposed to other teratogenic agents, and you also expose -- you also have concomitant control animals which are not tested -- which are not exposed to the agent under test. And, one reason for that is to try to contrast the difference in the birth defects or the cancers between the tests and the control animals, and also to take into account the possibility their may be some unknown environmental influence which is producing the effect which you want to exclude, and that is the reason why you want to have controls at the same time.
Q And, because there are these other environmental influences and there may be other things that happened to test animals, the governmental bodies that deal with this have standards which they have set up as to the

number of animals you have to use.

A Well, there have been various standards for this. And again, as I mentioned before, I have been involved in the setting of some of these standards.

For instance, the earlier standards for pesticides were known as the FIFRA guidelines. FIFRA is short for Federal Insecticide, Fungicide, Rodenticide Act. This is an Act of 1947 as amended in 1972. The Federal Environmental Pesticide Control Act, which basically gave the administrator initially of the United States Department of Agriculture, and subsequently the administrator of the Environmental Protection Agency, the right to require certain data on adverse effects of pesticides prior to their registration.

The FIFRA guidelines had a relatively small number of animals -- to be quite frank, I have forgotten exactly the number of animals they recommended in the teratogenicity tests.

The Good Laboratory Practices guidelines which came out later in fact recommended more animals. These are fairly recent, the Good Laboratory Practices, I think is about '78, or something like that. So, these are relatively recent guidelines. I don't think there is any question that if today you start and design a teratogenicity test, you want to build in a goodly number

of animals. But, that is different from saying, I am going to disregard data on positive effects prior to the development of those standards, especially if there is data coming from tests, repeated tests in different species and different strains, all of which have been positive or highly suggestive are positive.

The fact there are guidelines today doesn't invalidate data which existed prior to the development of the guidelines, especially if those data were positive.

Q Isn't it implicit in the fact that certain governmental agencies and others set guidelines, that in their judgment at least, if the guidelines are not followed you don't have an adequate study?

A Well, the object of this is to try and ensure that subsequent to the passage of the guidelines the people who do these tests will do them based on the cookbook recipe. That doesn't mean to say the cakes baked before then were ineatable. Nor does it mean to say that teratogenicity or carcinogenicity tests done prior to the formation of these guidelines have to be disregarded.

Q But, it does say, as far as present-day knowledge is concerned, there are too many concerns about small animal experiments, experiments with small numbers of

animals?

A. You couldn't be more right.

Q. And, by today's standards, they say we do not look at those as meaningful.

A. No.

Q. If I showed up with a four-animal study down in one of the governmental agencies, they would throw me out of there,wouldn't they?

A. Ah hah, let me say what they would do to you.

Q. Well --

A. First of all -- hang on a second, let me tell you what they would do.

If the data were negative, you are absolutely right, they would kick you out on your ass.

However, if you came in with studies, with birth defects in four mice or four rats, affecting all the progeny, and these animals had three heads on them and none of the controls had three heads, they would say -- in other words, an unusual birth defect, they would say, look, friend, these data statistically are not valid. You've got something pretty rotten here. You've got something pretty rotten here. You've got a birth defect here. You've got a very unusual birth defect in a small number of animals, none in the controls This, to say the least, is extraordinarily suspicious.

Now, make sharp distinctions between that and between claims on the negativity, on the absence of effect based on small numbers.

So, the way you would be received, sir, would depend on what gifts you brought; whether you brought the positive results of unusual effects, or the absence of effects and you said, look, there is nothing here, why don't I register this material and expose millions of people to it.

Q If I came in with four animals with one defect, the overwhelming probability is that no scientist in the area would pay any attention to it whatsoever, right?

A Well, when you say four animals, do you mean four pregnant rats, or four pregnant mice, each with one defect in all the litters of all of them?

Q No. I just mean there is -- there were four animals and I administered a substance.

A Four pregnant animals, okay.

Q Four pregnant animals.

A Fine.

Q And I administered a substance.

A And four controls. And how many controls then?

Q Four controls.

A Okay. Four pregnant animals in the test group, and four pregnant animals in the controls.

Q And I got an abnormality.

A In just one animal, in just one litter, one baby in one litter, one would say well, look, you now, this is nothing to write home about, go and get lost, chum. One would not be interested in that.

If, however, in two or three litters of these four animals you had unusual birth defects and none in the controls, and in fact when you looked up your agency files you found that there were half a dozen other of these experiments, all of which with varying degrees of animals showed positive effects, one would say, now, look, this is very interesting. Why don't we mount more studies on this strain of animals which has not been done, incidentally, on the two positive strains of rats, why don't we mount large-scale studies on the mammalian species like pigs and dogs? That's the respons for one to have. And, in fact, the results with the pigs and dogs you see down there are positive and equivocal, you have two positive results in rats, in two strains of rats, the Wistar rat, the Sherman rat, and the Ciba-Geigy you used a different strain.

Q Are you mad at me?

A No, not in the slightest. I am trying to explain. I think we are developing a reasonable pattern of communication at last.

Q Can't you turn off a little after I just ask you a simple question, can't you just give me a simple answer?

A Well, I am trying to be as helpful as I can to you, but it appears that a certain amount of repetition is necessary. Otherwise you ask the same question twice.

Q Well, I am simply trying to find out whether one unusual result in a litter of four animals would be taken seriously? I think you told me no, it wouldn't. Then you went on to a long explanation as to why --

A No. You changed your question. Initially you were talking about one litter -- one animal amongst four, and then I tried to find out from you whether you were talking about one baby in four litters which may be one in fifty. There is a difference.

Q At least then the process of evaluating these different studies to say whether they give you evidence that is meaningful should be done by people who know their business, and I assum you are holding out to me that you know your business. You say, by gosh, I am good at this.

A Well, those weren't my exact words, but I am willing to accept your paraphrase.

Q All right. Now let's go here. You have some studies up here and you have a plus mark on some egg

studies. Do they recognize egg studies as being good studies? Do they tell you something about --

A Well, to be quite frank, I have done a vast amount of egg work myself.

Q For godsakes, doctor, don't tell me what your opinion is. Do they?

A I was just going to comment to say, in general, I think the position amongst most people is that it would be pretty rash to develop clear inferences on the basis of egg data. And, I share that too. I would be very unhappy about accepting clear inferences of positivity on the basis of egg data.

All I think that the egg data can do is to show you whether or not the material is suspicious and the degree of suspicion. So, I would say the answer is, you shouldn't rely on egg data in a definitive fashion, but it is reasonable to take the position that it provides you suggestive data. That's the kind of thing. It is a screen test.

Q Is it reasonable to say that a subject is -- to be teratogenic, a substance has to cross the placenta barrier and affect the fetus?

A Yes, I think so. And, this is the reason why one has certain reservations about drawing hard and fast inferences from egg data. I fully accept this.

Q And the placenta barrier is the covering around the mammalian fetus?

A You are absolutely right. There are differences, clear differences between the egg, the physiology of the egg in chicks or ducks, and the physiology of a human egg, the human embryo. And, for this reason, I think one has to be cautious, although in fact the FDA studies have shown a fairly interesting concordance, or similarity between some of the chick egg studies and some of the rodent studies.

Q Now, Doctor, pick out for me, if there is one, the one study on which you put a plus that you think is the most important study supporting your opinion.

A Well, you know, I said very clearly in the deposition that I am relying on the aggregate of the data. I am not prepared -- I was not prepared then, and I am not prepared to say now that this study is the most important.

What I am saying is, we have several positive studies; each of them which have different strengths and different weaknesses, and the aggregate of all of these I find persuasive. As indeed many other authors in the literature also find persuasive.

Q Like whom?

A Well, I may be in contempt of court if I go into

this again, but we already had a chart this morning from which you insisted that I excluded several authors who made statements on teratogenicity of Diazinon. If you would like me to go over these and with the consent of the Court, I will do so.

Q Well, we have taken a lot of time already.

This Kimbrough and Gaines study in 1968, did that have an adequate number of animals by today's standard?

A Well, that is a good question. I said before that today's standards, in general, tend to like about ten or so animals per dose level. I would say that on a whole the Kimbrough and Gaines Study was a bit short on animals. It had four to six animals in a group, in a test group, and it had four to six animals in controls. But, there were three control groups in the Kimbrough and Gaines Study.

Furthermore, the losses, the birth defects which you got in the Kimbrough and Gaines Study were extraordinarily similar to the birth defects in found in the Dobbins Study. That is the study immediately above. Those two. Very similar birth defects.

The Dobbins Study was with Wistar strain of rats; the Kimbrough and Gaines Study was with the Sherman strain of rats, and both of them found renal

defects of the -- defects of the renal tract. Very interesting.

So, when you say to me, do I exclusively rely on the Kimbrough and Gaines Study, the answer is no. It is a study I would like to see more animals in it. However, there were three groups of controls, there were birth defects similar to the defects found in other studies, and these, I think, are very very interesting indeed.

Q Well, Doctor, I am basically going to give up on you because I just can't keep going and all I asked you -- the only question I asked was, in the Kimbrough and Gaines study was there an adequate number of rats by today's standards. It seems to me you can answer that yes or no, and it took -- it took 15 minutes.

At any rate, in judging whether these studies are indicative of teratogenicity in man, people could have a difference of opinion with yours, couldn't they?

A I would say that if you show data of this kind where you have several positive studies in animals, when some of these studies show similar birth defects in different species, on different strains, the most some people -- you might have a difference of opinion this way: Some people would say there is a high degree of probability

this is teratogenic in humans; others would simply say there is a possibility, or there is a suspicion. I am willing to accept the fact that there may well be a difference of opinion between some scientists who say there is a suspicion that this produces birth defects in humans, or those who go stronger and say there is a high degree of probability. In that respect I totally agree with you, between good men of -- and women, excuse me, but in good people of faith and training in the area, there could well be a difference of opinion between those who look at data of this kind and talk about suspicion of teratogenicity on the one hand or probability, that I fully accept.

Q Do you know Dr. James G. Wilson, don't you, or of him?

A Yes, I do.

Q Do you accept him as a competent authority in the field of teratogens?

A Certainly he is a most competent bench teratologist, but I wouldn't accept him as authoritative in the area of human risk evaluation.

Q Well, you would accept him as an authority in the field of deciding whether various tests indicate teratogenicity in the animals?

A As I say, I think the man, Dr. Wilson, is certainly

a most competent teratologist. There is no question at all.

Of his professional ability in the area of risk assessment -- and we have had differences of opinion on this which I would be happy to discuss with you if you care to, I would, with due respect, raise some guarded qualifications, and, these qualifications, incidentally, have been shared by governmental agencies, and the Administrative Environmental Protection Agency rejected recommendations of his committee of a committee which he chaired on ability of 245T to produce birth defects. Dr. Wilson looked at a great deal of data in 1972 on 245T, a herbicide for which there was overwhelming evidence on causes of birth defects -- this is the Agent Orange chemical -- and he came to the conclusion that there really wasn't much hazard in this and I took a different position and the adminstrator of the Environmental Protection Agency, in an action unprecedented in the regulated history of the United States rejected the opinions of his advisory committee, including the opinions of Dr. Wilson.

So, as I said before, I think in terms of experimental teratology, fine; in terms of human risk evaluation, with due respect and -- really, with due respect I would question his ability to make

inferences on risk assessment.

Q. If your are criticizing, Doctor -- I take it that was a criticism of Dr. Wilson?

A. No, no. I said that I think that he is highly qualified.

Q. It is just an attempt --

A. Excuse me.

Q. -- that he wasn't good.

A. No, no, not at all. I said I think he is highly qualified as a professional teratologist. In the area of professional risk assessment, of assessment of risk to humans, I have indicated that there is a history on which he has taken positions contrary to the positions of many many professionals in this country, and positions -- his positions having been rejected in an unprecedented fashion by the Environmental Protection Agency in 1972 -- '71.

Q. What was the reason for doing that?

A. Well --

Q. Again.

A. The reason basically --

Q. Do you accept him as an authority in his field or don't you?

A. Well, you know you asked me before why I give you lengthy answers. You are coming back and asking me the

same question repeatedly, and I am willing to repeat my answers, but I am afraid by doing this we are trying the patience of the Court. I have already answered very substantively, and if you wish me to repeat this, I will.

Q. I don't want you to repeat it. God only knows, I'm not sure where we are, to tell you the truth with that answer. You simply -- I gather you are saying, yes, you accept Dr. Wilson as am eminent authority, but there was an instance in which he and some other people in the government disagreed.

A. Sir, you do misquote me, and, really, this is most unfortunate.

What I said was that Dr. Wilson is a most experienced and an excellent bench teratologist. He has done very fine fundamental studies on teratology in animals.

When it comes to human risk assessment, the question of assessment of risk to humans, he has been characterized by many as highly conservative. And, the instance I have given you of a committee which he chaired and which is recommendations on public policy were ignored and rejected by the federal agency to whom he was reporting, this is an example of questions that may be reasonably direct on his qualifications in the

area of risk assessment.

Now, I hope that is clear, sir.

Q As far as you are concerned, what does "Nature Magazine," think of you?

A Well, "Nature Magazine" is a journal that publishes opinions from qualified scientific people. A journal never thinks of, be it all badly, of anyone. A journal is prepared to publish opposing viewpoints and opposing viewpoints of positions I have taken have been published in "Nature" and elsewhere.

Q So, we don't want to get into incidents where somebody has not gone along with somebody else.

A I am not really talking about incidents. I am talking about the fact that when recommendations on public policy effecting the lives of millions of women in this country are concerned, he made a recommendation that it was no hazard from 245T. The scientific data were contradictory to that, and I was involved in marshaling of the scientific data which took a contrary position and presenting this in Washington and the Admistrative Environmental Protection Agency decided with due scientific advice to reject the recommendations of Dr. Wilson that indeed 245T was safe. And, the subsequent experimental data in the last ten years has confirmed the fact. We have dozens of experiments now,

well-designed experiments with large numbers of animals demonstrating that 245T is teratogenic.

THE COURT: Excuse me, Dr. Epstein. I think to summarize, and I think we better drop it at that, you have said you do accept Dr. Wilson as a competent bench teratologist, but you would not accept him as authoritative on human risk evaluation.

THE WITNESS: Thank you, sir.

THE COURT: I think, Mr. Griffin, perhaps we move along.

MR. GRIFFIN: Well, sir, I am virtually finished.

THE COURT: I know, but we are now trying 245, whatever that is, and I am not interested in injecting new matters before the jury.

MR. GRIFFIN: I just wanted to recap where we were in this case.

THE WITNESS: Sure.

BY MR. GRIFFIN:

Q In this case, because we don't have human risk factor data, we are limited, really, in trying to decide whether there is a teratological effect in humans to a study of the effect in animals. And, we have to make sure that the animal studies do show what you say they show.

A Excuse me, two points. First of all, we have the absence of human risk data. We have the fact that she was not exposed to any known teratogen, that is point one.

Point two, when you talk about the statements which I make in teratogenicity, this is misleading. A whole series of statements on the teratogenicity of Diazinon have been made by a wide-range of experts in this field, some of which are allowable, some of which I have been barred from presenting to the jury. So, I am not expressing just a personal opinion. There have been a wide-range of statements by authoritative scientists in government and elsewhere that Diazinon is teratogenic. That, plus the absence of any risk fact, known risk factor in pregnancy. She didn't get rubella, she didn't get German measles, she didn't get x-rayed, she didn't have a previous child with birth defects. So, you have mischaracterized my position in summing it up in the way you have.

Q Doctor, I thought in this case all of your judgment on whether it is teratogenic or not come from animal studies.

A Two points: One, it comes from the animal data, which is one point. But, over and above my evaluation of the animal data, a wide-range of other experts have

come to a similar conclusion, that Diazinon is indeed teratogenic. And, therefore what I was pointing out to you, that my evaluation of the teratogenicity data is not unique, as you were attempting to suggest.

Q You talk of wide-range of experts, you are simply talking about people that show up in these studies.

A No I am not. I am talking about many others, and you have barred me from making reference to the statements of these other experts. If the Court permits me, I will do that.

Do you wish me to do so?

Q I am not -- I don't know whether I do or not, Doctor. I don't know what you have or what you don't have.

A Do you wish me to --

Q You have not given me an --

THE COURT: Mr. Griffin, why don't you stop arguing with the witness.

MR. GRIFFIN: All right, sir. I suppose I shouldn't. I suppose I shouldn't. I will let it go at that.

THE COURT: Do you have any questions, Mr. Candless?

MR. McCANDLESS: Yes, sir.

THE COURT: You may proceed.

CROSS-EXAMINATION

BY MR. McCANDLESS:

Q Doctor, is Diazinon teratogenic in horses?

A I don't have the slightest idea.

Q Why not?

A I don't believe Ciba has tested it, or if it has tested it it has not released the data and I don't know if any other scientist has tested Diazinon in horses. It is not a common experimental animal in teratogenicity to the best of my information.

Q What about -- I've got a list here. What about goats? Is it teratogenic in goats?

A To the best of my knowledge, Ciba has not tested this.

Q Well --

A To the best of my knowledge there are not published data on the teratogenicity of Diazinon in goats, which again doesn't happen to be a common or usual experimental animal.

Now, we can go through a whole zoo if you'd like and you will get a similar answer, except for animals which we discussed; namely, the mouse, the rat, the hampster, the rabbit, the pig and the dog, and perhaps more recently some experiments on primates. I don't know if that saves any time.

Q Well Doctor, is Diazinon teratogenic in elephants?
A I don't have the slightest idea.
Q Why not?
A For the same answer I have given you before for goats and horses.
Q Because what, you haven't read anything that says it is?
A No. No. No. Because I am unaware it has been tested.
Q Okay.
A If there were data on the test results, I would be happy to evaluate them and give you an opinion. Perhaps you have such data which you would like me to look at.
Q Well, let me go on, one more. Is Diazinon teratogenic in kangaroos? If you know.
A I am afraid I have to answer the same way as the previous answers.
Q You know of no tests having been done on kangaroos?
A No, I am not aware of it. But, it is possible I missed it.
Q Is Diazinon teratogenic in man?
A I would say that there is a strong presumption that it is teratogenic in humans on the basis of positive data in rats, in two strains of rats, and in rabbits and in pig and dog.

Q Well, Doctor, for a kangaroo you said no because there was no study in a kangaroo.

A I didn't say there was no study. I said I was unaware. That is very different.

Q Well, what is the study in man that you are aware of that says Diazinon is teratogenic in man?

A I didn't say teratogenic -- it was -- now look, I think we are going to waste a great deal of time if you misquote me. Please do not do this. I stated clearly and explicitly that there was a strong presumption or probability. Now, you have taken that and quoted me as saying that it is teratogenic in man. I object strongly to these legal tricks.

Q All right. So then you disagree with my statement and you would say that Diazinon is not teratogenic in man. You disagreed with how I characterized it.

A I have characterized it in the way which I consider proper; namely, that on the basis of experimental data, there was a strong presumption or probability that Diazinon is pregnant in humans -- is teratogenic in humans.

Q Do you know the names of any other human, other than someone conceivably involved in this case, that had a birth defect because of Diazinon?

A No. No. But, it is -- as I said before, you have

an overwhelming majority of cases with birth defects that are never investigated.

Q All right. Are you an investigator of birth defects?

A I think I have discussed my professional expertise in some detail this morning. I do not make a profession out of investigating birth defects. I have advised governmental agencies, I have advised and still advise the March of Dimes how to go about studying this, but I do not spend my time exclusively in these areas.

Q Okay. Are there people who do?

A Certainly. Certainly. There are some epidemiologists, particularly in the Center for Disease Control, who do their best with the very limited data they have. But, as I said before, the basic information which you need, namely a birth defects registry, or parental, maternal and paternal occupation on birth certificates, we don't have these data, but, nevertheless there are epidemiologists in CDC and elsewhere who study these matters, and there are experimentalists who study these matters, and there are people in the area of risk assessment too. There is a wide-range of areas for the data base. As far as humans are concerned, to say the least it is grossly inadequate.

Q Are you and epidemiologist?

A. No.
Q. Would you rely on another epidemiologist if you wanted to know something about epidemiology?
A. In general, when I have problems in epidemiology I discuss these with colleagues in the field and take opinion and advice from those who are recognized as being professionally competent in the area, certainly.
Q. Doctor, do you know when Diazinon was created?
A. Created? That is a strange word. What do you mean by that?
Q. Well, did it come to us with the formation of the earth? It is not a natural compound, is it, or is it?
A. Do you mean when was it synthesized?
Q. Whatever you want to make it.
A. Okay. Well, that is different. I believe a patent was taken out in about '51, to the best of my memory, and Ciba-Geigy started marking it in about 1954. That is to the best of my recollection. I may be off by a few years, that I think that is basically the -- I may have some -- I think that was -- yes. I think it was marketed in '54. Sure.
Q. How long has man been on this earth?
A. Well, you know, it depends on whether you are a creationist or not, and I am not sure this Court would permit a discussion of evolution in this area. I just

don't know.

Q Will you accept a million years?

A I am willing to accept any hypothetical you are willing to offer.

Q When did cleft palate first appear on this earth?

A Well, you know, in the ancient papyri, I believe there are records in times of Egyptians of birth defects, including cleft palates.

Q Did the Egyptians have Diazinon?

A To the best of my knowledge, no. I think I told you that Diazinon was synthesized about 1951, and I am not sure at what point the repetition of the question is. If it was synthesized in 1951, how could the Egyptians have been using Diazinon; the early Egyptians, the ancient Egyptians, I mean.

On the other hand, there have been many instances of acute toxicity in organic phosphate pesticides in Egyptians, Egyptians in the course of the last decade or so, including massive numbers of buffalo kills from organic phosphate pesticides which were manufactured in this country and exported without any labels or warning on these problems to Egypt. I am willing to discuss this, if you so wish. That was an Egyptian episode.

Q Well, let me just get this straight, leaving the

Egyptians in or out of this. Cleft palate and cleft lip certainly came long before Diazinon.

A Oh, you are absolutely right.

Q Thank you.

Well before Diazinon, what would we blame cleft palates on?

A I had gone through a list of risk factors in response to your colleague's question. Would you like me to repeat the same list of risk factors for humans? I think the record is very very clear as to what I said causes risk factors, but I am willing, if the Court wishes, to repeat the same list again.

Q You needn't do that. We heard it once.

A Well, you asked the question a second time.

Q It is pretty clear to say that certainly you couldn't blame any of those clefts before 1951 on Diazinon.

A In the absence of an exposure to a teratogen, you cannot blame the teratogen or incriminate the teratogen for the birth defect. That is fairly obvious.

Q And, Doctor, is that a yes answer or a no?

A I have answered, I think, fairly simply.

Q Can you blame pre-1951 birth defects, cleft palate, cleft lip, on Diazinon?

A I have already said no.

Q Thank you.

A For the reasons I have given.
Q Where are Diazinon's fingerprints on the McConnell cleft?
A There aren't any. In fact, the majority of adverse effects in the environment, whether cancer or birth defects, or genetic abnormalities, there are no pathognomic, or fingerprints to say this cancer is due to that chemical, or this birth defect is due to that particular chemical. It is very very rare that you can have -- you can state by looking at a particular cancer, or this or that, or birth defect, this is due to exposure to that agent.
Q You can't do that in this case either, can you?
A I just told you.
Q You said that in part you relied upon what you perceived to be an absence of exposure in Diane McConnell to known teratogens, is that correct?
A Yes.
Q Well, I think in your earlier testimony, and I know you will correct me if I am wrong here, but, you led me to believe that certainly almost no compound can be excluded simply because there is no data on it, is that correct?
A Yes, certainly. There is a great deal of differenc between actual data showing that a material is

teratogenic than the absence of data which would not allow you to pass an opinion one way or another. But here we have clearcut exposure to an agent which has been demonstrated to be teratogenic in several animal species and several strains. We don't have data on teratogenicity of any other materials to which she was exposed.

Now, I am not willing to exclude the possibility that there were other materials in the environment. I don't know. I am not prescient. All I can do is to offer the Court an opinion based on the evidence that is available.

Now, if you hypothesize on something on which I have no data, I am not in a position to be helpful to you.

Q Did you give Diane McConnell a checklist of possible teratogens so you can know this?

A I gave her nothing. I have never met Mrs. McConnell until this morning, but I asked Mr. Bolden if he would please inquire into a range of exposures and factors.

Q Mr. Bolden did this for you?

A I asked Mr. Bolden if he would get this information for me, and make this information available to me.

Q What checklist did you give him to find out what

the exposure to other--

A. I have already told you that --

Q. You gave him that checklist?

A. Would you allow me to finish before firing staccato questions?

I told Mr. Bolden that I needed information covering a wide-range of factors, including any drugs she took in pregnancy, tobacco, alcohol; I went into a very wide-range of possible environmental influences with Mr. Bolden and I got information on all of those.

I got information on drugs, lack of radiation --

Q. Doctor --

A. -- alcohol, tobacco, and all other exposures. So, the answer to your question is, while I do not have a formal checklist in front of me of factors one to twelve, I inquired about all factors which I considered.

Q. Okay. Well, Doctor, if something were carcinogenic, would you -- that means it causes cancer. Maybe we are bandying about words here that not everyone is totally familiar with. Doesn't it, carcinogenic means capable of causing cancer?

A. That's right.

Q. If you suspected a compound as being carcinogenic,

would you also have suspicions about its teratogenicity?
A Well, that is a good question. One of the difficulties of answering this is that we don't have good comparative data on a large number of carcinogens and a large number of teratogens. There have been suggestions based on smaller numbers that there is an association between the two. I don't think the association is an obligate one. I don't think it is a very clearcut association. But, there are some suggestions of an association.

It is clear that some carcinogens do induce teratogenic effects. But, that doesn't mean to say that there is a close association between them.
Q There is a lack of --

THE COURT: Just a moment, Mr. McCandless.

May I see counsel at side bar, please?

(Side bar discussion on the record, as follows:)

THE COURT: I don't want to limit anybody. By the same token, I don't want to cause unnecessary expense. But, I do not want to press the jury too hard. We have pushed them pretty hard.

I take it you are going to be awhile?

MR. McCANDLESS: I may well be.

THE COURT: Particularly if you are going

to go over the same ground Mr. Griffin has already covered.

MR. McCANDLESS: I don't think I have done too much of that already, have I?

THE COURT: It all depends if 80 percent of what you have done is too much or not too much.

In any event, I certainly am not going to cut anybody off. But, I am not going to push the jury any further. It is now 4:15. They have been sitting without a break for two hours. I am going to excuse them until 9:30.

Unless -- if I knew -- Mr. Griffin.

If I knew that five or ten minutes more would save a witness fee, I will -- but I --

MR. FERRONI: Your Honor, the witness does have a plane that he would like to catch at 7 o'clock tonight. With all due respect to the Court, if we could finish today, we would appreciate it.

THE COURT: Yes. But, you would have to say, with all due respect to defense counsel, and defense counsel are not about to accommodate this witness, I don't think.

Am I correct in my assessment?

MR. McCANDLESS: Yes, your Honor. I think you are right.

MR. SPALDING: Perhaps we could inquire of the jury if they would be willing to indulge us to hear the end of this witness' testimony.

THE COURT: I think as good citizens they would say -- they would stay here until 9 o'clock if I asked them to. I simply am not going to ask them to.

MR. SPALDING: All right.

(End of side bar discussion.)

THE COURT: Members of the jury, having due regard for the principle that the hardness of a seat after one has been sitting too long affects the ability to absorb, I think we will call an end to today's session, although I gather it will cause some inconvenience to the witness.

So, we will recess now until 9:30 tomorrow morning.

(The jury withdrew from the courtroom at 4:15 p.m.)

(There was an in-chambers conference at 4:17 p.m., concluding at 4:30 p.m., at which time court adjourned.)

(Proceedings for December 10, 1982.)

(Court convened at 9:55 a.m.)

THE COURT: Good morning.

The witness may return to the stand.

(Dr. Samuel Epstein resumed the witness stand.)

CROSS-EXAMINATION(Continued)

BY MR. McCANDLESS:

Q Good morning, Doctor.

A Good morning.

Q Did you meet with plaintiffs' counsel last night?

A Well, we had dinner yesterday together, yes.

Q Did you discuss this case?

A No. No.

Q Not at all?

A No. We talked about music and many other matters, but not the case.

MR. McCANDLESS: Your Honor, I would like to make a motion about this witness. I feel that during --

THE COURT: Come to side bar.

(Side bar discussion on the record as follows:)

MR. McCANDLESS: Your Honor, I think that

under these circumstances, the witness having met with counsel while he is under oath and in the process of being cross-examined, its impropriety, at least some sort of instruction should be given for that, or at least move to strike his testimony.

THE COURT: Motion denied.

(End of side bar discussion.)

BY MR. McCANDLESS:

Q Okay, Doctor, last night when we left off, I think we were asking about what you did to determine what other possible teratogens Mrs. McConnell might have been exposed to.

When were you asked to consult in this case?

A I think it was about in June or July of 1980.

Q At that time suit had already been brought, hadn't it?

A I beg your pardon.

Q Had suit already been brought at that time?

A I have no idea.

Q Who did this literature search for you?

A This was done Toxline and Medline, and commissioned by Mr. Bolden.

These are automated computerized literature searchers that you pay a fee. You feed in

the key words, like diazinon, or whatever you are interested in, and they produce the information for you.

Q Mr. Bolden supplied you with this literature.

A Yes.

Q In your deposition which we took in Chicago in August of 1981, you said that you had only been asked to consult in this case some five months before the deposition.

A That was a mistake. It was in fact the summer of 1980.

Q We did come to Chicago to depose you; you recall that?

A Yes, I do.

Q And, you charged us a thousand dollars for your time on that single day, isn't that right?

A Yes, that's correct.

Q And, that time, as now, you presented yourself as being an expert in reading literature, is that correct?

A That was not the language I used. I presented myself as an expert in toxicology.

Q And at that time you read the 1974 Baselt Rat Study backwards, did you?

A Yes. In fact, I got the Baselt report fairly shortly before the deposition, and I really hadn't had

an adequate amount of time to look into it as thoroughly as I did subsequently. I think I pointed out right at the beginning of the deposition that I had by no means completed my literature review.

Q But, at that time, your conclusion was that that showed some sort of teratogenic effect.

A That's correct.

Q And it in fact didn't.

A Well, I wouldn't say it is totally without any effect at all. But, there is no question that I misread one table. However, there are certainly some other interesting aspects to the Ciba-Geigy 1974 report, which make it not entirely without blemish.

Q But now you changed on your chart from a plus to a minus?

A That's right, yes.

Q Doctor, in the request that was presented to you about this case, were you asked to find the cause for the birth defect, or were you asked whether Diazinon was involved?

A I was just asked to review the files and to see if I could come up with an opinion as to the causes of the birth defect.

Q And, Diazinon had been suggested to you, hadn't it?

A I was presented with a background document and

asked to review them and asked to see if I could come up with an opinion.

Q. Diazinon was suggested to you at that time.

A. Well, to be quite frank with you, I don't remember exactly the nature of the original letters and the conversation, but I was told, among other things, that she had been exposed to pesticides in her early pregnancy, yes.

Q. You have the original letter with you, don't you?

A. I am afraid I don't, no.

Q. You didn't bring that?

A. No. But, I am prepared to concede there was a -- certainly in the correspondence, or in the discussion there was reference to spraying of pesticides, including Diazinon. And, that in fact was the basis for the literature search in Diazinon in fact.

Q. Okay. Did you consider the possible effect of Mrs. McConnell's having worked near a cathode ray tube?

A. I considered it, but didn't feel on the basis of the information I had that there was any evidence relati such exposure to birth defects.

Q. Did you do a literature search on that?

A. No, I didn't.

Q. What about her use of alcohol or tobacco? What did you do to find out about that?

A Well, I specifically inquired about all these matters, and you are quite right in pointing direction in those areas.

First of all, as far as tobacco is concerned, she did smoke certainly at one stage, but she gave up smoking as soon as she discovered she was pregnant. I believe that was the exact time.

Over and above that, she did take alcohol very very briefly. I think over Christmas when she was pregnant. She said that she had taken, I believe, one to two glasses, or something of that kind. So, in fact, she didn't take alcohol during pregnancy, with the exception of about one to two glasses of alcohol in Christmas of '78. And, as I said before, she stopped smoking as soon as she discovered she was pregnant with Kristine.

Q Isn't that somewhat contradicted by the medical records you were given on this lady's delivery and her health before that time wherein it was indicated that she was smoking one-pack-and-a-half a day?

A You are absolutely right. There is one record of Dr. Hayman, in which it was said that she smoked one-and-a-half packs a day. And I specifically inquired about that and was assured by Mr. Bolden, who in fact I asked him to go back and check with Mrs. McConnell,

that in fact that represented her past history, that she had in the past smoked one-and-a-half packs of cigarettes a day in her pregnancy, but that in fact she confirmed to me, via Mr. Bolden, that she did not smoke during this pregnancy.

In fact, in all the medical records I saw, there was only one reference to her smoking in pregnancy, and that was Doctor -- to the best of my recollection, that was Dr. Hayman's note, which I am assured is a mistake.

Q Doctor, have you brought all the records with you?

A No, I don't have the medical records.

Q Did you ever talk to Mrs. McConnell personally?

A Yes, I spoke to her yesterday and introduced myself and asked to see her daughter, and that is the first time I have spoken to her or seen her.

Q Doctor, I realize you are not what you call a bench teratologist, but you agree that in the field of teratology there is a wide margin of error when you ask a mother what it was she might have been exposed to after delivery?

A You are absolutely right. Human memory is, mine included, is frail at best. And, one can simply go on good faith.

If indeed you question and question

repeatedly and repeatedly and you get an answer, "I haven't smoked," or, "I didn't take alcohol," you know, what else can one do but accept.

I am not denying the possibility that an error was made, but all I can say is, I don't think so.

Now, if you ask me the basis for saying, "I don't think so," I can't really tell you. It is just my feeling that this is the truth.

Q Well, then, you are familiar, I take it, with the literature of people who are bench teratologists, that there is certainly a selective memory bias in women who have had children with birth defects as to what they have been exposed to during pregnancy.

A With due respect, I don't think bench teratologists would have any information at all on this. A bench teratologist is someone who works experimentally with animals and most of them have never seen a pregnant woman, let alone -- in the course of their professional activities -- let alone have any professional opinion on this.

The kind of person who I think would be qualified in this area would be, say, the clinical -- the clinical teratologist, or the pediatric teratologist on the one hand; alternatively, the psychiatrist.

But, you are absolutely right, there is selective memory. The most honest person can have selective memory deletions, and I think the psychological literature abundantly attests to that.

Q And, doesn't the literature also say that in cases such as this, a mother would be most inclined to select something outside of herself, or outside of her own responsible conduct to find to blame for the birth defect?

A Well, to be quite frank, I really don't want to qualify myself in this area. I am perfectly prepared on general grounds to accept the fact that we all have selective memories. More than that I think you should address your questions, with due respect to somebody who is more qualified, like a behavioral psychologist, or psychiatrist, or a clinical teratologist.

Q Doctor, in that Kimbrough and Gaines Study, when was that published, the one that you made reference to?

A The Kimbrough and Gaines Study was published in 1968.

Q About 14, 15 years ago?

A Sure.

Q And, another one of the ones you found positive is Dobbins.

A Dobbins, yes.

Q 1967.

A That's right. Yes.

Q And Green, you found -- what is that, positive, 1969? Is that right?

A Green, no. We have a plus-minus, which really means equivocal.

Q Okay. What is the latest positive study that you found?

A The latest? I would say the Earle Study.

Q 1973.

A In 1973, yes. That's correct.

Q Nine years ago.

A Yes.

Q And, I think you have already explained that date you know of no federal regulatory agency that has ever restricted the use of Diazinon with its relationship to pregnant women.

A That's correct. But, I also pointed out, I believe, I am unaware of any federal regulatory action with relation to teratogenesis, with two possible exceptions. With two exceptions: One, the FDA's position on drugs, which originally required three-generation tests in rats and subsequently after the thalidomide episode, subsequently required teratology studies; and also the Occupational Safety and Health Administration Regulation

on lead, in which there was consideration of a variety of effects, including teratological.

I should also just explain, NIOSH, the National Institute of Occupational Safety and Health, who has been credited with statements on teratogenic actions and in whose Registry of Toxic Effects of Chemical Substances, Diazinon is listed as a teratogen, NIOSH has no regulatory authority. It simply makes recommendations and does research and reviews of literature, but has no regulatory authority per se.

Q But, pesticides are regulated by EPA, isn't that true?

A Yes, that's correct.

Q And, you made reference on your chart to the NIOSH document; is that true, NIOSH, what was it, recommended standard for environmental exposure? You made use of that?

A Well, I think the original standards on this were developed by the American Conference of Governmental Industrial Hygienists, or ACGIH.

Q I didn't ask you about the source. I am asking you whether or not you made reference to the document?

A No. Excuse me. You asked me about the standard, and you asked me -- you implied it was a NIOSH standard.

Could we have that read back?

Q. Let me withdraw the question, and I want to get it clear.

Do you or do you not make reference in your charts to the NIOSH document, Recommended Standards for Occupational Exposures.

A I see. Now, that's different. You said recommended standard.

The document is called, "Recommended Standard for Occupational Exposure," but, in fact the actual recommendation for the standard came not from NIOSH, came from the American Conference of Governmental Industrial Hygienists. The document is entitled, "Recommended Standards for Occupational Exposure." That is the basis of the ambiguity.

Q Did you make reference to that document?

A Yes, sir.

Q Thank you.

Have you had the opportunity to read Dr. Farrow's deposition?

A Yes, certainly.

Q And, you know then that he was the author of the pertinent sections -- well, I know he prepared the draft of it.

A Okay.

A Yes. But, this draft --.

Q You know he based it specifically and only on Kimbrough and Gaines.

A That is correct.

Q What was the birth defect, or teratogenic effect in Kimbrough and Gaines?

A Well, there were a series of different birth defects

Q With respect to Diazinon.

A Excuse me. I am just --

Q I just want to limit the question but --

A I am coming to the answer on the Diazinon, and if you please don't interrupt me I will give you your answer.

Q Thank you.

A There were a series of birth defects induced in rats from the Diazinon, and they included renal abnormalities, congenital renal abnormalities, which incidentally were very similar to those observed in a previous Study by Dobbins in Wistar rats. So, they had renal abnormalities in 100 percent of -- I beg your pardon, at one particular dose level of 100 milligrams per kg, effecting about six-out-of-fifty animals. And then at another dose level, at the 200 milligrams per kilogram dose level, there are a series of birth defects including hydrocephalus, which means a big head, that is

due to blockage of drainage of the spinal fluid, and the head gets enlarged, progressively enlarged.

There is one hydrocephalus, one missing phalanx, and another defect. In fact, there were about, in the 200 dose level, there were three-out-of-six defects.

Those were the basic defects which were reported, and, you know, the study is certainly by no means conclusive. It is -- there are defects in the study and there are suggestive pointers in the study.

Q Let me ask you about the high-dose range, they were giving 200 milligrams per kilogram.

A Yes, that's correct.

Q Okay. Now, as a toxicologist, you would agree, wouldn't you, that virtually every substance is toxic, depending upon the right dose.

A Absolutely.

Q So, the fact that a substance may be toxic doesn't mean it is particularly dangerous.

A Sure.

Q Okay. Now, they gave at 200 milligrams per kilogram, Kimbrough and Gaines, enough of this Diazinon at that very high dose level to have induced toxic effects in the mothers, isn't that true?

A Yes, there was some weight loss, among other things

the mothers showed.

Q Two-out-of-five of them died.

A Yes, there was weight loss and mortality, sure.

Q Under current teratological practice, with the bench people now, as you understand it, don't the scientists in that field now regard that type of test as not showing teratogenic effects because you are inducing toxic effects in the mother?

A No. In any teratology experiment you aim to give a series of doses, the top dose being -- the highest dose being a near-toxic-dose, or just short of toxic, very often called MTD, or Maximally Tolerated Dose. That is standard practice.

Then you give fractions of those doses. So, it is standard practice, as I said, to have in your high dose, as I said before, doses which approach toxicity.

In fact, in the Ciba-Geigy 1981 Study, they had mortality at the high dose and they had also symptoms at the high dose, and I wouldn't criticize the Ciba-Geigy Study on that basis. I think it is a correct and proper approach.

Q I am not criticizing the Study. I am asking you whether under current teratological practice, in the experimental fields of teratology, isn't it true that

teratologists would tend to ignore any findings where they have shown toxic doses in the mother?

A No.

Q She just showed toxicity.

A The answer is no. One wouldn't ignore them. One would weigh those findings accordingly.

Q But, they are not of value, or the same value as compared to an effect shown at a subtoxic dose?

A As I said, one would wait until those data are recorded.

Q What weight would you put on it?

A One would not ignore them, but one would note that there is toxicity. But, toxicity alone -- hundreds and thousands of chemicals are toxic, but hundreds and thousands of chemicals are not teratogenic. So, therefore, toxicity per se does not confer teratogenicity. That is exactly what I mean by -- I am saying, one would weigh those observations accordingly.

Q You would give it less weight?

A I would certainly give it less weight, yes, but I

a teratological effect, but something that is seen in the normal development of rats, and depending upon when you take your sample you may well it, you may well not?

A Oh, certainly. But, it is regarded as a birth defect. Developmental abnormalities are birth defects.

For instance, a cleft lip and a cleft palate, I presume you would regard as birth defect.

Q Well --

A But, they are -- they occur at a stage in pregnancy that the palate and the lip haven't fused. So, therefore, one can't say because that is just simply developmental, therefore, it isn't a birth defect. It is a birth defect.

Q Well, these rats weren't born, were they, in Kimbrough and Gaines.

A No. The standard practice in most teratological experiments is to deliver the young by cesarean section, the test in the control before birth.

Q And, you disagree with me then, I take it, that under current practice in the field of teratology, in experimental teratology, teratologists would not regard a dilated renal pelvis as being a teratological effect.

A I beg your pardon? I am sorry, I was just looking at something else. Would you mind repeating that?

Q Then I take it that you disagree under normal present teratological science in the field of experimental teratology, that scientists who found dilated renal pelvis, hydroureter in a rat, would not accept that as being a teratological effect.

A No, I think those are teratological effects.

Q You think they are.

A Yes.

Q And you think that is the general opinion in the field?

A That is what the authors of the Study considered, and there are numerous statements in the literature attesting to the fact that on the basis of the Study Diazinon is teratogenic.

Q Kimbrough and Gaines concluded with a certain qualification, didn't they?

A Certainly.

Q They qualified any finding they might have found by saying that it only occurred at toxic level doses?

A Well, that is not entirely true. I share the qualifications of Kimbrough and Gaines, that the Study is not a perfect one, and I pointed that out very clearly and very explicitly in the deposition, that there are criticisms that can be made against the Kimbrough and Gaines Study. However, it is incorrect

to state that the birth defects were only noted at the highest dose level. In fact, as I indicated before, birth defects were noted at the lowest dose level of 100 mg per kg where there was no evidence of toxicity at all. And, I explained that very clearly to you before when I said at the 100 milligram per kg dose, that birth defects were noted.

Q Doctor, I would like to read to you from the Study, at page 807 and 808.

A I understand what the authors say. But I am telling you -- you asked me my opinion, and my opinion is that in fact the data in the Study show clearly, and we can go to the data, if you like, by looking at the results of 100 mg per kg, that birth defects were produced. In fact, there was a 12 percent incidence of congenital renal abnormalities at the 100 dose level where there was no toxicity.

Q The people who did the Study, didn't say that.

A I answered very clearly that the data show this. The data show very clearly that there were birth defects at the 100 mg per kg where there were no dose levels.

One of the things that the evaluator of literature has to do is to read studies, to look at the author's conclusions, and to compare the author's conclusions with the data that they -- which they present

Now, in general, the authors' conclusions on this are consistent with the data. There is one area in which the authors' conclusions are inconsistent with their own data, and that is the point that I have just told you. At the 100 mg per kg -- and, we have been discussing the renal abnormalities for the last four or five minutes, and those occurred at the low-dose level where there was no toxicity.

Q So, you disagree with the people who did the Study?

A No, I don't. Their data show defects at the 100 mg per kg. There is, however, an inconsistency between one statement in the paper and the results. But, when such inconsistencies occur, you always give precedence and priority to the data. The data are the important things.

There are numerous examples in the toxicological literature when people make conclusions that are not justified and that are not warranted by the data. It is the data that are the scientifically sacrosanct elements. The authors' conclusions are interesting, they should be carefully considered, but they are not sacrosanct. What is sacrosanct are the data, the scientific data.

Q Do you read the journal "Teratology"?

A What I do is, I look at the cover of it and find --

pull out any articles that interest me, and I do this with about 30 journals, and flip them over about once every since months or so, something along those lines.

Q. Are you familiar with the article that appeared in "Teratology" written by Woo and Hoar, which shows their findings that dilated renal pelvis really is not a teratological effect?

A. No, I haven't seen this paper.

Q. Okay. It would be unfair of me then to ask you questions.

Would you agree, Doctor, that many teratologists, in fact most if not all, would feel that it is impossible to extrapolate data from animal studies into man?

A. Well, no, I would disagree. If this indeed were true, what would be the point of doing -- of the FDA requiring teratology studies on drugs, what would be the point of any requirement for toxicological testing in animals. If this would be the case, why don't we just release all chemicals into the environment, into food, into consumer products, into foods, into drugs, and not bother to do any testing if you cannot extrapolate the results from animal data to humans.

Now, it is clear that you can't equate results in animal studies with human risk. You can't

say because it occurs in one animal that it will necessarily occur in humans. But, all you can say is that there is a probability, or a strong presumption, that this will occur.

So, it is not an obligate association. It is a presumption or a strong probability.

Q In fact, in may studies they have shown what happens in animals just doesn't relate to man at all, isn't that true? Did you mention meclizine yesterday?

A Yes. Now, this is not the case. There is a difference between the absence of an effect in the literature, or the absence of data and the absence of an effect. It is true that meclizine, in animals, has clearly been shown to be teratogenic.

There have been some human studies done on meclizine, and in the human epidemiological literature on meclizine, there is no evidence of teratogenicity. However, as I pointed out yesterday, to develop negative inferences needs very very large populations followed up for long periods of time. And, I have to explain this again by pointing out that with tobacco it took several decades of research, including many, many millions of people before causal associations could be developed between smoking and lung cancer. Therefore, if one wants to develop inferences as to the

safety or otherwise in meclizine in human populations, you need very large numbers of pregnant women taking meclizine, some of whom have taken high doses, some of whom who have taken moderate doses, and some of whom have taken low doses, and a vast body of data which you analyzed exclude other exposures before you can develop inferences.

Q Based on that reasoning, Doctor, what is safe?

A Well, toxicology, as best as I indicated, is an imperfect science. All one tries to do is, one tries to determine by the best type of animal tests whether a material produces adverse effects, whether it be cancer, whether it be birth defects, or what have you, and then arrive at a reasoned extrapolation to humans.

Now, if you find these effects in animals there is a suspicion, a probability, a strong suspicion and ignore that information at your peril.

If, however, the data are negative, it doesn't mean to say it it safe. It may simply be, you have tested too small numbers of animals. It may well, be that this chemical by itself doesn't produce the adverse effect, but that chemical together with another chemical does.

So, like lawyers, scientists do the best they can. And, the best we can do in terms of

safety is to test thoroughly and extensively in animal tests. If you find a positive, you act on it. And, in some instances -- when I say a positive, there is different degrees of positivity. There may be strongly positive data which very very clearly sound warning signals, or there may be positive data which have less clarity and strength and persistence to them, but which again raise beacons.

On the other hand, if the data are negative in a series of studies, then in fact you can say, as far as we know, there is no evidence of hazard. That doesn't mean to say it is safe. And, there are numerous examples in the literature to attest this.

Q All right. Now, answer my question, please. What is safe to expose a pregnant woman to.

A Well, the position which March of Dimes and various other organizations take is that it is rash to expose a woman in pregnancy to any foreign material, to any drug, to any chemical, and with recent evidence which we have even relatively small amounts of alcohol.

So, the pregnant woman is an extraordinarily sensitive -- the growing fetus is extraordinarily sensitive, and it is rash and extreme to expose this highly sensitive collection of growing and dividing cells to the possibility of any toxic

insult. That is as a general statement.

If you do have evidence that a chemical is teratogenic, or there was a suspicion of its teratogenicity, this becomes all the more clear: Don't do it. Or, if you are considering exposing people, warn them. But, don't do it once you have suggestions in the literature or evidence in the literature, even if this evidence is not watertight.

Q The fact is, the theory or the feeling is that we know so little that virtually anything might do it.

A The consensus of opinion is, it is rash to expose pregnant woment to environmental chemicals, to drugs, to radiation, to any known insult. It is a rash thing to do, even in the absence of data on teratogenicity.

However, in the presence of data on teratogenicity, this is, to say the least, very, very, very rash.

Q What I am saying is, again, we know so little that our current suggestion is to avoid virtually everything.

A No. You are paraphrasing my answers and I have already answered exactly what I mean to say. Ignorance is no excuse for failure to act on available information There is -- there are available data. Act on those available data.

The absence of vast amount of other

information is not relevant to public health decisions which have to be based on available information. That is the point.

Q I am not here to ask you to make points you choose to make. I just want an answer to the question. The fact is right now the advice to pregnant women is virtually avoid everything.

A Avoid all exposures, again, to environmental and toxic chemicals, now much more so to chemicals which are suspected of being teratogenic or which are teratogenic.

Q Doctor, your principal line of work has been in cancer, isn't that correct?

A It has been in a pretty wide-range of areas, ranging from human pathology, I have extensive experience as an M.D. pathologist in hospitals; my experimental work has included a very wide range of areas, including genetic -- tests for genetic effects using pregnant animals; enzyme disturbances from toxic chemicals; the use of protozoa, or single-cell systems for studying cancer chemotherapeutic agents. I have also done extensive work in cancer, and also extensive research in the whole question effects of chemicals in air, water, food and the workplace.

Q Well, then, with such a wide-range, there must be

certain literature that you relied upon in keeping yourself abreast of things. Let me ask you this. There are a few journals in the world that are pretty highly regarded: "New England Journal of Medicine" is one of them, isn't it?

A Yes.

Q "Harvard Medical Journal"?

A I am sorry, I missed that.

Q "Harvard Medical Journal."

A Okay. Fine.

Q "Nature."

A As an ex-Harvard alumnus I would be happy to agree with it, but I am not sure everybody would agree, but --

A "Nature." Do you think "Nature" is a respected journal?

A I think -- I must say I have a very high opinion of "Nature," yes. American scientists tend to not have such a high opinion, and tend to like "Science," an American equivalent, more.

Q A few years back you wrote a book called the "Politics of Cancer," didn't you? Is that true?

A True.

Q And, this was reviewed in an article in "Nature."

A Correct.

Q The title of that article was, "Distoring the

Epidemiology of Cancer, the Need for a More Balanced Overview."

A That's correct.

Q And in that article you were criticized for such things as distorting scientific evidence?

A I was accused of that.

Q Statements appear in there that say, "However the political punch is often achieved at the expense of scientific accuracy and balance."

A That accusation was made. But, those accusations were refuted by an article of mine published subsequently in "Nature" which analyzes each one of these charges and in open print demonstrated their untruthfulness and there has not been a rebuttal or criticism of my reply to that article, which was a very long and a very extensive article which appeared in "Nature" in January 15, 1981.

Q So, you took exception to this anyway.

A Well, it is not a question of taking exception. It is not a question of personal feelings. My interests are on the underlying scientific data. And, the scientific data were inconsistent with the criticisms of that article. And, I demonstrated this in open print and there has been no criticism or challenge of my very detailed rebuttal of that article. In fact, I

have had numerous letters and contacts from people all over the world applauding my response and saying that that article was, to say the least, scientifically misplaced.

Q Nonetheless --

A The author, incidentally, comes from an institution which is -- which receives overwhelming industry support. I am not saying there is any necessary association between the support of the institution and his position, but it is a fact that should be noted.

Q I take it equally then that your position ought to be noted as a fact where you have been waging wars against industry.

A That is a gross misrepresentation of the facts, and I propose to reply to that as you have, I think, made a statement which casts doubt on my professional status.

From the late '60's I was consulted by Congress and by government for a wide-range of purposes. Many of these purposes included federal regulations and the development of congresssional legislation. For this purpose it was necessary to go into industry files and to examine them in great detail. And, in may instances when I did this I was able to document, clearly and precisely, without any question

of legal challenge, a pattern of suppression, manipulati
and distortion and distruction of data, all of which I have documented in detail in my book, "The Politics of Cancer," which, among other things, has been called a white collar -- primer on white collar crime.

This book which names names in industry, and which describes events of actual manipulation and suppression, including the fact that industry data is often generated on secrecy in-house -- either the industry's scientists do it -- and, this information is submitted secretly to the regulatory agencies without the opportunity for the scientific community to look at it, and in my book I named various industries and demonstrate what practices they have done, and there has not been a single legal challenge to the specific details of what I have published. In fact, there have been a series of court proceedings which have amply confirmed by position, first of all in asbestos where I have a section known as "The Asbestos Pentagon Papers, which makes it clear that the asbestos industry, as early as 1930, had detailed intimate information on the cancer-causing effects of asbestos and suppressed this information, and invovled in this suppression, this conspiracy, were lawyers, were doctors, were insurance companies, and in fact the record speaks for

itself, and this has been abundantly attested to in several subsequent litigations since I published the book.

Q Nonetheless --

A There is a fine tradition in this country of publishing data --

Q Well, Doctor, please answer my question. There is no question outstanding.

A I have not completed my answer. There is a fine tradition in this country of investigative journalism on the one hand and also of publishing the facts and letting facts speak for themselves. And, in the book, "The Politics of Cancer," besides having a detailed scientific analysis of many causes of cancer, there is abundant documentation of improper practices by the chemical-pesticide industry, the pharmaceutical industry, in actions relating to the improper handling of information and data; either the generation or the interpretation of the data.

Q Okay. Essentially, what that document is though is a political document, isn't it?

A I don't know what you mean by political document. "The Politics of Cancer," which is referred to by many people now as the "The Silent Spring of Cancer," is a scientifically precise --

MR. McCANDLESS: Your Honor, I would ask to terminate this answer.

He originally stated --

A It is a scientifically precise --

THE COURT: Mr. McCandless, when you ask questions like that, you encourage answers like this.

MR. McCANDLESS: I got an answer.

THE COURT: None of which has anything to do with the issues before this jury.

MR. McCANDLESS: I understand that. I was about to ask --

THE COURT: So, if you will go on to the next question and avoid that kind of question we won't have to listen to these extended lectures.

MR. McCANDLESS: Yes, your Honor. I thought we had received an answer when he said he didn't know what I meant. But then somehow from not knowing we appeared to be going down the road.

BY MR. McCANDLESS:

Q Okay, Doctor, that's all I have. Thank you.

A Thank you.

MR. BOLDEN: May I have a moment, your Honor?

(Pause)

(Off-the-record discussion among

plaintiffs' counsel.)

MR. BOLDEN: No questions, your Honor.

THE COURT: You may step down, Doctor.

MR. GRIFFIN: If your Honor please, based on the examination by Mr. McCandless, I have just a couple of questions.

THE COURT: All right.

MR. BOLDEN: I will object to that, your Honor.

THE COURT: No. He has a right to cross-examine further after the other cross-examination, if he wishes.

MR. GRIFFIN: I think it will be very short, your Honor.

FURTHER CROSS-EXAMINATION

BY MR. GRIFFIN:

Q Dr. Epstein, in answer to some questions Mr. McCandless asked you, you said Ciba had patented Diazinon back in the mid-fifties.

A Well, it may be a mistake. They developed it. They developed it right about '51 and marketed it around about '54. But --

Q Well, you know if there was a patent, it only lasts for 17 years anyhow, don't you?

A Yes.

Q So, that by the mid-seventies, this was a product that could be produced around the world without any limitations by anybody who wanted to produce it.

A I take your word for that.

Q Now, Doctor, I have had a chance over the evening to look at those other references you have. And, if there is anything in there you really think is important I don't want to hold you back from telling the jury about it.

A Well, I don't want to be --

THE COURT: He has now withdraw his objection to your reference to the -- is it the subsequent studies and articles?

MR. GRIFFIN: Yes, sir. He had three references yesterday I knew nothing about, and over the evening I was able to look at them, and if the Doctor thinks they are important and the jury should know about them, you can tell them.

MR. BOLDEN: I think that is unfair. We were not permitted to question the witness in direct examination about them.

THE COURT: You will have full opportunity.

If you wish now to inquire, I will do that before he resumes his cross-examination.

MR. BOLDEN: No, your Honor. I think it is probably best if Dr. Epstein wants to refer to it, to let Mr. Griffin conduct the examination.

THE COURT: All right, you may bring it out and you may, in your redirect examination, which you have a full right to do, then explore it as fully as you wish.

Mr. Griffin, you may proceed.

BY MR. GRIFFIN:

Q Doctor, I can just short cut it, Doctor, by saying, you had three additional references. One had to do with egg and chick studies, didn't it?

A Are we talking about one chart, or all my charts? Are you withdrawing your objection to all my charts, or are you being selective about what I can --

Q I was talking about the literature references. That is the only thing I have been able to check.

A Well, there are several literature references, and essentially what are you saying, that I can refer to all three charts, or would you like me to be selective about my suppression of information?

t10 Q I may have misunderstood you. I only thought there was three additional literature sources to which you went in making up the chart.

A In one particular chart, on the chart on the

teratogenicity of Diazinon, that is true. There are however, also statements on quotations from the literature on precautions to be taken with Diazinon and persistence with Diazinon, and quotations in the literature on teratogenicity of Diazinon.

Now, essentially what are you telling me you want me to do? Should I suppress some information, all information or no information?

Q Doctor, I simply want to give you a chance to tell the jury if there is anything in all of that that you consider particularly important on this question of whether in fact, whether in fact, there is a teratogenic effect in Diazinon demonstrated in animals.

A I see. So you are being selective about what aspects I can inform -- discuss with the jury.

To be quite frank, I must be guided by the Court on this --

THE COURT: No, no, no. Mr. Griffin's question, whether he intends it or not, eliminates all restrictions.

THE WITNESS: Thank you, sir.

THE COURT: You may now answer to your heart's content and disclose to the jury all that which you have said up to this point you have been bound not to disclose.

THE WITNESS: Thank you, your Honor. I will return almost immediately. I just want to --

(The witness withdrew from the witness stand and approached the easel.)

A May I have a red pen, please? Again.

(A red pen was handed to the witness.)

First of all, let me say I appreciate this change of position which I think would be helpful in presenting my thoughts on this matter.

The first chart is on the teratogenicity of Diazinon. It is a summary of data which I am aware of in the literature.

This involves certain studies involving eight different species of animals.

I have made changes here to reflect my present evaluation of the data. And, as you see that in eight-of-the-thirteen studies, Diazinon was shown to be teratogenic.

As was made clear yesterday, there are some discrepancies between these results and the results which I discussed at the time of the deposition, and the reason for this -- I would like you to be clear of the reasons for the discrepancies is that while I did have a great deal of information in my files at the time of the deposition, I hadn't reviewed it all. And, in fact,

if you look at the very first two studies, the duck egg and the chick egg, at the time of my deposition I said they were negative. The reason for that being is in the original study described by the author, Khera and Lyons, in which eggs were injected with Diazinon, there was no reference at all to teratogenicity to defects and abnormalities. And, I took the position that in the absence of this, it means there is nothing there.

However, in more recent review of the literature, including material which I offered counsel for the defense at the time of the deposition, I found an abstract written by Khera, the first author there, which states very clearly that Diazinon was teratogenic.

Similarly, if you look at the two bottom -- the two studies at the bottom by Earle, the pig and the dog, I had previously said that the results in the dog were equivocal, and I now have changed that to the results in the dog are positive, not equivocal. And, the reason for this being is that I had in my file an abstract which I hadn't read, again by Earle, which points out that in the dog Diazinon was clearly teratogenic. So, that is the first chart.

(Witness withdrew from the witness stand and presented another chart to the jury.)

So, in other words, in

eight-out-of-thirteen studies involving five species, different studies, Diazinon was shown to be teratogenic.

Now, I had made clear yesterday that some of these studies are better than others, none of them are entirely perfect. In fact, some of them have major defects. But, the studies in the aggregate, creat at least a probability of Diazinon being teratogenic, if not a strong suspicion.

Now, let us leave my evaluation alone. Let us assume that you haven't heard my evaluation for the moment, and let's see what the literature says on the teratogenicity of Diazinon. Let's see what are the statements in the literature on the teratogenicity of Diazinon which could have allowed the development of an opinion as to whether this was teratogenic, or suspected to be teratogenic, or probably teratogenic. Now, here I have a series of quotations from literature, including some authors of some of the previous studies.

Now, the very first study was by Khera. This is based on the Khera and Lyons first study which I told you the abstract makes it clear that Diazinon is teratogenic.

The statement in the literature reads that Diazinon induced -- and I quote, and there is quotations marks, "congenital foot deformities," in eggs

in duck and chick eggs. "Congenital foot deformities" is in quotes.

The next is the Kimbrough and Gaines Study. "Diazinon produced some malformation."

Kimbrough and Gaines go on to say, and I haven't written that down there, "The spontaneous incidence of these malformations is very low in the control strain of rats."

So, it produced malformations, and the incidence of these is very low in the untreated controls.

The next is the Study by Green in which it says, "Diazinon produced teratogenic activity in all chicks."

The next is the Earle Study, and, -- incidentally, I should point out, underneath Khera, it says, "Canadian FDA," Canadian Food and Drug Administration, "CDC," Center for Disease Control -- that is a big federal research center in Atlanta, which has major responsibility in birth defects and congenital abnormalities; that Earle came from the Food and Drug Administration.

Nishimura is the next author, a Japanese author, who says, "The following chemicals were proved to have a teratogenic effect: Diazinon."

The next is NIOSH, National Institute for Occupational Safety and Health, the official government agency that makes recommendations to the Department of Labor on standards governing exposure of workers to toxic and chemical -- adverse agents in the environment. And, it reads, "Based on available evidence -- Diazinon -- can be considered possibly teratogenic and should be handled with caution by women of childbearing age."

The next, Sax, a standard textbook of industrial toxicolgoy, refers to Diazinon as "an exper." -- exper. is an abbreviation in the text, short for experitmental -- "an exper. teratogen."

The final is NIOSH, RTECS. RTECS is Registry of Toxic Effects of Chemical Substances, which, in 1977 -- and this lists detailed accounts of toxic effects of a wide-range of almost 50,000 chemicals are listed in these registries. And, in the year 1977 and 1978, 1979 and 1980, Diazinon is listed as a teratogen.

I regret that I haven't checked the 1981 and the 19- -- I don't think the 1982 version is out, but there you are.

Could I have the next, please?

(Another chart on the easel is being presented to the jury.)

The final chart relates to quotations from the literature on precautions to be taken with Diazinon, and whether or not -- and what is the persistence of Diazinon.

Now, the first first statement comes from Menzie in 1969, and Menzie is USI, that is short for United States Department of Interior.

Q Excuse me, Dr. Epstein. It is true, isn't it, whatever you are quoting here has nothing to do with the teratogenic effects?

A Not in the slightest. It has everything to do with it, because if indeed there is no exposure to Diazinon then my interest in Diazinon as a possible teratogen ceases. So, this is very relevant to the question.

Q This goes to the issue of exposure?

A -- of the -- the problem of the birth defect rests on two issues. One, is the agent teratogenic, and was there exposure. This speaks to the exposure aspects, and in fact, you never consider teratogenesis under any circumstances unless you take into account two facts, namely: the effect on the experimental system, and the question of human exposure.

Q And, did you gather in the course of gathering these quotations, anything from those authorities which said what the exposure level should be or could be?

A Well, would you let me finish and then I --

Q I want to know whether you did.

A Yes. I will be very happy to respond to any questions if you will allow me to finish.

Q Go on.

A Menzie, 1969, United States Department of Interior, quotation: "Diazinon half-life varies from 21.6 to 80.2 days."

Now, what this amounts to -- let me explain,if I may, what a half-life means. A half-life is the standard way of expressing the time taken for material to degrade and to disappear.

If you say the half-life of a chemical say, in soil, is four days, it means by four days 50 percent of that chemical will have disappeared, okay? Four days after that, another 50 percent would have disappeared. So, in other words, by eight days there would only be 25 percent of the original. So, half-life is an expression of how long it takes for half the stuff to disappear.

Now, in soil, the half-life of Diazinon can extend up to nearly three months.

Now, take into account that in soil you have air movement, constant air movement; wind, sun, rain and bacteria that are breaking down the Diazinon.

Very very different from the situation in a house, or in a carpet where you don't have constant wind movement, air movement; you don't have constant wind, you don't have constant sun, you don't have light, you don't have bacteria which break the stuff down.

So, the statement already -- by 1969 it was known that Diazinon was a relatively stable material, that it could vary up to three -- almost three months, eight days. By eighty days, only half the stuff would have disappeared. Okay.

Now, let's see what the industry says about Diazinon -- about exposure to Diazinon. This is a statement from a book by Cornwell, a British textbook by a manufacturer, director of a pesticide group known as Rentokil. And it says, "...inhalation should be prevented in confined areas."

The next, Ciba-Geigy, 1975; the literature of Ciba-Geigy. "Do not breathe spray mist. Do not get in eyes or skin or clothing." "One half of the original application (in soil) was lost in two to four weeks." Now, this is quite interesting.

Ciba-Geigy, in 1975 says, about two to four weeks, up to four weeks, the half-life of Diazinon is up to four weeks. It is interesting that the same Ciba-Geigy statement that says that, also has

a reference to the authority on which this is based. This statement is based on an author known as Braugh Rasmussen, which is cited in the Ciba-Geigy document. But, Ciba-Geigy states that one-half was lost in two to four weeks. It doesn't say one-half was lost in eighty days. But, be that as it may -- even though the Ciba-Geigy document says that, half the stuff can remain after four weeks, okay.

The Environmental Protection Agency, Allison and Hermanutz. What do they say? This is a study in water. "Diazinon may persist many months in some fresh water environments." Again, with exposure to air, to sun, constant air movement; not just a 10 or 20 percent loss, or what have you, but constant air movements, bacteria even can exist for many months.

Now, the United States Army, in Fort Detrick, the Center for Bacteriological Warfare Research -- and, there is a paper in 1978 by a man called Meier, who determined that there was an impurity in Diazinon, a highly toxic impurity known as sulfotep, which is highly persistent, very stable and highly toxic, and he noted that this information was known to Ciba-Geigy and that Ciba-Geigy had failed to warn people on its label, and had failed to produce any information in the open scientific literature, or its own literature on sulfotep,

it's highly toxic, highly persistent impurity. And, I quote, "Sulfotep is an impurity common to all formulations. It is much more toxic. It is not more stable. It may concentrate. Sulfotep presents a previously unidentified potential hazard to health." No warning by Ciba in its literature, no reference in the total scientific literature.

NIOSH, 1978, National Institute of Occupational Safety and Health, 1978: "Diazinon can be considered to be possibly teratogenic and should be handled with caution by women of childbearing age."

Baselt, in 1978. Dr. Baselt is the Connecticut Medical Examiner who, I don't know, but I am told has extensive experience in poisonings and pesticides and other agents: "Diazinon itself --" and I quote, "-- accumulates in fat at concentrations over 100 times those in blood."

So, in other words, even when you look in blood, say about a few days afterwards, a few days after a pesticide spraying, you find no diazinon in the blood, but, it is accumulated in the fat.

And, he goes on to point out that a particular breakdown product, some breakdown products of Diazinon, which I will tell you what they chemical is, but it doesn't make any difference --

diethylphosphoric acid -- and, the metabolites were found in urine specimens collected 23 and 58 days after exposure. So, two months after exposure you could still find metabolites of the Diazinon in the body.

Now, I don't know how many of these metabolites, or which of these metabolites are teratogenic. I have come across no information on the teratogenicity of some of the metabolites. But, the fact remains that the Diazinon persists in the fat, and even as long as two months after exposure you can demonstrate metabolites of Diazinon in the body.

Thank you. I appreciate the opportunity you gave me.

Q All right, Doctor. Now, as far as the talk on all the labels that you have given us, is the purpose of that to get the jury mad at Ciba?

A No. I think the purpose very simply is the following: The purpose is, as I indicated before, in an analysis of any adverse effect, one needs to have two pieces of information. One, information on the inherent toxicity of the material, which in this case was the experimental teratogenicity; the second is information on exposure.

As far as information on exposure is concerned, one needs to know, does the material break

down immediately; is it persistent; does it degrade, and information of this kind. And, this, I submit, is highly relevant to the question of the persistence and exposure.

Now, I am sorry if you take a different opinion, but in my view this is critical to an analysis of the problem.

Q Let me just ask you: This case doesn't involve in any way Diazinon in the soil, does it?

A Certainly not. But, Diazinon in the soil breaks down --

Q Excuse me, Doctor --

A Excuse me. Diazinon in the soil breaks down --

Q Doctor --

THE COURT: Dr. Epstein --

THE WITNESS: I am sorry.

Q Just answer my question and we will get over this quickly. This case doesn't involve Diazinon in the soil.

A Correct.

Q This case does not involve Diazinon in water.

A Correct.

Q Did you make any searches through the literature to see what the breakdown of Diazinon would be in the environment that we are talking about?

A To be quite frank, this is an issue that came -- that arose --

Q Did you make any searches to see --

A No.

This is an issue that only arose relatively recently. I had already -- at the time of edition I was aware of the Ciba-Geigy statement. The other references are more recent ones. As I was told, the questions of exposure have cropped up. But, there is a Ciba-Geigy Study which I would like to refer to, if I may --

Q Doctor, I don't want you to get into that. Answer my questions, and if you and your counsel want to bring something up, bring it up, all right?

A Yes.

Q Just --

A The answer is yes.

Q Just answer the few questions I have so I can get over this recross.

You have already said that you do not know what effect there might be if such Diazinon is found in the blood after a period of time.

A What I said was, I don't know -- I am unaware of information on the teratological effects of the metabolites of Diazinon.

They would not be in the blood. I think it is unlikely -- it disappears from blood fairly rapidly. It would be in the fat in the body.

Q Now, if you will go back to the charts with the quotations that you had in what you call the various studies.

A Sure.

Q In your studies we have Khera -- and that was a Study involving eggs, correct?

A Yes. Do you want the quotations from the literature?

Q No. I want to find out what the studies were about. I will ask you just a few questions about it.

Khera was about eggs, correct?

A Well, there were two studies by Khera. One was on duck eggs and the other was on chick eggs.

Q All right. Duck eggs and chick eggs. And, you and I talked about the significance of those yesterday.

A Correct.

Q All right.

Then, Kimbrough and Gaines --

A Well, excuse me. You have left out a couple.

The Green Study and the Procter Study are both on chick eggs.

Q I was going to come to them. I listed them in the

order you presented them.

A. I am sorry. I beg your pardon.

Q. Kimbrough and Gaines, Mr. McCandless talked to you about them, and you have discussed them.

A. Sure.

Q. Right.

Then Green was also one egg.

A. Correct.

Q. Earle was on a dog and a pig or pigs and dogs?

A. Correct.

Q. Now, Nishimura, in Japan, that was not a Study at all.

A. No, that's right. That was quotations from the literature. This is headed, "Quotations From Literature."

Q. And, so far as you know, Nishimura was simply going back to Kimbrough and Gaines.

A. I am not sure exactly what he based his opinion on, but he expressed that position that it was teratogenic.

Q. Well, if he had studied the world literature, as far as you know, because you have studied the world literature, you would have to go back to a study. So, you would have either Kimbrough and Gaines or Earle, those are the only two studies --

A It is pretty likely, but I honestly don't recall exactly what he based it on.

Q But, you don't have any other basis for judging what he based it on.

A No, that's right. It was a review of the literature.

Q It was just a literature review.

A That's right.

Q Also, when he used the word -- was it, "proved" to be?

A He states, "The following chemicals were proved to have a teratogenic effect."

Q All right. Now, "proved," do you know whether that was the word he used, or wasn't?

A God knows, my Japanese is pretty poor.

Q Well, there are actually a hundred different Japanese languages, aren't there? Dialects?

A I am more than prepared to concede that there are infinite subtleties in the Japanese language.

Q And he could just as well have said, reading the articles you can see the author's claim and you don't know how somebody translated it?

A No argument.

Q All right.

Now, the NIOSH Report, the first

NIOSH Report, that simply references Kimbrough and Gaines, doesn't it?

A. Correct. And a reference which was looked at by -- and a statement which was looked at by a wide-range of reviewers, governmental reviewers, industry reviewers, professional groups; a wide-range of people.

Q. But, all it references, the only study it refers to is the Kimbrough and Gaines Study.

A. You are correct, sir.

Q. All right. Then, the Sax book you talked about, it says, "experimental teratogen." And it has a reference.

A. Correct.

Q. And, the only reference it referenced is NIOSH.

A. Correct.

Q. So again, you're referenced back to Kimbrough and Gaines.

A. That's right.

Q. And then the final NIOSH statement you had was simply a repetition of the earlier NIOSH.

A. That's correct.

Q. So, as far as all this learning is concerned, what you've got is Kimbrough and Gaines and Earle.

A. What you have is statements in the literature expressing the position that Diazinon is teratogenic.

The basis for this rests on a relatively small number of studies. As I indicated before, in eight-out-of-thirteen studies Diazinon was shown to be teratogenic.

Q. Doctor, I just want to make sure I have this clear now.

A. I think you have.

Q. Except for eggs -- we discussed eggs yesterday. Except for eggs, the only studies that you can put a finger on having to do with -- where you can even put a plus, are Kimbrough and Gaines and Earle, as far as animal studies.

A. Not correct, sir, not correct.

Q. No?

A. No.

Q. Dobbins.

A. The studies, fine.

Q. Dobbins.

A. Dobbins, in the Wistar strain of rats, Kimbrough and Gaines in a different strain of rats, were remarkably similar congenital abnormalities; Earle, in a pig, pigs, which are not very often used in these studies and Earle in a dog. So, we have a pig, dog, two strains of rats, quite apart from chick eggs and duck eggs.

Q. To the extent that you know the literature and you

know other studies, everything else is negative.

A Well, as I indicated, there are one, two, three, four -- one, two, three, four, five negative studies.

Q All right.

Now, Messrs. Kimbrough and Gaines, they are not teratologists, are they?

A Well, I would say that they are toxicologists, not primarily teratologists. I would say that is correct. But, I would say they have substantial experience in translating toxocological data into areas of human risk.

Q And, Dobbins was a medical student, wasn't he?

A To be quite frank, I am not sure.

Q All right. All right, sir, that's all I have in addition.

REDIRECT EXAMINATION:

BY MR. BOLDEN:

Q Just one question. Of the five negative studies you referred to, you said there were thirteen studies, eight positive and five were negative.

A Right.

Q Of the five negative studies, how many of them if any, are Ciba-Geigy studies?

A Well, if by Ciba-Geigy studies you mean studies --

Q Performed for Ciba-Geigy.

A Performed for Ciba-Geigy as opposed to done in-house, two-of-the-five were Ciba-Geigy studies. That's the Harrison-Holson 1981 Rabbit Study, and the Fritz 1974 Rat Study.

MR. BOLDEN: Thank you. No further questions.

RECROSS-EXAMINATION

BY MR. GRIFFIN:

Q Ciba-Geigy's studies, as you understand both of the studies to which you have referred, they were done by independent laboratories at the request of Ciba-Geigy.

A They were done by contract to outside laboratories, yes.

Q And that is standard in the industry?

A Well, I can't answer that terribly briefly. I will try not to --

Q Well, then don't bother.

A Are you withdrawing the question?

MR. BOLDEN: Thank you.

THE COURT: All right, anything more?

MR. McCANDLESS: No.

THE COURT: Thank you. You may step down, Dr. Epstein.

We will take a ten-minute recess.

THE WITNESS: Thank you.

(Witness excused.)

(Court recessed.)

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