ORIGINAL

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF OHIO
WESTERN DIVISION

Mary A. Dendinger, et al.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	Case No. C87-7117
	)	
Chrysler Plastic Products Corp. et al.,	)	
	)	
Defendants.	)	
	)	

DEPOSITION upon oral examination of PROFESSOR SIR RICHARD DOLL taken on behalf of the Defendants before Christine Mary Armstrong, Accredited Court Reporter, commencing at 11am at Green College, Oxford, England on the 26th day of July, 1988.

URL 1140

APPEARANCES

For the Plaintiffs:

KIRK J DELLI BOVI Esq. of
Murray & Murray Co. L.P.A.
300 Central Avenue,
Sandusky, Ohio 44870

For the Defendants:

ROBERT A BUNDA Esq. of
Fuller & Henry,
Attorneys at Law,
One Seagate,
17th Floor,
P O Box 2088,
Toledo, Ohio 43603-2088

- - - - - - - - - - - -

I N D E X

- - - - - - - -

E X H I B I T S

No.	Description	Page
Defendant 1	Curriculum vitae	Marked for identification prior to the commencement of the deposition
Defendant 2	Review by Dr. Doll published 1988	

Plaintiffs' exhibits were marked by counsel and not released to the reporter.

Plaintiffs' exhibits subsequently supplied and attached to transcript.

11.10am

MR BUNDA: My name is Robert Bunda. I am attorney for the Defendants in the case of Mary A. Dendinger et al v. Chrysler Plastic Products Corporation et al, a case arising in the United States District Court for the Northern District of Ohio, Western Division.

MR DELLI BOVI: I am Kirk Delli Bovi, representing the Plaintiffs, Mary A. Dendinger and Etta Wallace.

MR BUNDA: (To the Reporter) Would you swear the witness?

PROFESSOR SIR RICHARD DOLL, having been duly sworn, testified and gave evidence as follows:

MR DELLI BOVI: Before we begin Dr Doll's testimony, I would like to make an objection for the purposes of the record to both the place and the time of the taking of Dr Doll's deposition. The taking of Dr Doll's testimony in Oxford, England, has imposed a great financial burden on the Plaintiffs in this case. There has been no showing by the Defendants that Dr Doll could not have been produced in the United States to give testimony which would have been far more cost-saving in terms of time and money both for the Plaintiffs and their counsel. Second, I want to register an objection to the time of the deposition. On July 19 I corresponded with you and requested that I be provided on July 25th with all the articles and other information upon which Dr Doll will base his expert opinions

URL 11543

today. Because of plane mis-connections in Pittsburg, instead of arriving in London at 8.30 yesterday morning, I arrived in London at 8.50 yesterday afternoon. Yesterday morning, I had my secretary contact you here in Oxford and request that the documents that I had requested from you on July 19 be made available at my hotel so that I could review them upon my arrival. At my hotel, which incidentally is located within a mile of Dr Doll's office and your hotel room here in Oxford, upon arriving in at the hotel, none of the documents were there. I immediately contacted you, you indicated that the documents could not and would not be made available to me until 9 o'clock this morning. When I arrived here at 9 o'clock this morning I did receive some of the documents that Dr Doll is going to be relying on and some of the documents I requested that he had authored and were in his curriculum vitae. However, I did not receive this morning a number of unpublished papers that are listed in the references to Dr Doll's report and accordingly, I have not had an opportunity to review those. I have not had an opportunity to thoroughly review the hundreds of pages of documents first presented to me at 9 o'clock this morning and accordingly we object to the time of the taking of Dr Doll's deposition this morning.

MR BUNDA: For the record in response, my understanding is that you arrived in Oxford at midnight last night. The

information was of waiting for you all day on the 25th. The unpublished documents which serve as the basis for Dr Doll's review were requested by him to remain in his office and under his control, to which request I acceded and I so informed your secretary when she called. We also made available to you this morning, the 26th July, at approximately 10 o'clock, an opportunity to review those documents. You were also provided with an opportunity to take a discovery deposition of Dr Doll which request you declined - - let me finish. I have asked Dr Doll to provide you with those articles which you requested from me which had been listed in his curriculum vitae, many of which are published. He brought with him those he had in his possession, this morning, which documents were made available to you between 10 and 11 o'clock.

THE WITNESS: May I interject. All the ones I was asked to produce were produced, with the exception of one Canadian article which I have used in my evidence which has been in the public domain for several years.

MR BUNDA: Which were you not produced?

MR DELLI BOVI: The ones I listed as references in Dr Doll's report are the following unpublished articles: Bar, 1981; Bennett, 1986; Barnes, 1987; Downes, 1977, and Equitable Environmental Health, 1978---

MR BUNDA: For the record, to my knowledge those were

never requested. The request I understand you made was for the four primary articles which serve as the basis for his opinion. Three of those four were provided and the fourth, as Dr Doll has indicated, is in the public domain as having been published.

MR DELLI BOVI: For the purposes of the record and we can mark this as Plaintiffs Exhibit 1, is a copy of my correspondence to you dated July 19, 1988 in which I requested: "All of the articles and other information upon which Dr Doll will base his expert opinions."

THE WITNESS: For the record, I do not think I shall base any opinion on any of the articles to which Mr Delli Bovi referred.

EXAMINATION

BY MR BUNDA:

Q Dr Doll, would you please state your name and age, for the record?

A My name is Richard Doll. I was born in 1912 so I am 75.

Q Doctor, what is your profession?

A I am a medical practitioner and have, for some years now, been a professional research worker. I then became a university professor and I am now working on cancer research in an honourary capacity.

Q Doctor, where are you employed presently?

A In the Radcliffe Infirmary in the Gibson laboratory for the Imperial Cancer Research Fund.

Q Where is physically that Cancer Research fund located?

A The Head Office is in London but they have a number of independent units and at the moment I am an honourary member of their unit in Oxford, acting temporarily as the Director of that unit - - as the recent Director has just resigned and the new Director cannot yet take up his post.

Q That is Oxford, England?

A Oxford, England, yes.

Q You indicated you were a medical practitioner. Is that the same as a medical doctor?

A Yes.

Q Where did you get your medical degree?

A In the University of London, St. Thomas's Hospital.

Q In what year?

A I got the degree in 1937.

Q Have you received a Doctor of Science degree?

A Yes.

Q When was that?

A The first one I got from the University of London, I cannot remember precisely, late 1950s, early 1960s, I am not sure.

Q Let me hand you Defendants Exhibit 1. (Document handed to the witness) Could you identify that for us, please?

A D.Sc., 1958.

URL 11547

Q Yes, the document itself, is that your curriculum vitae?
A Yes.
Q It also has attached to it a list of your publications, is that correct?
A Yes.
Q Have you received subsequent degrees since that time?
A I have received several honourary degrees, yes.
MR DELLI BOVI: For the purposes of the record, and I believe there is a local court rule that pertains to this, we will stipulate to the qualifications of Dr Doll. It is my understanding that you have in fact offered his curriculum vitae into evidence and we will stipulate as to his qualifications also to render expert opinions in the areas in which you choose to enquire.
BY MR BUNDA:
Q There are certain items listed in the curriculum vitae not familiar to an American jury so I would like to go through your qualifications, if I could?
A Yes, sir.
Q What were the honourary degrees?
A I was given an honourary D.Sc. in the Universities of Newcastle, Belfast, Reading, England. Newfoundland in Canada, the degree in Tasmania of Doctor of Medicine and honourary degrees of science in two universities in the United States, the New York State University and Harvard.

Q Those last two are not listed on your curriculum vitae they are new awards?

A No, I was awarded those this year.

Q What professional awards have you received?

A It is difficult to remember.

Q You can refer to your curriculum vitae.

A May I?

Q Yes.

A Are you referring to prizes and that sort of award for cancer research and that sort of thing?

Q No, sir. If I could see your curriculum vitae for a second - (document handed to counsel) - you have listed on ther professional awards immediately beneath Honorary Degrees and what those are. (Document handed to the witness)

A These are either examinations I have taken to qualify Fellow of the Royal College of Practitioners and Fellowship of the Faculty of Community Medicine; Fellowship of the Faculty of Occupational Medicine of the Royal College of Physicians. I also have the Fellowship of our Royal Society in England which is, I suppose, the nearest equivalent of the Acadamy of Sciences in the States.

Q Below that on your listing of Honours, you have Kt

listed. What is that?

A Oh, that is an English peculiarity. It stands for Knight. It is an old custom to award this title to some people in this country, twice a year on the Queen's Birthday and also on the 1st of the year.

Q And you have been awarded that honour, sir?

A Yes.

Q I have heard you referred to as Sir Richard Doll. Is that as a result of the Knighthood, sir?

A Yes.

Q How do your colleagues refer to you, as Dr Doll or Sir Richard?

A If they do not know me very well, as Sir Richard. If they know me well, just as Richard.

Q Sir, what is the purpose of the knighthood. Do you know why you were knighted?

A No, they do not tell you, it just says "For public services", and I presume this was for the results of our research.

Q Which research?

A Primarily, I imagine, our research into the causes of lung cancer, particularly the effects of smoking, but also into the effects of ionizing radiation and their relation to production of cancer and other studies of national concern like the effects of oral contraceptives and the effect of asbestos. These were all early studies which I imagine influenced whoever it was that

made the recommendation that I should be given this honour.

Q Now, sir, you also have listed an award, the OBE. What do those initials stand for?

A Order of the British Empire.

Q What is that?

A That is a decoration which is given by the Queen on the Prime Minister's recommendation. I do know what this was for. It was for our early work on demonstrating the relationship between ionizing radiations and production of leukemia and the first estimate of the amount of leukemia that might be produced by a given dose of radiation.

Q Did you serve in the World War II in Europe and the Middle East?

A Yes.

Q Sir, if you would for the jury, could you outline some of the medical posts which you have held leading up to your present position?

A Yes. I started as an internal physician and, of course, the war came shortly after I qualified. I was first of all a medical officer to a battalion. Then I became a medical specialist in a hospital but I immediately after the war ended, I started research and I have been doing research ever since, employed by the Medical Research Council until I was appointed to be Regius Professor of Medicine in Oxford in 1969 when I continued with the research but also had some acamedic and

administrative responsibilities. For the first twenty years or so after the war I also continued with some clinical medicine, with the care of patients suffering from gastrointestinal diseases because I was doing, at that time, clinical research into the methods of benefits of different sorts of treatment for gastric and duodenal ulcers, but I have not done any clinical work since 1969.

Q Sir Richard, you have also listed on your curriculum vitae that you are a warden of Green College. What is that?

A Well, that title, warden, means the Head of the College and we have some 35 colleges in Oxford. When I retired from the professorship I was made Head of this new college, Green College, which has a special interest in clinical medicine.

Q Could I see your curriculum vitae, please? (Document handed to counsel and returned to the witness) Can you confirm for the jury, sir, that you have been honoured with the following awards: The William Julius Mickle Fellow Award from the University of London in 1955?

A Yes.

Q The David Anderson Berry Prize from the Royal Society of Edinburgh in 1958?

A Yes.

Q The Bisset Hawkins Medal from the Royal College of Physicians in 1952?

A Yes.

Q The United Nations Award for Cancer Research in 1962?

A Yes.

MR DELLI BOVI: Excuse me for interrupting. This time I would like to renew our objection to at this point reading from Dr Doll's curriculum vitae. That document presumably will be in evidence. At this point it speaks for itself and again I believe there is a local rule that governs qualifying the witness.

MR BUNDA: Again I believe that the Awards need explanation.

MR DELLI BOVI: May we show a continuing objection?

MR BUNDA: Yes.

BY MR BUNDA:

Q The Awards I mentioned, are they for specific work or is that a general award for the work you have done until that time?

A They usually referred to specific items of work, principally the effects of smoking, the effects of ionizing radiation and the effects of asbestos.

Q The Gairdner Award, Toronto, 1970.

A Yes.

Q The Buchanan Medal of the Royal Society in 1972. Did you receive that Award?

A Yes.

Q What was that for?

A For epidemiological work.

Q In 1973, did you receive the Nuffield Medal? —

A Which, I am sorry?

Q Nuffield Medal?

A There must be a misprint. Oh, Nuffield. I cannot remember what that was for.

Q You have had so many. The Presidential Award, New York Academy of Sciences in 1974. Do you recall that you received that?

A Yes, for general epidemiological research.

Q This is a French word now, Prix Griffuel, in Paris in 1975.

A For cancer research.

Q John Snow Award, Epidemiological Section, American Public Health Association in 1976. Did you receive that?

A Yes.

Q What was that for?

A Epidemiological research in general.

Q And the Gold Medal, Royal Institute of Public Health in 1977, did you receive that?

A Yes.

Q What was that for?

A I cannot remember.

Q The Charles S. Mott Prize for Cancer Research, in New York in 1979. Did you receive that?

A Yes.
Q That was for cancer research?
A Yes, that specifically mentioned the work on smoking, ionizing radiation and asbestos.
Q And you received the Gold Medal of the British Medical Association in 1983?
A Yes.
Q Do you recall what that was for?
A General medical research and helping other people in their research, I think.
Q The Wilhelm Conrad Rontegen Prize. You received that in Rome in 1984?
A Yes.
Q What was that for?
A I do not know what was specified for that.
Q There was another that appears to be a German or Austrian prize awarded in Hannover in 1985. The Johann-Georg-Zimmermann Preise?
A Yes, for cancer research.
Q And the Founders' Award from the Chemical Industry Institute of Toxicology in 1986, do you recall that?
A I expect that was for the book I wrote with Mr Peto. on the causes of cancer.
Q The Royal Medal from the Royal Society in 1986. Do you recall that?

A Yes, that was for epidemiological research in general.

Q Which Royal Society?

A The British Royal Society which I think is the equivalent of the American Academy of Sciences insofar as there is any equivament.

Q I would ask you also to review the committees on which you have served or which you are presently serving and indicate whether those listings are accurate. (Pause)

A Yes, they are accurate.

Q Sir Richard, attached to your curriculum vitae is a list of publications. Is that right?

A Yes.

Q Is that a list of the articles which you had published in your career?

A Yes.

Q Are there additions to that list?

A None of any importance, no.

Q There is at least one article not listed on there, a recent publication of yours regarding the effects of exposure to vinyl chloride?

A Yes, that only appeared in April this year and I forgot I had not brought the list up to date.

Q Well, I remembered for you. Could you identify Exhibit 2 for me please? (Document handed to the witness)

A Yes, that is the article.

Q Doctor, of your 345 articles approximately, what percentage of these deal with cancer?

A Oh, at a guess I would say about three-quarters.

Q What are some of the carcinogens you have studied in your career?

A Apart from tobacco smoke, ionizing radiation and asbestos, nickel compounds, chrome compounds, mustard gas, vinyl chloride - - oh dear. Combustion of fossil fuels, urban smoke and the fuels from combustion of coal gas retort houses. I cannot remember if there are any more.

Q This body of literature you have produced, do these articles deal with the causes of cancer?

A Yes, mostly.

Q And has the Office of Technology Assessment of the United States Congress ever asked you to publish any study?

A Yes, my colleague Richard Peto and I were asked to write a report on the causes of cancer in the United States and of the proportion that might be avoidable by different means. We were asked to do that several years ago and that was the reason we wrote our book on the causes of cancer.

Q Do you recall from that study, sir, what percentage of cancers approximately can be attributed to occupational sources?

A Yes, we made an estimate that approximately 4 per cent might be. It is very difficult to give a precise figure but that

seems a reasonable estimate of the proportion of fatal cancers.

Q Doctor, I would now like to discuss with you the field of epidemiology. Sir Richard, are you an epidemiologist?

A Yes.

Q How would you describe your role in the development of the modern field of epidemiology as it relates to known infections, diseases?

A I was very fortunate when I came out of the Army after the war. I worked for the Medical Research Council with Doctor Avery Jones on the causes of gastric and duodenal ulcers and the occupational causes in particular and in the course of doing that, I met Professor Bradford Hill at the London School of Hygiene and he asked me to work for him and from 1948 until he retired in 1961, I worked with him and he really was the man, the father of modern epidemiology. I think I can say in the world. Up until then epidemiology had been principally a science studying the causes of infectious diseases and as infectious diseases became controlled , it became of less general interest, but since that period, the period of the war, the techniques of epidemiology have been applied to known infectious diseases such as peptic ulcers, coronary heart disease, as well as cancer and Professor Bradford Hill was really the person who developed the techniques for deciding whether or not a particular factor was a cause of a known infectious disease by epidemiological means. I was fortunate enough to work with him at that time and so I

helped him develop some of these techniques in the very early days of the subject.

Q Doctor, can you explain for our jury what epidemiology is?

A Yes. Epidemiology is a study on variation in the instance of disease in different groups of human beings. By studying the way the incidence varies in different environments and with people who behave in different ways, we can discover what are the causes of the diseases from which they suffer.

Q Doctor, are you familiar with the field of medicine called occupational medicine?

A Yes.

Q How does the work that an epidemiologist such as yourself does, differ from what an occupational physician does?

A An occupational physician will have clinical care of people working in the industry, but the greater part of his research will be epidemiological research. The majority of occupational health researchers nowadays use epidemiological techniques so it is very much a part of epidemiology.

Q How long have you been doing work in the field of epidemiology?

A Since 1946.

Q And in the area of epidemiology of cancer causation?

A Since 1948.

Q Have you taught epidemiology?

A Yes.

Q When and where?

A Mostly post graduate teaching which I have done ever since 1949 or 1950. Once I knew something about the subject. A little bit of under graduate teaching in Oxford and elsewhere, but mostly post graduate teaching.

Q Where did this occur?

A All over the world really. At the London School of Hygiene in England, in Oxford University, but in universities all over England and in many parts of the world as well.

Q Have you consulted with researchers in epidemiology from different countries?

A Yes.

Q I would like you to explain to the jury a few terms which they may have already encountered in this trial or may encounter later. What is a case report?

A A case report is an account of the development of the disease in an individual. It is a clinical description of a disease in an individual.

Q Is it necessarily concerned with determining the cause of the disease in the individual?

A Well, it can help to suggest causes if a number of case reports all point to the same type of behaviour in the individual or the same type of exposure and, in very rare cases, even one case reported in the light of knowledge generally, can

lead to the discovery of a cause, but this is quite exceptional if the type of disease produced is a disease which is extremely rare normally. I will give you an example in which two cases, two case reports led to a discovery of a cause when a GP in South Wales had two patients with cancer of the ethmoid sinus of the nose present in his practice, both of whom were working in the same plant and he knew from his teaching as a student that it was unlikely he would see one such case in the whole of his practising life and he was able to draw the conclusion that almost certainly their cancer was due to their work.

Q Generally, does medical science use case reports to describe cause and effect in an occupational sense?

A Oh no. They are of very little value in relation to common diseases.

Q Is a case report the same as an epidemiologic study?

A No, it is quite different.

Q What is an epidemiologic study. How do you go about doing it?

A Well, an epidemiologic study requires two things. It requires the determination of the number of cases of a particular disease or condition and also the determination of the population in whom those diseases occurred because we very seldom have a situation in medicine in which a person is exposed to a cause and automatically gets the disease. 100 per cent exposed get the disease. When that happens it is very easy to discover the

cause. For most of the chronic diseases, exposure to a cause only gives rise to a risk. 1 in 100 people may get the disease. 1 in 1,000, 1 in 10,000 even and epidemiology requires constructing the relationship between the development of the disease and the population of people who were exposed to the cause of that disease.

Q I have heard the term cohort used. What is that?

A Cohort is a technical term which was introduced to describe a group of people who are defined and who are then followed forward over a period of time to see what happens to them. It was introduced in the first place to describe a group of people born in a certain period. You would speak of the cohort born before the First World War or the cohort born in the 1930s. That would define a group of people and you could see how their experience, their medical experience differed from those born before or afterwards, but you commonly now use it to describe all the employees of a particular factory. That would be a cohort. I have been studying a cohort of doctors who gave me their smoking habits in 1951 and I have been following them ever since as a matter of fact, or rather the survivors.

Q You observe them over time to determine what is happening to them?

A Find out if they are still alive at a given date later. If they are not, if you cannot find out if they are alive, you discover if they have died or if they have perhaps left the

country or what has happened to them. You may not, you are not always concerned with whether they are alive or dead, you may want to discover the diseases they have developed in the course of the period. That is a more complicated study than one which just requires you to find out the causes of their death.

Q Are there different types of epidemiologic studies that are done?

A Oh yes, quite a number of different types.

Q Have you heard of proportionate mortality study?

A Yes.

Q What is that?.

A That is one in which you just record the causes of death of a defined group of people, let us say, people working in a particular industry and then you compare the proportions of death from different causes in that group with the proportions that you might expect from some other standard population, usually the population of the whole country. It does not require you to know precisely the number of people that you had originally in which these deaths occurred. You just require a list of all the deaths you can get hold of. Let us say the deaths of all the people actually working in a plant over a given number of years in which you do not have to find out what has happened to all the people who have left there, as in a cohort study, you will find out what has happened to everybody. In a proportionate mortality study you are merely concerned with the deaths that

you know about and you have not got any details of the whole group in whom these deaths occurred.

Q What is it used for. Why is it done?

A Well, it is commonly called a quick and dirty study. You can get this information quite easily very often and can get it quickly and by looking at the distribution of deaths, the different causes of deaths in this list of deaths that you have, you can get an idea as to whether there is any excess or gross excess of a particular disease and this will then provide you with a hypothesis which you will then want to test by doing a full scale cohort study or by doing another type of epidemiologic study known as a case control study.

Q Are proportionate mortality studies used for cause and effect of particular occupational disease?

A Not in general, no. In an extreme case you might say the evidence obtained from a proportionate mortality study was sufficient to give you pretty strong indications about a cause, but normally speaking they are regarded as hypothesis-forming, the basis for a full scale scientific study.

Q Are there weaknesses associated with the proportionate mortality study?

A It is a question of the data. The data are fine, but you may get an increased number of deaths from some causes, or it appears to be an increased number of deaths because you have a deficiency of deaths from other causes. You have a group of

people who have very few accidents, let us say, or who have been selected in such a way that they have very little chronic respiratory disease. Automatically, the deaths that occur in this group will be disproportionately due to other causes, so you cannot say there is an excess of one group of causes in these workers because the alternative explanation may be there is a deficiency of other causes.

Q I believe you have already described, but are there other types of epidemiologic studies that are more accurate or are more valuable to you?

A From the point of view of assessing cause and effect, yes. There is another whole group of studies which we call case control studies in which you start from the diagnosis of a particular condition, let us say cancer of the lung. You get a list, if you can, of all the patients admitted to a number of hospitals with cancer of the lung and then you interview them to find out what their past lives have been like, what chemicals they have been exposed to in the past, if that is what you are interested in and then you take a group of people who have not got cancer of the lung and find out what exposure they have in their past lives, how they behave and compare the two and see if there is any peculiar characteristic of the people who develop the disease you are interested in. That can give very important information about potential disease, but, of course, to say that something is the cause of a disease, that is only

done on the basis of the totality of the evidence of all sorts and you have to take into account all the evidence that you can obtain from many different sources, including, for example, the extent to which a new agent has been introduced into society, the variation in the prevalence of it from one country to another and how this correlates with the prevalence of the disease. All sorts of evidence like that has to be taken into account before you can conclude that something is the cause of a particular disease.

Q Is epidemiology usually used to prescribe a particular cause of a disease in a particular person?

A No, very seldom. It is used to discover the cause of a risk to which a group of people - - of which a group of people suffer. It can on occasions, epidemiological evidence will be so strong that you can conclude that a particular individual has developed a disease because of exposure to a particular cause, but that is unusual.

Q Sir Richard, I have heard of a term used called the power of an epidemiologic study. What is that?

A Well, that is a complex concept. If you start from the assumption that a particular mode of behaviour or exposure to a particular chemical is going to cause a certain risk, let us say a risk of someone developing a particular cancer, of 1 in 100 in the course of five years, then the power of the study, what it means by the power of the study is the extent to which

you will be able to be precise about the actual risk that people in that group suffered. Your postulate was that 1 in 100 might develop it in five years. You may say, well the power of this study is only such that we will be able to exclude 5 per cent of people developing it in five years because there are not - - or the power of the study is such we will only be able to say that not more than 5 per cent of the people will develop the disease in five years. On the other hand, if you have a very powerful study you might say, well we can boil down our conclusions to a very fine limit. We can say that the risk in this group must have been something between ½ per cent and 1½ per cent to developing the disease in five years. Then you would say that is a pretty powerful study.

Q So it refers to the accuracy of the conclusions and the ability to be accurate in those conclusions?

A It refers to the precision of the conclusion you can draw, not to the qualitative conclusion, but to the quantitive conclusion.

Q What does the term standardized mortality ratio mean?

A This is a term we used to show we have taken account of the peculiar age distribution of the population we are studying. Many, many diseases vary in instance with age of the individual, particularly diseases like coronary heart disease or cancer, they tend to become much commoner as people get older. Therefore, if you are comparing two population groups, you must compare

people of the same ages. Obviously, also of the same sexes and a standardized mortality ratio is a figure which you obtain from your study, taking into account the peculiar age distribution of the population you are studying.

Q When you are studying two populations and trying to determine the causes of cancer, what is the difference between those two populations?

A I am afraid I do not quite follow.

Q Say you are studying something like vinyl chloride and you are trying to discover what effect it has and you have two populations, one population would be exposed to vinyl chloride and one would not?

A That is right.

Q Would you expect to see cancer in the group that was not?

A It depends on the type of cancer. Most cancers occur for reasons which we do not know, throughout the whole world. There is a background incidence of all types of cancer. Some cancers are really quite common as a result of background factors that are affecting the whole population. Others, on the other hand, are extremely rare. So, when you are looking at your group of workers, for example, exposed to vinyl chloride, the importance of the background incidence will vary with the type of cancer you are studying. If you are studying cancer of the lung which is very common in the population for other reasons, then it will

be quite difficult to tell whether vinyl chloride is causing cancer of the lung in that population. On the other hand, if you are looking at an extremely rare disease like angiosarcoma of the liver, a disease which only affects 1 in 10m people a year, then if you find two or three cases in a group of 200 men, you do not need any other evidence to indicate you have found something pretty extraordinary. The conclusions you draw depends very much on the type of disease you are studying and its general incidence.

Q What does the term statistical significance mean?

A This is a term we use purely arbitrarily to indicate the probability that your observation may have occurred by chance and not be in any way due to the peculiarities of the group you have been studying. Quite arbitrarily we take a probability of 1 in 20 as being something that we would not normally accept as something that is likely to turn up, so if we find an excess of a particular disease which would only have occurred by chance once in thirty times in that group, then you call that statistically significant and you think you have probably got some peculiarity about the group, but it is only a guide. Statistical significance does not tell you definitely whether a disease is due to a particular environment or particular type of behaviour. It just helps you draw a conclusion as to whether it is likely to be due to the peculiarities of the group or whether it is something that could be purely chance event because, after all,

not only 1 in 30, but 1 in 100 chances turn up every now and again or otherwise no one would ever buy a lottery ticket?

Q Sir Richard, are you familiar with animal studies which are used in cancer research?

A To some extent, yes. I am not a specialist in that field but I have to take account of them in determining epidemiological observations.

Q What are the advantages and disadvantages of an epidemiologic study versus an animal study?

A Well, an epidemiological study, the great value of that refers to the animal whose disease that you are trying to prevent and you know that your findings are relevant to human beings. The difficulty with it is that you usually cannot do an experiment. You cannot do an experiment to produce disease in man so your interpretation of epidemiological evidence is often open to question. You can only take into account all the evidence and eventaully you may be able to say it is sufficiently strong to prove that a particular agent is a cause of a disease. With animals you can actually do an experiment. You can cause disease in animals and so you can be confident about what the factor is that has produced the increased incidence of disease in a particular group of animals. What you do not know of course, is whether humans will react in the same way as animals. You have to extrapolate from one species to another and that is always risky. By and large we can get good indications of what is

likely to happen to man from studying different animal species, but there is always the doubt in one's mind, perhaps a man may not behave like a rat in this particular case. Perhaps he may behave more like a guinea pig, in which case the reaction would be quite different.

Q Do animals, different animals react differently from time to time?

A Yes, they do.

Q I would like to change the subject. Are you familiar with some of your colleagues in the field of cancer research and epidemiology in the United States?

A Yes.

Q Have you heard of a gentleman called Richard Monson?

A Yes.

Q Have you heard of Leonard Chiazze?

A Yes.

Q Also have you heard of an Italian researcher by the name of Dr Maltoni?

A Yes.

Q Have you heard of an occupational physician from Cincinnati by the name of R. Michael Kelly?

A No.

Q Now I would like again to change gear. If we can go and discuss a little bit the specific matter involved in this case, vinyl chloride. Have you done any research involving

vinyl chloride?

A Yes.

Q Would you describe that for me?

A Yes. It was not a very important piece of research, we just used the information that had been collected by the chemical industries in this country on the number of cases of angiosarcoma of the liver, a particular cancer which is characteristically produced by vinyl chloride and we use the information collected from factories, industries throughout the world where vinyl chloride had been used to try to get an estimate of the amount of liver cancer because this disease, angiosarcoma of the liver is commonly described as a liver cancer. We used this information to try to predict how many more cases might be expected to occur in industry. That was all this particular piece of research was aimed at doing.

Q Since that time have you recently done a review of the literature or epidemiologic work of others on vinyl chloride?

A Yes, I have done a review of the diseases produced by vinyl chloride.

Q And that has resulted in the paper that has been marked as Exhibit 2?

A This was published in the Scandinavian journal, "Work, Environment and Health" in April this year.

Q Can you explain briefly what vinyl chloride is?

A Vinyl Chloride is a gas, a molecule, very important

A I gathered a great deal of information about the health of the workers exposed to large doses of vinyl chloride.

Q Did you do a comprehensive survey of the medical literature?

A Yes.

Q How did you go about doing that?

A I was provided with a list of publications by the chemical industry, to which, of course, I then sought to add by asking medical libraries to find out if there were any additional articles that were relevant. I had to get some of the foreign ones translated and I read them all, decided which of them were giving important information and then tried to summarise that information and then when I had summarised all the information, tried to make up my mind what it all meant.

Q Is this an area where the epidemiologic research has been fairly extensive. Are there a lot of studies?

A There are quite a lot. There have been more studies on some other compounds but there have been quite a lot of studies on vinyl chloride.

Q Did you do this research before I ever contacted you regarding working and testifying in this case?

A Oh yes, I was asked to do this, I cannot remember how many years ago, about five years ago. I could not do it initially, I could not fit it into my timetable, but I effectively did it in 1986 and finished the report in 1987.

Q And the results of that research have been recently published?

A Yes, I made it a condition of doing the report that I should be free to publish the results.

Q Was there any review of the results or change of the results before they were published, not by editors but by the CMA?

A Not of necessity. I did, in fact, send it to a colleague of mine who worked in the industry to read through and he suggested there were two points he thought I had not made clear and I tried to improve in that respect and I then sent it to the industry but there was no review from them after that.

Q In your opinion, was there any censorship or portions of the article that they found unfavourable, that they asked you not to publish?

A No, there was no such thing and indeed I made it a condition of doing the review that I would publish exactly what I thought. There was no possibility of any censorship.

Q Where was that published?

A In the Scandinavian journal "Work, Environment and Health".

Q Is that a juried publication?

A Yes.

Q What does that mean?

A That is not a phrase we use in England. We say

refereed. But yes certainly, that is a refereed journal.

Q What does that term mean?

A That means the editor does not publish articles unless he has sought opinions of other people in the field that it is a reliable paper that deserves publication.

Q And this was done with your article?

A Yes.

Q What were the general conclusions you reached in this study?

A I concluded that intense concentrations of vinyl chloride such the people in the industry were exposed to before the mid-60s in the United States and in England would produce a normally very rare disease, angiosarcoma of the liver, a type of cancer of the liver, that vinyl chloride might possibly produce a small hazard of lung cancer. I could not be quite sure about that, the evidence was not conclusive, but suggestive. But, I thought that the evidence did not really suggest that vinyl chloride caused any other type of cancer in humans. Two or three other types of cancer had been suggested as being likely to be caused by individual studies, but if you looked at the totality of the evidence, you really did not find that there was enough to bear this out. I would like to see some more work done to check that there is not an excess of cancer of the brain and cancers of the lymphatic system. On the whole I do not think there is, but I think it would be important to confirm this

negative conclusion by further observations.

Q Doctor, from the research that you have done, do you have a general idea about the level of exposure to vinyl chloride which existed and exists today in the vinyl chloride and polyvinyl chloride manufacturing facilities?

A Yes. When vinyl chloride was first used in industry it was not thought to be likely to be a hazardous agent and people were exposed to very high concentrations of it of the order of thousands of parts per million in the air, but it became clear it did have a number of toxic effects, acute effects on individuals. It was poisonous at that level and the levels were reduced in the early 1960s, mid 1960s by ten-fold to something of the order of several hundred parts per million, but it was not until these cancers turned up that people realised that the amounts that workers had been exposed to were still hazardous and the levels were then quickly reduced to something of the order of ten or five parts per million and then Government agencies came in and said: "That is not low enough." I know the industry really at first thought they could not get it much lower but they have it down now so that no one is exposed to more than one part per million. Very much lower than they used to be exposed to when the risk of cancer was produced.

Q Do you have a general idea about the amount of vinyl chloride exposure which existed in those factories where polyvinyl chloride resin was used to make plastic products?

A I have not much knowledge of that. I decided in my review not to study those plants, the workers in those plants, because my understanding was that they really were not exposed to levels of more than ten or twenty parts per million or even less and so it did not seem relevant. I wanted to find out what vinyl chloride could produce and, therefore, I wanted to look at groups of people who had been exposed to hundreds of parts per million and I did not cover the people that used polyvinyl chloride and who might be exposed to small amounts of vinyl chloride in my review.

MR DELLI BOVI: I am going to object to Dr Doll's last answer dealing with levels of vinyl chloride monomer, for lack of proper foundation.

BY MR BUNDA:

Q I provided you, Doctor, with documents relevant to the levels of vinyl chloride exposures that existed in the Ohio plant that Mr Dendinger and Mr Wallace worked in, have I not?

A Yes.

Q What is your general understanding of what those levels were as to what you have said before?

A My understanding is that those levels were low but not as low as we like to see them now.

Q Sir Richard, have you come across any statistics which are important to you with regard to the decrease and level of exposure. I am speaking now of statistics involving those who

have incurred angiosarcoma of the liver?

A Yes. Well, the angiosarcoma of the liver we take as the marker of exposure to substantial amounts of vinyl chloride. My understanding from studying the register of angiosarcoma cases which is maintained by Imperial Chemical Industries in England and they send me copies of this up-dated register every year, my understanding is that there has not yet been a case of angiosarcoma recorded in anybody who was first exposed after 1969. That was someone, a case that developed in Germany. I think I am right in saying that no cases have been recorded in American workers who were first exposed after 1964.

Q What is the significance of that statistic to you?

A Well, it is suggestive, but it is not conclusive. It is suggestive that the reductions in level in concentration that took place in the mid 1960s had reduced the exposure of vinyl chloride workers in the developed countries to levels at which the risk of developing angiosarcoma of the liver is so low that you may not see any more cases. I cannot say you will not see any but you would only see one in a very large number of people. I have to qualify that though to some extent because cancers take some time to be produced after individuals are first exposed and this particular diaease tends to occur only fifteen, twenty years or more after first exposure. We had had one case occur, I think nine years after, is the shortest, but we are just coming up to a time now in which it is becoming really interesting that

no new cases are being recorded that have occurred as a result of exposure limited to the period after the mid 1960s because we are getting twenty, twenty-five years after first exposure, but it will still take another five years, I would say, before we can be confident that the reductions that took place in that period were really adequate to eliminate or, if not eliminate, nearly eliminate the risk of the disease.

Q Doctor, I would now like to address the specific gentlemen involved in this case, Mr Dendinger and Mr Wallace and the facts surrounding them. I provided you certain materials regarding these two gentlemen?

A Yes.

Q You have seen certain medical records regarding their cancers?

A Yes.

Q You understand that Mr Dendinger died of a colon cancer and Mr Wallace died of a mucoepidermoid of the parotid gland?

A Yes.

Q Do you have an opinion to a reasonable degree of medical certainty about what is known by medical science about these two types of cancers?

A I wish I could tell you what the causes of those two types of cancers are. Cancer of the parotid gland is cancer of the group of glands, the salivary glands and we really do not know any causes of these particular types of tumours. They are

a little more common among Canadian Indians than any other population. That may be a clue, but I do not know what Canadian Indians do that would produce these diseases. They also occur in families that have a high incidence of cancer of the breast. These types of cancer sometimes occur in families with a genetic susceptibility to cancer of the breast but I know of no cause of cancer of the salivary glands and there is nothing to suggest that vinyl chloride would cause that disease. Cancer of the colon is a different matter. This is a common disease in developed countries. There is quite a good deal of evidence to suggest that most of the cases are determined by the diet of developed countries, particularly the high content of fat and the relative lack of fibre in the diet, but the evidence is not conclusive. I think it is strongly suggestive that both these two factors contribute to the development of the disease but I do not think any epidemiologist would wish to say he thought it was proved that those factors were important. It is something to do with conditions of life of the developed world throughout Europe and North America and Australasia that leads to the production of these diseases but I cannot put my hand on my heart and say what it is. I am confident that vinyl chloride does not produce this disease.

Q Sir Richard, could you explain to the jury what is known by medical science about the types of cancers which are caused by vinyl chloride?

A Yes. We must divide this into two categories of animals and humans. In animals vinyl chloride produces the angiosarcoma of the liver as it does in humans. It also produces squamous sarcoma of the zimbal gland in rats. It possibly produces a few other cancers of the lungs. There was a belief that it produced cancer of the haematopoeteic system and lymphatic system originally but this I think is differently interpreted.

Q Let us focus on humans.

A In humans it produces a particular type of cancer of the liver and I frequently referred to angiosarcoma of the liver intentionally. Cancer of the liver is rare in North America and England but those cancers that do arise in the liver are usually haepatomas, liver cancer cell tumours, but there is this very rare type of cancer of the liver which arises from another type of cell in the liver called an angiosarcoma and this is characteristically produced by vinyl chloride. I think there is reason to suspect that it may also cause cancer of the lung to a small extent but that is not proven. I do not think it causes any other cancer in humans.

Q Sir Richard, does the fact that as you have indicated, there is research which indicates that vinyl chloride causes cancer in one part of the body, the liver, mean that it can be said that if there is cancer in another part of the body of someone exposed to vinyl chloride, that vinyl chloride is the cause of that cancer?

A No, it certainly does not mean that. From what we know of the causes of cancer and we know now quite a lot, I could give you a list of about fifty agents which cause cancer in humans and with one exception of ionizing radiations which will cause cancer in practically every tissue, these are all site specific. They cause cancer in one or perhaps two or three associated organs but none in more. Tobacco smoke might be regarded as an exception. That causes cancer in about seven or eight organs. I am not sure of the recent count, but that is hardly relevant to your question because tobacco smoke contains 3,000 chemicals and at least 25 different carcinogens. So, the fact that produces cancer in so many organs is irrelevant to your question. A specific chemical so far as human experience goes, produces cancer usually or pretty well always in a very limited number of organs. The only exception I can think of is ionizing radiation which will produce cancer in practically every organ.

Q Doctor Doll, I would ask that you base your answer now and give us an answer to this to a reasonable degree of medical certainty because that is what the American Courts require. My question to you is this: Based upon your training, experience and knowledge in the field of medicine and epidemiology and based on your research into the area of cancer, specifically as it relates to vinyl chloride, do you have an opinion to a reasonable degree of medical certainty as to whether vinyl

chloride was a contributing cause of the parotid gland cancer of Mr Wallace?

A Yes I do have.

Q What is your opinion?

A That it did not cause that cancer.

Q What is the basis of that opinion?

A The basis of that opinion is that of the workers who have been studied, that had been exposed to very large amounts of vinyl chloride, there has been no excess of tumours of that sort and it is not produced in animal experiments either.

Q Mr Wallace was exposed, you indicated, to a lower dose?

A I have only the data that you presented me with of the report of the industrial hygienist and that certainly implied it was a much lower dose.

Q Does that have any relevance to your conclusion?

A Well, it just strengthens the conclusion because one would not expect doses of 1,000 parts per million to produce that type of cancer.

Q What did your review of the literature indicate? Are there any indications that that type of cancer was caused by higher levels?

A No, no indications at all.

Q Based on your training, experience and knowledge in the fields of medicine and epidemiology and your research and review of the medical literature in the area of cancer,

specifically as it relates to vinyl chloride, do you have an opinion to a reasonable degree of medical certainty as to whether vinyl chloride was a contributing cause to the colon cancer in Mr Dendinger?

A Yes, I do have.

Q What is your opinion?

A That it was not such a contributory cause.

Q What is the basis of your opinion?

A Studying these statistics of men exposed to very high doses of vinyl chloride and comparing the risk of colon cancer in those men compared with the risk of developing colon cancer of people in the country at large who were not exposed to vinyl chloride.

Q Are these conclusions of yours borne out or indicated in the article you recently published?

A Yes.

Q Sir Richard, are you familiar with the 1981 study done by an epidemiologist by the name of Leonard Chiazze?

A Yes.

Q This was done of workers developing cancer using poly-vinyl chloride resins?

A Yes.

Q These were in areas like Mr Dendinger and Mr Wallace?

A My understanding is that that is correct.

Q What type of study was that?

A That was a proportionate mortality ratio study.

Q And we have already discussed the purpose of that?

A Yes.

Q Can you remind the jury what that study is used for?

A It is used as hypothesis-forming to see if there is any suggestion there might be a specific hazard among a particular group of people investigated.

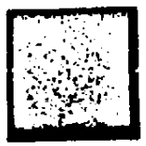
Q Do you recall in that particular study there was a suggestion or a hypothesis that perhaps digestive cancer showed some increase in this group?

A Yes, there was indeed.

Q How do you resolve that study with the results of your study?

A This, as we have said, was a proportionate mortality ratio study and the relatively high proportion of deaths due to cancer of the colon on that study in comparison with deaths of people of the same sex and age in the United States as a whole, was influenced by the fact that the people investigated had a very low proportion of deaths from other diseases, some other diseases, particularly accidents and respiratory disease and this low proportion automatically results in there being a high proportion of some other cause of death, particularly cancers and the proportion of deaths due to cancer as a whole was increased in that study. Now, many people - I am surprised Dr Chiazze did not do this - prefer to use what we call a cancer

proportional mortality ratio study in which you just look at the proportion of different cancers attributable to cancers in different sites. This is a better indication of a possible risk because cancer as a whole is not really influenced by the selection of workers into a particular industry as the risk of developing cancer as a whole has been shown in many studies where there is no special hazard, to be much the same as in the general population. So, if you look at the distribution of different types of cancer within all the cancers you are much more confident you have something odd if you find that one of those cancers, one type of cancer, shows a higher ratio. I cannot do precisely a proper cancer proportional mortality study on the basis of the published data, but I can make an approximate estimate. If you do that, if you examine the different types of cancer that have caused death, then the excess - and there is some excess from colon cancer - ceases to be what we call technically significant. It is not quite significant. Mind you, if it was significant it would not lead to the conclusion that the work had caused cancer of the colon because if you look at some twelve or fifteen types of cancer, the chances are that you will find that one is unexpectedly common. After all, a 1 in 20 chance turns up 1 in 20 times. The statistical test is only a guide to one's thought, that my assessment of the data is that if you look within the different types of cancer there is not really any surprising excess numbers of deaths from cancer of



the colon.

Q Of the other studies that you have reviewed, have you found any that have concluded that there is an increased risk of incurring cancer of the colon from vinyl chloride?

A I have to qualify my answer to that. My principal studies that I thought gave the best indications of hazards irrelated to vinyl chloride which was 49 plants in the United States, England, Canada and Italy, they actually gave rise to a smaller number of deaths from cancer of the colon than would be expected from the general population. I think it was 30 deaths whereas you might have expected 43. This is not a surprising deficiency, it is quite within reasonable chance variation. Then I looked at another 7 studies that I called subsidiary studies which, for a variety of reasons did not give such good evidence. The latent periods were not long enough. Various other reasons. There was a small excess, I think 39 against 35 expected, but even if you added those into what I call the principal studies, you still find a deficiency of deaths from cancer of the colon. I am not suggesting vinyl chloride protects against developing cancer of the colon, this deficiency is just the sort you would expect quite easily by chance in a study of this size, but looking at the evidence as a whole I am quite confident that there is no suggestion at all of any excess of cancer of the colon on people exposed to high doses of vinyl chloride.

Q We talked about the power of studies before. The study which you recently published based upon a review of the other studies that you looked at, the subsidiary studies and the four main studies, how does the power of your study compare to that of Dr Chiazze?

A Well, it is qualitatively entirely different. The studies I reviewed give firm evidence. Dr Chiazze's study does nothing more than throw up a hypothesis for testing. Nobody with any experience of epidemiology could draw a conclusion about the cause of disease from the results of Dr Chiazze's study.

Q Dr Chiazze's study calls for further investigation?

A Yes.

Q Was your study the type of further investigation that was called for?

A My review was of vinyl chloride workers specifically exposed to the gas itself or the manufacture of polyvinyl chloride. I think Dr Chiazze would say that he was calling for a study of people working with polyvinyl chloride because after all, there are other chemicals to which those people are exposed and the fact that we do not see anything in these diseases that he hypothesized might be produced by vinyl chloride, the fact that we do not see them appear in people that were intensively exposed to it, does not mean to say there was not something in that industry that caused a risk of colon cancer. That, I think, needs investigation, but that is a working hypothesis, nothing more.

Q In your opinion, again to a reasonable degree of medical and scientific certainty, is there any scientific basis for claiming either of these two cancers were due to the exposure to vinyl chloride?

A There is no reason for concluding that at all.

MR BUNDA: Thank you very much, that is all the questions I have.

(Whereupon there followed a discussion off the record)

(Whereupon there followed the luncheon adjournment)

CROSS EXAMINATION

BY MR DELLI BOVI:

Q My name is Kirk Delli Bovi, we have been introduced before. I represent the Plaintiffs in this case and I have a few quesitons I would like to ask you this afternoon. Is it your understanding that Mr Dendinger and Mr Wallace were employed not in the vinyl chloride industry or in the polyvinyl chloride producing industry, but in the PVC fabrication industry?

A Yes.

Q Can you tell me what epidemiological or other studies you are aware of that pertain to workers in the industry in which Mr Dendinger and Mr Wallace worked, that is the PVC fabrication industry?

A There is one by Dr Chiazze and a colleague. There is a Swedish study, I am afraid I forget the names of the authors and there has been a recent study, I think unpublished, by a

doctor of the particular industry in which Mr Wallace and Mr Dendinger worked. Those are the only three that I can recall at the moment.

Q In terms of your opinions in this case, have you relied upon any of the three studies that you have just cited, pertaining to workers in the PVC fabrication industry?

A I have not specifically studied the PVC fabrication industry. I have studied the effects of exposure to vinyl chloride and the evidence I have given has been in relation to exposure to vinyl chloride.

Q In the paper that you wrote for the Scandinavian journal "Work, Environment and Health", you indicated, did you not, that in formulating opinions concerning the aetiology of cancer, it is important to look at all of the evidence?

A Yes, whether I said it in the paper I do not know, but I certainly believe it.

Q Now, when you prepared your paper for that Scandinavian journal, did you include at the end of it a list of the references that you consulted in preparation of that work?

A Yes.

Q And there are a list of some fifty references that you consulted that you relied on in whole or in part or to a limited extent in preparing that work?

A Yes. I did not read one of them actually, it was a Russian one. I only quoted it on the basis of somebody else's

analysis of it.

Q Did you rely to any extent on Dr Chiazze's study in authoring your paper entitled "Effects of exposure to vinyl chloride - an assessment of the evidence"?

A No, I did not. I read the paper but I specifically excluded it. As you will see, I stated in that paper that I did not include in my review, reports of polyvinyl chloride fabricators as it was my understanding that the amount of vinyl chloride which people in that industry would have been exposed to was substantially less than people were exposed to in the PVC manufacturing industry and my specific concern was with vinyl chloride, not with the effects of any other chemicals that might be found in the fabricating industry.

Q What was the source of your assumption or your understanding that the levels of worker exposure in the PVC fabricating industry were lower than those in the PVC resin producing industry?

A Two items of information. One, the information that I was given by medical officers in Imperial Chemical Industries with whom I am on professional terms and the other was the absence at that time of reports of angiosarcoma of the liver which I regard as an indicator of vinyl chloride exposure in people in industries other than the vinyl chloride monomer of polyvinyl chloride manufacturing industries.

Q Have you ever seen any data from any plants in the

United States comparing levels of vinyl chloride in the work-place atmospheres in fabrication plants as opposed to resin manufacturing plants?

A I have no direct knowledge of levels in American fabrication plants other than the information provided to me by the investigators at the particular plant in which Messrs Wallace and Dendinger were employed, but as to the rest of the industry I have no personal knowledge of it.

Q When you were presented with the data from the Chrysler facility where Mr Dendinger and Mr Wallace were employed, were you given any understanding as to the time frame encompassed by that data?

A Yes. I am speaking from memory now. I would like to check it, but I think the observations were made around the middle 1970s but if I am wrong, please tell me.

Q Are you aware that the observations all the data that was furnished to you regarding vinyl chloride levels in the work-place atmospheres in that plant were all subsequent to the public announcement of the Goodrich nagiosarcoma deaths?

A I think they must have been, yes. I am assuming they were.

Q Is it your understanding, based upon your knowledge of the industry, that the workplace levels of vinyl chloride would have been higher prior to the public announcement of the Goodrich angiosarcoma deaths?

A The levels in the manufacturing industry were certainly higher before that but whether they could have been higher in the PVC fabrication industry I do not know because I do not know how much vinyl chloride could have been released from manufactured PVC. I would be guessing. It does not necessarily follow that they were higher, but they could have been higher.

Q Do you have any knowledge as to the mechanism by which workers in a PVC fabrication plant would become exposed to vinyl chloride?

A No intimate knowledge, no.

Q Have you been provided with any information by the PVC manufacturers as to the method by which PVC fabrication workers can be exposed to vinyl chloride?

A Not that I would call any serious account, no.

Q I am going to hand you what I have marked as Plaintiffs Exhibit Doll 2. Could you identify that, sir, as the work of Dr Chiazze that appeared in the scientific journal in the United States in 1981. (Document handed to the witness)

A Yes.

Q In terms of the size of that study, looking at the number of deaths Dr Chiazze analysed, how does the size of Dr Chiazze's study compare to the size of all the studies that you considered in preparing your Scandinavian journal?

A Insofar as it relates to exposure to vinyl chloride, I cannot say, because Dr Chiazze's study does not say what

proportion of the 17,000 odd workers that were probably involved were exposed to vinyl chloride, though he does say somewhere that the proportion - at least if my memory is correct - that it was only a relatively small proportion so I cannot answer that question except to say to the best of my belief it is a very much smaller total number of people exposed to vinyl chloride than in the studies which I reviewed.

Q My question, Dr Doll, dealt with the number of worker deaths that Dr Chiazze analysed compared to the total number of deaths analysed in the review that you did.

A The total number is slightly less than the total number in the review that I did.

Q Dr Chiazze's study involved the deaths of 3,847 workers?

A So I believe, yes. I think my studies covered some 5,000 workers, if I remember correctly, but I would need to check. Some 5,000 deaths, I mean.

Q Why don't we take a look at that if we could. Do you have a copy of your report handy? Could you indicate to me, Dr Doll, the total number of deaths that were analysed by you in your review?

A Yes, I am just trying to check. It must have been less. (Pause) No, I am sorry, my memory was at fault. I was thinking of another review I have just done on formaldehyde. The total number is nearer 2,000, not 5,000.

Q Could we break that down please for the individual

studies you analysed. How many deaths were involved in the United States?

A 1,136.

Q And in the United Kingdom study?

A 780.

Q Canadian?

A 59.

Q And the Italian study?

A 66.

Q So in terms of the total number of deaths encompassed by the studies, the Chiazze study looked at substantially more deaths than all of the studies covered by your review?

A Yes, that is true.

Q As a result---

A Just a minute, let me see what the subsidiary studies were. Where are we now? We will have to add these up. (Pause) Yes, I think the total of the subsidiary studies still probably come to somewhat less than the total reported by Dr Chiazze.

Q Now in terms of the conclusions that Dr Chiazze drew from his proportional mortality ratio study, he determined that there were statistically significant increases in cancers of the large intestine in both the male and female deaths, did he not?

A No, he did not. His sort of study can tell you nothing about the incidence and consequently the increase in the amount of cancer. What he showed was that if the distribution of deaths

were to be expected to be the same as the distribution of deaths in the American population of people of the same sex and the same age, then the sort of distribution that he observed was unlikely to have been obtained by chance, but that says nothing about an increase or decrease in them because that is a purely proportional distribution and a high proportion of one cause of death may be due to a low proportion of another type of death, so you can draw no conclusions about the actual incidence of the disease, of mortality from the disease as Dr Chiazze is careful to point out in his study.

Q Let me read to you, doctor, one of the sentences from Dr Chiazze's conclusion and ask you whether you agree or disagree with his statement: "PMRs are significantly different from unity for all cancers and for cancers of the digestive system among both white males and white females".

A Yes, that is what I have just been saying. It is in a different form, but essentially what I say.

Q So, in terms of comparing PVC fabrication employees to the general population, Dr Chiazze found statistically significant increases in the proportion of large intestine cancers in both the male and female PVC fabrication workers?

A No, I do not think you could say significant increases. He would say significant differences in the distribution and this may have been due to significant decreases in the other causes. So, a proportional mortality study of the sort he did

is not capable, as Dr Chiazze points out in his article, of telling you whether there is an increase or not. He is showing that the distribution is different and now we have to assess and try to determine why the proportion is different.

Q One of the limitations you indicated in your direct examination on Dr Chiazze's study, was that the increases in the large intestine cancers may have been attributable to corresponding decreases in other causes of death, for example, accidental death, suicides, heart disease, things of that nature?

A Yes.

Q And you indicated in your direct examination that a cancer proportionate mortality ratio study would have been a better indication of the possible risk and that if that calculation had been done, you would have been much more confident that something odd had occurred?

A Yes, it would have been a better basis for producing a hypothesis.

Q Dr Doll, since reviewing Dr Chiazze's work, have you made any effort to take Dr Chiazze's data and determine the cancer proportionate mortality ratios for the total number of cancers and for the large intestine cancers?

A Yes.

Q Have you brought any of those calculations with you?

A No, I have not brought them with me on paper, I have brought them in my head.

Q Your opinion was that if Dr Chiazze's PMR calculations for total cancers and large intestine cancers were converted to CPMRs, that the increased proportions of total cancer deaths and large intestine cancer deaths would not be statistically significant?

A I must qualify that statement as I did earlier by saying I could only make an approximate calculation on the basis of the data available to me and the approximate calculation I made suggested they were not statistically significant but I would not exclude the possibility that if a proper cancer proportionate mortality ratio was done, they would just be on the other side of the 1 in 20 significance level which we usually use, purely arbitrarily, to decide what is significant or not. I think only Dr Chiazze could make such calculations, as you need to have the basic data by broken down small age groups and different calendar years.

Q So, it is your belief then that if Dr Chiazze's PMR figures were converted to CPMR figures, that they would still show an elevation in the incidence of large intestine cancers?

A I am sure they would show an elevation in comparison with the proportion of deaths normally attributed to cancer of the large bowel in the American population, but I am not at all sure that that elevation would be such that one would regard it as being a particularly unusual event.

Q Do you attach any significance to the fact that in his

PMR study, Dr Chiazze found increases in the proportion of large intestine cancers of statistical significance for both males and females?

A Not particularly, no. I suppose insofar as it implies anything, if it were to be regarded as implying an occupational hazard, it would weigh against it as women would be unlikely to be employed on the same type of occupation as men.

Q Was there any indication in Dr Chiazze's study that the women employees that he surveyed were performing different jobs than the male employees?

A I cannot remember.

Q Would you like to take a look at his study and see if it draws any such distinction?

A I am afraid it might take me five minutes to read it.

Q Certainly. Would you like to go off the record?

A Yes please.

(Off the record)

BY THE WITNESS:

A Yes, I have read the paper and there is a strong implication that there is different exposures for men and women but no specific statement to that effect. I have drawn that conclusion from ordinary experience of factories and the fact that 72% of the women had no exposure to vinyl chloride and 12.6% had improbable exposure and that a proportion of the workers were office and clerical workers. So, it seems to me the ordinary

URL 11600

conclusion to be drawn from that was that the women did different jobs from the men but Dr Chiazze does not state that in his paper.

BY MR DELLI BOVI:

Q That is am implication you have drawn from his work?

A Yes an implication I have drawn from his paper.

Q In his study, Dr Chiazze found statistically different increases in the proportion of total cancers, large intestine cancers and others and unspecified cancers in both males and females, did he not?

A Would you mind repeating that, I missed the first part of the question?

Q In his study, Dr Chiazze reported statistically significant increases in the proportion of all cancers, large intestine cancers and other and unspecified cancers in both males and females?

A No, I do not think he reported significant increases in the proportion of cancers due to large intestines. He reported significant differences in the proportion of total deaths due to large bowel cancers. We pointed out earlier that a cancer proportionate mortality study probably did not show a significant increase in the proportion of cancer deaths due to large bowel cancer.

Q I would like you to take a look, if you would, at either Table 3 of Table 4 from Dr Chiazze's study, which ever one you prefer to work with.

A This is the second publication, is it not?

Q Yes, it is. The first one reports it in terms of United States mortality. You do not mind if I look over your shoulder, I did not bring another copy. Table 3 reports using U.S. mortality up to 1968. Table 4 shows U.S. mortality figures for individual years between 1964 and 1973. Would you feel more comfortable using the individual years?

A It is not that I would feel more comfortable, the data for the individual years are the data that are remotely relevant. The data for using the single year for comparison was something to provide a further indication of what the results might be but neither Dr Chiazze nor myself would attach any significance to the data in Table 3 when we have the data in Table 4 available.

Q Let us use Table 4 then. In terms of all cancer among male PVC fabrication employees, what was the PMR that Dr Chiazze calculated?

A For what?

Q All cancers among male PVC fabrication employees.

A 1.1567.

Q Did Dr Chiazze determine that that figure was statistically significant?

A Yes, he showed it was significantly different from the proportion to be expected from the distribution of the deaths in the U.S. population at the same period.

Q Can you determine by what percentage the figure

represented an increase over that expected in the general population?

A I do not think that necessarily indicated any increase in cancer mortality in the general population at all. It is reflecting the fact that there were relatively few deaths from accidents in this population and very few from diseases of the respiratory system and cirrhosis of the liver.

Q And the decrease in those deaths is largely attributable to what has been called a healthy worker effect?

A Healthy worker effect is a very complex phenomenon which has two or three components in it. In this case it reflects what is a common - - it partly reflects what is a common experience of any employed workers compared with the national expectation, that is a reduction in the mortality of a number of important diseases but, of course, in some industries the accident rate may be a good deal higher than in the population at large. Here we have an industry with a relatively low accident rate. I would not call that a healthy worker effect. That is an effect of a well run industry or an industry with very little hazards. The healthy worker effect is composed of several components, one of which is the effect of observing a mortality in a group of people who are healthy enough to start employment when you begin and the first few years of any follow up study invariably shows a low mortality for the first few years because you have, by definition, included only people who were healthy

to be in employment at the beginning, but then this wears off with the passage of time. Then there is a second aspect of the healthy worker effect which is that people with certain chronic diseases that are liable to give rise to high death rate, do not get employed in industry, so that they are a selected population and this often gives rise to low mortality, for example, from chronic respiratory disease or from cirrhosis of the liver.

Q Before you finish your answer, the Court Reporter has indicated we are about to run out of video tape so why don't we change the tape.

(Whereupon there followed a discussion off the record)

(Whereupon there followed a short adjournment)

BY MR DELLI BOVI:

Q Dr Doll, have you concluded your answer?

A Yes.

Q With that answer in mind, can you tell me whether or not the lower reported death rates/were that proportionately lower death rates in Dr Chiazze's studies for causes other than cancer, are attributable to a significant extent to the healthy worker effect?

A I cannot say for certain, I would expect they were.

Q Going back to the male fabrication employees and all cancers and the PMR of 1.1567 that Dr Chiazze reported, what does that indicate in terms of the proportion of male employees who died of cancer versus the proportion of people in the general

URL 11604

population that died of cancer as opposed to some other cause of death?

A I am not sure. I should have to do a calculation. Of course, another factor which has to be taken into account is this comparison is a comparison with the whole of the United States and not with a comparison with the people of Ohio which would, of course, again alter the proportions, but I am afraid I cannot answer your question without some calculations.

Q Let me ask it another way. If male PVC fabrication workers were dying of cancer as a proportion of the total deaths, at the same rate as the general population was, would the PMR be 1.00?

A I think I will have to ask you to repeat that question.

Q Sure.

A Would you take it at dictation speed so I can get it down?

Q Certainly.

A Or perhaps the simplest thing would be to ask the Court Reporter to read it to me.

Q Whatever your preference is. (To the Reporter) Would you read the question back, please?

(The Reporter read back the relevant passage)

BY THE WITNESS:

A Yes, well I have got that question now and I am afraid it is a nonsense question because it is confusing proportions

and rates so there is no possible way in which I can answer it.
BY MR DELLI BOVI:
Q How would you like the question phrased so you can answer it in order to tell me why Dr Chiazze concluded that his figure of 1.1567 for the male PVC fabrication cancer employee deaths was statistically significant?
A That is quite simple. That is a different question altogether. What he was testing was the comparison of the distribution of the causes of death as recorded in the deaths that he knew about with the distribution of the causes of death as recorded nationally at the same time and what he was able to conclude was - and I would agree with him in this - that the proportion of deaths in this group was a different proportion from that recorded in the general population and that the fact that it was different was unlikely, though not impossible, unlikely to be due to chance, though it might be, but I would agree with him that it probably was not.
Q That it was not due to chance?
A I would agree with him that it was probably not due to chance because I can think of a lot of better reasons, but, of course, it could be.
Q The probability that it was due to chance as opposed to some other factor was less than 20%?
A I think you mean less than 5%.
Q Less than ---

A Well again, you cannot answer that question. That is not what the statistic says. That statistic does not tell you what the probability is that it was a particular figure. What it tells you is that if the distribution had been the same as that of the national population over the same period, in only 1 in 20 comparable studies would the PMR have been as great as that found, or greater.

Q So, the odds are 1 in 20 that that particular finding was a chance finding?

A This could have occurred by chance once in twenty times or actually he says the probability is less than 1 in 20. I do not know how much. Something between 1 in 20 and 1 in a hundred.

Q Can we fairly say then that he was confident to the 95% level that his finding was due to something other than chance?

A No, that is deduction which no statistician would make. You cannot have levels of confidence. You might be 100% confident it was due to chance even though it was, it appeared on paper to be a very improbable thing. For example, if I took a dice out of my pocket and threw it six times and it came up six every time, I would not be 95% confident that was not due to chance. I would be 100% confident it was due to chance although it was a very improbable event, so you cannot draw any conclusions about the confidence with which you draw a conclusion about the meaning of the findings. That is based on a whole lot of other evidence.

Q In terms of the male PVC fabrication employees cancer deaths, the proportion of deaths among those workers was different to a statistically significant level from the proportion of deaths in the general population?

A In the United States over the same period, yes.

Q And Dr Chiazze came to an identical result and identical finding with respect to the female PVC workers?

A Yes.

Q Again, as with the male, the odds of that finding in the female PVC fabrication workers was 1 in 20?

A Less than.

Q Less than 1 in 20?

A Yes.

Q And Dr Chiazze came to a similar conclusion with respect to the proportion of large intestine cancer deaths among male PVC fabrication employees?

A Yes.

Q And also with respect to the female employees in that category?

A Yes.

Q Then with resepct to the other and unspecified cancers, Dr Chiazze again came to a statistically significant finding, did he not?

A Yes.

Q Both with regard to the male employees and with regard

to the female employees?

A Yes.

Q Have you reviewed at all, Dr Doll, in preparation for your testimony today, the 1976 study of Baxter and Fox?

A No.

Q Do you know whether or not in their study they reported an increase in mortality due to stomach cancers?

A I am afraid you will have to remind me of this study, I forget it.

Q Baxter and Fox Angiosarcoma of the Liver in PVC Fabricators, an article that appeared in the Lancet at page 245 in 1976. Have you reviewed that study of PVC fabricator employees prior to testifying here today?

A No. I am sorry, I will have to look at the paper. I do not think I have.

Q I did not bring the paper with me. All I have is the reference to the paper.

A Can you remind me of the reference again?

Q Baxter and Fox, Angiosarcoma of the Liver in PVC Fabricators, an article that appeared in the Lancet on page 245 in 1976.

A I cannot recall having reviewed that. Why I am hesitating is because I am not sure whether those workers were subsumed subsequently into the study done by Jones of all vinyl chloride workers in this country. I am not sure if they were

subsumed into this.

Q Well, the Baxter and Fox could not be subsumed in Jones' work because Baxter and Fox dealt with PVC fabrications while Jones dealt with PVC manufacturing employees and vinyl chloride manufacturing employees.

A If it was purely PVC fabrication and did not involve the manufacture of vinyl chloride or polyvinyl chloride in the same plant, then I have not reviewed it and I have specifically stated that I excluded such data from my review.

MR BUNDA: I am going to object to the characterization of counsel of the Baxter and Fox study presetned to the witness for his review.

BY MR DELLI BOVI:

Q Let me refer you, Dr Doll, to an article entitled: "Occupational hazards in the PVC industry", written by William Nicholson. You know Dr Nicholson?

A Yes, I do.

Q In which he states at page 170: "Interestingly, an excess of stomach cancer was seen in the proportional mortality study of Baxter and Fox." The last sentence. Do I quote accurately from Dr Nicholson's article?

A Yes.

MR BUNDA: What page was that?

MR DELLI BOVI: 170.

BY MR DELLI BOVI:

Q In addition to the Baxter and Fox article that you did not review and the Chiazze article which you did not rely on, you referred to a Swedish study and you forgot the name of the author of that study?

A Is that Molina?

Q Yes.

A I specifically excluded that for a number of reasons.

Q What I would like to ask you, Dr Doll, is in your paper that you wrote in 1988, you did refer to two studies done in Sweden at page 66, the top of the right-hand column?

A Yes.

Q The Swedish study that you relied on that covered two plants was done by Byren and others in 1976?

A Yes.

Q And that involved workers in plants producing vinyl chloride and polyvinyl chloride?

A Yes.

Q It did not include PVC fabrication workers?

A No.

Q So for purposes of your article and the opinions you have given here today, you have relied on a 1976 Swedish study of vinyl chloride and PVC manufacturing employees, but not the 1981 Swedish study of PVC fabrication workers?

A I read the one on PVC fabrication workers and decided