IN THE HIGH COURT OF JUSTICE

QUEEN'S BENCH DIVISION

1990 R No 860
1989 H No 3689

ROYAL COURTS OF JUSTICE
THE STRAND
LONDON

Wednesday 2 December 1992

Before

THE HON. MR JUSTICE FRENCH

ELIZABETH REAY

Suing on her own behalf and as
Mother and Administratrix of the
Estate of DOROTHY REAY (deceased)
and as Widow and Administratrix of the Estate
of GEORGE REAY (deceased) (Plaintiff)

V.

BRITISH NUCLEAR FUELS plc (Defendants)

AND

VIVIEN JANE HOPE (Plaintiff)

V.

BRITISH NUCLEAR FUELS plc (Defendants)

APPEARANCES:

For the Plaintiffs:

MR B A HYTNER QC
MR B F J LANGSTAFF
MR G S READ and MISS T GILL
(Instructed by Messrs Leigh, Day & Co. Solicitors, London)

For the Defendants:

MR K S ROKISON QC
MR M G SPENCER QC
and MR C J BUTCHER
(Instructed by Messrs Freshfields, Solicitors, London)

From the Notes of J L HARPHAM LIMITED
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INDEX TO TRANSCRIPT

SEVENTEENTH DAY'S PROCEEDINGS

WEDNESDAY, 2nd DECEMBER, 1992

STEPHEN JAMES EVANS Recalled

Cross-Examined by MR. ROKISON (Continued)

Q. Good morning, Prof. Evans. May I try to pick up with you where we left off when we were discussing case 00106?
A. Yes.

Q. I pick it up right at the end of yesterday afternoon's transcript of evidence, just to remind you how far we had got. On page 79, where I was putting to you part of the Gardner Methods paper?
A. Yes.

Q. The part in particular to which I have invited your attention was at the bottom of page 431 on the left?
A. Yes.

MR. ROKISON: My Lord, the reference is G.89:

Q. You will recall we read that passage?
A. Yes.

Q. I think that subject to your saying there was a clearer description of it in Dr. Snee's thesis, you agreed at 79D that what they appear to have done initially in relation to controls is to go to the Family Practitioner Committee register, and they would ascertain from that where the control was registered?
A. Yes.

Q. They would only be registered in one place?
A. If they went to a local...

Q. No, no, what they do is go to the Central Registry, see where they are registered?
A. At the Central Register?

Q. Yes, and see where they are registered.
A. At the local FPC they may not be quite as up to date as they are at Southport, at the Central Registry.

Q. Then what they do is they go and look and see whether the control is registered with the Cumbria FPC?
A. Yes.

Q. One has got to distinguish between Cumbria and West Cumbria in this context because it tends to get a little bit confusing if one does not. They first check whether they were registered...

MR. JUSTICE FRENCH: If this point is important I had better make a note of it. They find where the

control was registered. If registered with Cumbria FPC - not West Cumbria?

MR. ROKISON: My Lord, that is right.

MR. JUSTICE FRENCH: At the moment I don't grasp the importance of the difference but it will no doubt emerge.

MR. ROKISON: It is simply that I am taking Prof. Evans through the various stage that they went through in either including or excluding controls.

MR. JUSTICE FRENCH: I follow that entirely. It is simply that at the moment the significance of the distinction is not presently to my mind.

Q. MR. ROKISON: Of course, what they were seeking to do is by laying down a series of ground rules, if I can put it that way, hoping to end up with controls who were resident in West Cumbria at the date of diagnosis of the case?
A. Yes.

Q. They start by looking to see whether they are registered with the Cumbria Family Practitioner Committee?
A. Yes.

Q. If they were not registered with the Cumbria FPC then they were excluded?
A. Yes.

Q. They had fallen at the first jump, if we can use that expression?
A. Yes.

Q. That is made clear in the Methods paper at page 431, and we can come to look at the Snee thesis if we want further clarification in just a moment. If they did get over the first hurdle, that is, being registered with the Cumbria FPC, then further questions were asked via a questionnaire? Correct?
A. Yes.

Q. Inevitably not all the questionnaires were returned?
A. I am not absolutely sure that it went in that historical order. I think the questionnaires were sent to controls...

Q. No, with respect, that may be your error. What I will put to you is what we understand the position is and then we can check the documents to see if we are right. It was if they were registered with the Cumbrian FPC then they were sent a questionnaire. If that questionnaire was returned and indicated that they were not resident in West Cumbria, then they would be excluded?
A. Yes. I am sorry? In West...?

Q. Yes, because what they were seeking to do...

MR. LANGSTAFF: I hesitate again to rise to my feet but Prof. Evans has been asked in particular about the method set out at the bottom left hand corner of page 431, where it appears to say:

> "Residence particulars for controls with a Cumbrian registration or no registration were examined in questionnaires sent to parents..."

My Lord, I am not sure if he is putting the questions about questionnaires with the suggestion that the methods paper may not be entirely accurate, or what the suggestion is about that passage.

MR. ROKISON: My Lord, I know my learned friend was intervening and trying to help, but I would rather take it, if I may, in stages. We have agreed what stage 1 was, or what the first jump or hurdle is that you have to cross:

Q. It is true there are three possibilities, Prof. Evans, and I must do this through questioning. There are three possibilities...

MR. JUSTICE FRENCH: Let me just make sure I am up to date. If not resident in West Cumbria...

MR. ROKISON: No. If the questionnaire stated, "not resident in West Cumbria", then they were excluded.

MR. JUSTICE FRENCH: If the answer stated "not resident in West Cumbria", they were excluded?

MR. ROKISON: Yes:

Q. If the questionnaire was not returned... Let me put it this way: if the questionnaires said they were registered in West Cumbria, then so far as that control was concerned they were home?

A. Yes.

MR. JUSTICE FRENCH: If "Yes" they were entered.

Q. MR. ROKISON: The difficulty, or potential difficulty arose if the questionnaire wasn't returned?

A. Yes.

MR. JUSTICE FRENCH: If questionnaire not returned, then what?

MR. ROKISON: In those circumstances the basis for inclusion or exclusion is described in Prof. Snee's thesis? Is that right? We can look at it. Perhaps we can look at that now. We think it has been given a reference number. It was first referred to in Dr. MacRae's second report. I think it will therefore be a MacRae reference.

MR. JUSTICE FRENCH: At the moment I have it in a separate bundle - Snee's Thesis.

MR. ROKISON: I am happy your Lordship should have it in that separate bundle:

Q. I was going to take you to basically pages 75 and 76 and just through on to 77, because you actually quote in your third report a passage near to the bottom of page 75?

A. Yes.

Q. Can we start at page 74? I will just read it quite quickly with you:

> "In order to be suitable for analysis controls had to be eligible to become cases, that is, had they developed lymphoid malignancy before the age of 25 then they would have becomes cases in a study. In effect this meant they had to be resident in West Cumbria at the date of the diagnosis of their matched case. This residential qualification was ascertained initially by a search at the NHSCR..."

That is the Central Registry of the National Health Service?

A. Yes.

Q. "...where the FPC..."

That is the Family Practitioner Committee:

> "...posting of each control at the date of diagnosis of the index case was noted."

That is step 1:

> "If the control was registered with Cumbria FPC at the relevant date then the child was considered to be in West Cumbria at the date of diagnosis of the index case and hence acceptable as a control in the study provided that the questionnaire where returned did not give the residential address as outside West Cumbria at the relevant date."

Pausing there, there are two stages of possible exclusion; one is not being registered with Cumbria FPC and the second is, if you were registered with Cumbria FPC, but the questionnaire said you weren't resident in West Cumbria,then you were excluded? Correct thus far?

A. Yes.

Q. "Questionnaires were also forwarded to those parents where the control had registered with Cumbria FPC up to 1 year after the date of diagnosis of the matched case. This was to allow for the inevitable delay between moving back into Cumbria and registering with a doctor in that area. However by adopting

this procedure I had no confirmation that the controls for whom there was no questionnaire information were actually in West Cumbria at the relevant date and hence were eligible for the study."

So those who became registered with Cumbria up to a year later? That is a way in which they were included even though they might not have been resident in West Cumbria? Correct?

A. Yes.

Q. "This is because there are three health authorities within Cumbria, namely, East, South and West Cumbria. Thus a registration with Cumbria FPC only implies residence within Cumbria. Therefore a search was performed at the offices of Cumbria FPC to determine if residence within West Cumbria could be confirmed for the controls in the study."

They wanted to find out if they were resident in West Cumbria so they conducted a search in order to verify:

"A sample of subjects were submitted to this search. These were all those controls who were resident in Cumbria at the relevant date according to NHSCR, but for whom information from a questionnaire was not available, plus a small number of controls where residential information was available from the parents."

They refer to the results of that tracing.

"The records of the Cumbria FPC contain, in the form of cards, all past residential addresses of patients as notified to the committee by general practitioners. These cards therefore provide an independent means of assessing residence. However dates are given on the cards for only a small minority of the addresses and therefore the exact date of a person's movement cannot always be determined from this source. Some 863 controls for whom questionnaires were not available were submitted for tracing at Cumbria FPC in order to determine place of residence at the relevant time. The results of this procedure are shown in table 5.3.2. The main reason that records could not be found was that the person in question had moved out of Cumbria at the time of the search."

Then one sees - this is a trace of selected controls at Cumbria FPC. One finds there set out 162 weren't found; 608 were in West Cumbria at the index date; 15 were not in West Cumbria at the index date and 78 were unknown.

"The classification of majority of the 78 subjects..."

That is the last mentioned:

> "...into the category ' Unknown whether or not in West Cumbria' occurred because a single address outside West Cumbria was given in the record but with no mention of when the change of address took place. Therefore the residence of these subjects at the index date was unknown, though it is likely that they were still resident within West Cumbria at the date in question."

In other words they didn't know because they hadn't got a date of when they moved:

> "The 15 (2%)..."

I think this is the passage which you quote:

> "The 15 (2%) of controls who according to the records of the FPC..."

That is the Cumbria FPC as referred to in the table above:

> "...were not in West Cumbria at the index date and the 78 controls for whom location was not certain, were not excluded solely on this basis for the following reasons:
>
> 1. The same exercise could not be carried out for cases as the majority of their records were not available at the FPC (due to death)."

They wouldn't have a residence, or they may not have their residence recorded there because they had died?

A. Yes, and they may not even have their records there any longer.

Q. It doesn't say that, but it may or may not be so. It may be that some of their records would no longer be there?

A. That's right.

Q.

> "Therefore if such an exclusion criterion were applied to controls it could not be applied to all cases.
>
> 2. For 3 cases and 10 controls the residential record according to the questionnaire did not concur with the information at Cumbria FPC. These subjects were included as it was felt the questionnaire was a more reliable source of residential data than the FPC records."

Just pausing there, if we may, to see where we have got to. We have looked at the first step which is to see where they are registered. If they are registered in Cumbria then a number of things happen. A questionnaire is sent out and also searches may be done?

A. Yes.

A Q. Depending on what the questionnaire shows, or what the searches show, the control may be included or excluded?
A. Yes.

Q. They go on and say:

> "Therefore for the purposes of this study I have assumed that a person born in West Cumbria and
B registered with Cumbria FPC at a given date, was also resident in West Cumbria at that date."

In other words, the presumption is that if they were born there and if they were registered with the Cumbria FPC, then unless there was strong evidence to the contrary in the questionnaire saying they were not registered there any more, they were assumed to be resident in West
C Cumbria?
A. Yes.

Q. "Inevitably adopting this method of determining residence at the relevant date has meant that some subjects who were not in West Cumbria at the date of diagnosis will have been included in the study. However, from the above analysis it would seem that
D the proportion of such subjects would be no more than 2%. (that is 15/701). Furthermore, inclusion of such misclassified individuals is unlikely to have produced any significant bias in the results...

Therefore, if a control was traced as alive, did not have cancer and was registered with Cumbria FPC at
E the date of diagnosis then that control has been included in the analysis."

They refer to 242 controls not fulfilling the criteria and having been excluded. One sees this very conveniently set out. If you go back to page 73 one finds a very helpful figure which describes in a figure form the process?
F A. Yes.

Q. If you go down to where you are dealing with controls, which is the lower part of the page, it says:

> "Control alive at date of diagnosis of matched case?"

G "No", they excluded them. "Yes", they go on to the next step:

> "Control registered with cancer before date of diagnosis of matched case?"

If the answer were to have been - I think they have got
H this wrong - if it were to have been "Yes" I think they would have been excluded, but none were?
A. You are quite correct.

Q. I think the "Yes" there should be a "No"?
A. That is right.

Q. Moving down to the next box:

> "Control registered with Cumbria FPC at date of diagnosis of matched case?"

If the answer was "No" they were excluded?
A. Yes.

Q. If the answer was "Yes" then they had to consider whether they were resident in West Cumbria at the date of diagnosis of the matched case according to the questionnaire, and if the answer was "No" they were excluded, otherwise the presumption was that they were there?
A. Yes.

Q. We are agreed that that seems to have been the procedure?
A. Yes.

MR. JUSTICE FRENCH: I had better make the alterations of "Yes" and "No" appropriately. Would you tell me precisely where they are?

MR. ROKISON: Yes, my Lord. If you look at the box which says:

> "Control registered with cancer before date of diagnosis of matched case?"

It is immediately below that. It should say "No", and there ought to be to the right where there is nothing written there should be a "Yes" in brackets, because in theory they would have been excluded but in fact there weren't any so it doesn't matter. It is academic. The design was that they would have been excluded.

MR. JUSTICE FRENCH: Yes, I quite follow that none in fact were.

Q. MR. ROKISON: We are agreed, I think, from that, and I agree it slightly expands what is said in the methods paper and that was the procedure that was followed. Now the point made by Dr. MacRae I think one can pick up most clearly because it is dealt with more fully in his second report. May I ask you to look at that? It is MacRae 2, paragraph 3.2 on page 22. We can look through it quickly and you can indicate the extent to which you agree or disagree with what is stated:

> "Leukaemia and lymphoma cases were eligible for inclusion in the West Cumbria Study if they were diagnosed during 1950 to 1985 while under 25 years of age 'with a residential address in the area served by West Cumbria Health Authority'. The included cases, therefore, had to be resident in West Cumbria at the time of diagnosis."

Do you agree?
A. Yes.

Q. "Each case was matched with two (possibly overlapping) sets of up to 8 controls, and 'to have the potential to be a case in this study at the appropriate time, controls had to have been resident in West Cumbria at the date of diagnosis of their associated case'."

Yes?
A. Yes.

Q. "To determine whether a particular control was resident in West Cumbria at the appropriate date, the National Health Service central register was consulted to identify the relevant family practitioner committee area of registration at the time. Controls registered outside Cumbria were excluded from the Study, and, in this way, 195 otherwise eligible controls were omitted from the West Cumbria Study."

Right?
A. Yes.

Q. "On examination of the documents held at the MRC Unit, I have found that Case Identification Number C00106 (a case of chronic myeloid leukaemia affecting a young man aged 19 years at diagnosis) was diagnosed in April 1978 at the Southmead Hospital in Bristol. The case died at the age of 21 years on 1st August 1979 at the same hospital in Bristol. The death certificate shows this young man to be a student at the time of death although the 'usual address' given in this certificate is an address in Seascale which I take to be the parental address, the 'informant' on the certificate being the father who gave an address in Seascale as his residence.

Case C00106 was included in the West Cumbria Study. I take it, therefore, that the decision to include this case is based upon the parental address being in Seascale."

We will see what Prof. Gardner says in a moment:

"However, if the residential address at diagnosis of the case <u>himself</u> (rather than that of his parents) was outside West Cumbria, then this case should <u>not</u> have been included in the West Cumbria Study. I am of the view that the residential address of this individual should be taken to be his residence as a student (presumably in the Bristol area), and that this case should have been excluded from the West Cumbria Study. This view is confirmed by the following:

1. For controls in the West Cumbria Study, area of residence is taken to be that covered by the FPC area of registration at the appropriate date. If at the date of diagnosis Case C000106 had a FPC area of registration which was outside Cumbria (as must be a distinct possibility for a student in the Bristol area living away from his parents)..."

Just pausing there. You have seen evidence to the effect that this was indeed the case, that he was registered with the FPC in Bristol?

A. I have not seen evidence that the records of West Cumbria had been amended at that date.

Q. What happened was that at the NHS central registry his FPC at the relevant date was Bristol and not Cumbria.

A. It is not simply a question of "at the relevant date". It is the date at which that amendment was made and the NHSCR can be up to - and at that time certainly was - up to one year out of date with recording such things.

Q. Forgive me, is the point that you are making, which seems to be to be rather different from the point you are making either in your statement or in your evidence yesterday, that you do not know whether the Bristol case at the date of diagnosis was actually still registered with the Cumbria FPC as opposed to being registered with the Bristol FPC? Is that the point you are making?

A. It is the point I am making but it is also the point that Prof. Gardner did not have the ability to go to the Cumbria FPC to find that information out at that point.

Q. I don't understand?

A. Well, I presume that as far as one can tell that was something he had not been able to do.

Q. On the contrary, he did that for all potential controls. That is indeed what he did.

A. We are talking about a case.

Q. Well, he did it in relation to all controls and if they were to be treated in the same way, as you have agreed it is very important that they should, and indeed the paper states that they were treated in the same way, and your own evidence actually positively makes the point that they were treated in the same way.

A. Yes.

Q. If the first step in relation to a control was to see whether they were registered with the Cumbria FPC, if the position was there was a case that was to be potentially included in the study, one would assume that the same exercise would be carried out?

A. Yes, but you are doing this with the benefit of a retrospectoscope rather than saying what was being done at the time.

Q. With respect, I am not. With respect, what I am saying is that if it was not done for cases but was only done for controls then that would have been a defect in the methodology, wouldn't it?
A. If the same facilities were available for cases, but the point being that the same facility is not available for cases by nature of the way the records are held by the fact that those who have died will disappear from FPC records.

Q. The NHSCR, the central registry, as I understand it - my instructions are and my understanding is that the NHSCR will tell you where a person is registered at what dates. Is that correct?
A. They will attempt to do so...

Q. All right, they attempt to do so, and no doubt they make mistakes as other people can make mistakes, but that is what they tell you. If you go to that and if it says, for example, that at the date of diagnosis, being April 1978, that the case 00106 was registered with the FPC in Bristol, then had that person been a control he would have been excluded?
A. Yes.

MR. JUSTICE FRENCH: Now is it establishable what information appeared on the NHSCR at the date of the search? That surely is a matter of significance?

MR. ROKISON: Indeed, and what we have at the moment... My learned friend is very helpful in saying that Gardner says he had a family practitioner address in Bristol, but I think what is not - we will check this - but I cannot at the moment call to mind a positive statement by anybody to the effect that that was what was stated on the NHS central registry:

Q. The position would be this, and we can speculate a little bit about this: Prof. Gardner is looking for relevant information as to registry at the relevant date when he is carrying out his study some time in 1989?
A. Yes. The thing is you have said the evidence is from Dr. Barker and not from the NHSCR, so it isn't actually evidence that...

Q. Let's not argue about that for the moment. I am putting to you a separate thing. The point is this that in 1989, Prof. Gardner and his team are carrying out this exercise?
A. Yes.

Q. They go to the National Health Service central registry in order to try to ascertain where, if they are treating them in the same way, cases and controls were registered at the relevant date?
A. Yes.

Q. One would assume that by that time the NHS central registry would have picked up, if it was the case, that case 00106 some time before April 1978 had become registered at Bristol? It is pretty likely, isn't it?
A. It could well be, but whether... You are asking me to speculate here.

Q. Indeed I am, but you are making the point... As I understand it, the only point you are now making about this, which as I point out to you is not the point you never made before, is that it could be that the data was not sufficiently up to date to have shown this. As I understand it that is the only point you now make?
A. I also make the point made by Dr. MacRae in his third report, that:

> "This information was not present in the documents made available in this litigation by the MRC Unit."

Again, I have...

Q. They wouldn't have that information. Of course they wouldn't have the information. They go and search and they look. They won't have the documents, presumably?
A. No, but they don't have the information in regard to the search.

Q. Let's come on to the third report. That is the same point, with respect, and not a different point. As I understand it, and is this correct, that the point you are now making on this vexed question which has occupied an awful lot of time and words about the inclusion of the Bristol case is that if the Bristol case was shown on the NHS central registry as having been registered with the Bristol FPC at the date of diagnosis, rather than the Cumbrian, then that case should have been excluded as a case? Do you agree?
A. According to the strict application of the protocol, yes.

MR. JUSTICE FRENCH: If, at the date of search the Bristol case was in fact shown on NHSCR records as registered with a FPC in Bristol, then according to the protocol it should have been excluded?

Q. Now, did you say "Yes"?
A. Yes.

Q. MR. ROKISON: Before we leave MacRae's second report, I have established the main point that I wanted to establish with you but as we are looking at it I would perhaps like to pursue it just a little more. He makes the point at page 24, which is a point you yourself have made, well, perhaps at the bottom of 23:

> "If at the date of diagnosis Case C000106 had a FPC area of registration which was outside Cumbria...then, under the same circumstances, a

control would not be regarded as being resident in West Cumbria at that date and would have been omitted from the Study."

I think you agree with that, although it depends on how up to date the information is?

A. Yes, and how certain it is, because some controls were included where the information was uncertain.

Q. No, that is not right, with respect. They were excluded if they had - we have been through this this morning. They had to get over the first hurdle and it was only if they got over the hurdle, that is, being registered with Cumbria FPC, that any assumptions were made in their favour, if I can put it that way, in the absence of evidence to the contrary?

A. Yes.

Q. He goes on to say:

> "Cases and controls should be treated impartially within a case-control study;..."

Then he makes the point which you yourself have observed, and my Lord has observed, that the Bristol case, as we call it, was excluded from the Draper 1992 Study?

A. Yes, for entirely different reasons.

Q. Well, it was excluded because he had an addressed in another part of Britain which was regarded as his area of residence for the purposes of the National Cancer Registration scheme. Now we don't know - there hasn't been evidence before my Lord about what the criteria are for residence for the purposes of the National Cancer Registration scheme, but one thing is clear and that is that Draper and his co-authors didn't say to themselves, "Oh, well, he has lived most of his life in West Cumbria so let's put him in"?

A. No. The issue in regard to Draper's Study is calculating an incidence rate and there are good scientific reasons for saying that it is very important that the numerators and denominators in an incidence rate study are treated in the same way. However, in a case-control study there is no scientific reason of itself to have excluded, and this is a point made by Dr. MacRae, cases that are resident outside Cumbria. There are no scientific reasons to have done so. That is an arbitrary decision of the protocol.

Q. Absolutely, but of course if you do that for cases then you should also do it for controls. The important thing is that if you are doing a case control study you have got to treat your cases and controls in the same way.

A. Yes, particularly in regard to anything that relates to a risk factor of interest.

Q. You have got to treat them in the same way, haven't you?

A. No, it is in regard to risk factors, is the key issue. You cannot treat cases and controls in the same way

because the information you have about them may be entirely different. A control is likely to be living and a case is going to be dead and so the real key issue, and I think the key scientific issue here, is that it is most important, absolutely vitally important, that they are treated in exactly the same way in regard to risk factors.

Q. You are wriggling now, aren't you, Prof. Evans, because you realise that you are wrong?
A. I don't think so.

MR. JUSTICE FRENCH: At some stages, wriggle or no wriggle, the higher the temperature the less the light. Let me see if I can record the essence of that exchange because I think it is important to both sides:

Q. You were drawing a distinction - I cannot, I am afraid, recall the exchange with accuracy - but you were expressing a distinction between case-control studies and - what was the other expression?
A. This is an incidence rate study.

Q. An incidence rate study. Draper was conducting an incidence rate study?
A. Draper was conducting an incidence rate study, so there what is important is that the addresses of residents ....

Q. There, or in such a study?
A. In such a study.

Q. What is important is ...?
A. That address of residents should be ascertained in the same way for those with and without the disease. The way that the ascertainment is done for those without the disease is by the Census.

Q. "Census" with a capital "C"?
A. Yes, the National Census.

Q. MR. ROKISON: Do you mean the NHS Cancer Registry?
A. No, I am talking about the Census that takes place in 1961, 1971, 1981 and 1991.

Q. I simply do not follow ....

MR. JUSTICE FRENCH: Sorry, can we have the answer and then examine:

Q. "Is by the Census", yes?
A. So that is how you find out where the population is.

Q. You have, I think, expressed the ascertainment if you are conducting an incidence study and then you drew a contrast between that and a case-control study?
A. Yes. I do not know, shall I just try and explain, what I am saying is that in the incidence study we have people

with the disease divided by the population at risk, and it is particularly the population at risk, we find their address of residence is determined at Census time.

Q. "Is by the Census and therefore is determined at Census time", is that right?
A. That is right.

Q. Then, in brackets, what you are doing is comparing what with what?
A. You are attempting to compare cases with the population at risk of being a case.

Q. Does that complete your answers as regards an incidence study?
A. Yes.

Q. You then went on to contrast such a study with a case-control study?
A. Yes.

Q. A case-control study, on the other hand ...?
A. A case-control study, on the other hand, is not necessarily required to match for area of residence.

Q. To match for?
A. To match for area of residence. It is not necessarily required to do so.

Q. I underline "necessarily" then?
A. Whereas an incidence rate study very clearly is absolutely determined, that is absolutely vital.

Q. Incidence, for incidence rate study purposes it is absolutely vital to do so?
A. Yes.

MR. JUSTICE FRENCH: I think that covers the exchange. Now, examine it by all means, Mr. Rokison.

MR. ROKISON: Thank you, my Lord:

Q. Would you agree that in a case-control study what you are doing is examining cases as against matched controls?
A. They do not have to be matched but in this instance we are talking about matches, yes.

Q. This was a matched controls study?
A. Yes.

MR. JUSTICE FRENCH: By "this", I can put "Gardner", can I?

MR. ROKISON: Yes:

Q. And the parameter which had been laid down by Black was, put loosely, residence in West Cumbria?
A. Yes.

Q. What those carrying out the study had to do was to define their parameters in relation to the ascertainment of residence in Cumbria, or West Cumbria?
A. Yes.

Q. It was you yourself who made the point, both in your statement and indeed in your evidence yesterday, and I read to you from Day 16 at page 77, from the top:

> "Q. You then deal with the selection of cases and controls and I think you have already agreed with me, Prof. Evans, that it is important to set your parameters in advance and it is important that, once you have set your parameters, you should stick to them?
> A. Yes.
>
> Q. You yourself make the point, in relation to the selection of controls, that the selection methods for controls used by Gardner and colleagues is reasonable and does not exclude or include children of controls unless they would also have been, and I take it you should say, excluded or included, as the case may be, as cases?
> A. Yes.
>
> Q. Would you regard that as being important, that you should treat your cases and controls in the same way?
> A. That is the most important aspect of a case control study."

Then when I asked you about the Bristol case, so far as your evidence went yesterday, as I understood it your justification for saying the Bristol case was rightly included, is a passage which we find at page 79H. What I said is this:

> "Q. Perhaps you might refer us to it ...."

- this was with reference to Snee -

> "... if it is of importance tomorrow. May I just put the very short point to you in relation to the Bristol case, that, trying to be fair and to paraphrase the statement of Prof. Gardner and the letter of Hazel Inskip, that what it appears that those carrying out the study did was that, in relation to cases, they took a broader, more judgmental view and, if they formed the view that, for example, the case had spent virtually all its life in Seascale and had had parents who were there, etc., the fact that it so happened that at the date of diagnosis a case was registered with a Family Practitioner Committee outside West Cumbria would not necessarily exclude that case from the study."

Now, you did not say then, "Oh, but they might not have had the right information". What you said in answer to that is:

"A. They did the same to some of the controls."

I then asked you:

"Q. That is something which you derive, do you, from the Snee thesis?
A. Yes."

We have looked at the Snee thesis from which it appears that what you were saying there was wrong, that they did not take that broader judgmental view for the controls, but they excluded controls if they fell at the first hurdle?

A. Yes.

Q. I suggest to you that Dr. MacRae, and indeed others of our epidemiologists, in particular Prof. Doll, will also support this view, that it was wrong of those carrying out the Gardner Study to adopt a different test or approach when considering the eligibility of cases on the one hand and controls on the other. Would you agree with that?

A. No, because I think that in practice in doing studies of this kind the rigid criteria that you set out in practice have to be blurred at the edges. What is the most important thing, when I have said that they should be treated the same, the really vital thing is that they should be treated the same in respect of risk factors. This is the danger, of course, in relying on questionnaire data, that even though you treat them the same, the issue of recall bias that we talked about before is a difficulty, that even though you treat them the same, the people themselves are not the same in their memories. So I would argue with Prof. Gardner that what is the most vital thing to do in this, in carrying out your scientific judgment, is to be absolutely sure that you have not done it having known what the doses are.

Q. MR. JUSTICE FRENCH: This is a compression - tell me whether it is an accurate compression: "I think that in practice the rigid criteria may be blurred at the edges"?

A. Yes.

Q. "What is vital is that the risk factors be the same. It is vital you should not do it knowing what the doses are"?

A. Yes. It is "ascertainment of the risk factors should be the same", rather than "the risk factors". The risk factors may or may not be the same.

Q. Yes. "What is vital is that the ascertainment of the risk factors should be the same".

Q. MR. ROKISON: It will be apparent from my questioning that we do not accept that is an adequate answer, and in particular you say that rigid criteria may have to be blurred at the edges. Why?
A. Because there is very often uncertainty over things, and this is one of the things that is left at the bottom of page 75, that you end up being uncertain about the exact date of something. You find that records are in error, that there is missing data, and you have to apply your judgment to that and to do it in an even-handed way.

Q. Exactly, and if the position is that in a matched case control study you apply it in a particular way in relation to controls, you should do the same with cases and vice versa, shouldn't you?
A. Yes, insofar as it is possible to.

Q. Because it will not have escaped your notice, Prof. Evans, that although the Bristol case was included in the study, the Bristol case, so far as the study is concerned, only had one local control out of eight?
A. Yes.

MR. ROKISON: My Lord, for the benefit of your Lordship's note, that is something that appears ....

MR. JUSTICE FRENCH: It has been agreed.

MR. ROKISON: It is accepted. It appears in the figure which you find on page 427 of the Results paper. I do not necessarily want your Lordship to look at it but it there appears.

MR. JUSTICE FRENCH: If something is accepted by the witness it is perhaps a time-saving exercise if one avoids going to the table but obviously on occasions one has to.

MR. ROKISON: The reference is in the transcript if your Lordship at any time wants to look at it:

Q. Of course, the Bristol case being a young man aged 19, it may very well be that the reason, or at least one reason, why his matched local controls were excluded from the study may be for a similar reason, namely that they had finished their school days and gone off to university?
A. Yes.

Q. And who knows, some of those seven controls who were excluded because of the rigid application of the criteria which were determined in advance may have had fathers with high doses, for all we know?
A. For all we know, yes.

Q. That is why it is important, is it not, that you should not only set the same criteria but adhere to the same criteria, as between your cases and your controls, in a matched case-control study such as this?
A. Yes.

Q. May I just, in relation to the point you made about whether the position might have been unclear, or there might have been some error in the documentation available to those carrying out the study, if you could look in bundle P4, tab 2, where we find the statement of Prof. Gardner, you see near the top of page 6 - page 18 of the bundle, Prof. Gardner says:

> "No hospital notes were available, although the case had registered with a general practitioner in Bristol two months before diagnosis."

So that it appears that Prof. Gardner was aware of the fact that the case had registered in Bristol, and if you go on to page 23, which is the last page of Hazel Inskip's letter, the penultimate paragraph:

> "From the information available at the time that case C00106 was assessed, his permanent address was given as being in West Cumbria (on the death certificate) ...."

- which is a point that has been dealt with by Dr. MacRae -

> "... and he appeared to have been away from home for only a short time (on the basis of his age and FPC registration)."

So again it would appear that they were aware of the fact that he was, at the relevant time, registered with an FPC outside Cumbria, doesn't it?

A. From Hazel Inskip that certainly appears to be so, though there is nothing in the documentation to state it.

MR. ROKISON: We have not got all the documentary evidence, fortunately, before the Court. My Lord, my learned friend says we have the documentation. What we have is the documentation, the documents, which MRC had, but what we do not have, of course, is in a sense their workings; what we do not know is what they observed or noted down when they did their initial exercise of examining the first hurdle, but it would appear that they did ascertain the relevant FPC for this case:

Q. Can I come back to your report in relation to this matter and get it out of the way, if I may? It is really to clear up the points you are making in your third report, in relation to this point raised by Dr. MacRae. You deal with it at page 19 of your third report. It is paragraph 49, sub-paragraph 3. The first point you make is this. You say:

> "Dr. MacRae has picked on this case knowing that the dose was very high. Examination of particular cases when 'unblinded' induces considerable bias as Dr. Macrae notes. The impartiality which is so vital for case/control studies has not been exercised in respect of this criticism."

Are your really saying that if he looks through the data and finds that a case has been included incorrectly that ought to have been excluded, that in doing that he shows bias?

A. If he has done it in regard to knowledge of doses and has looked at those cases only, and has not applied exactly the same criteria to every single case ....

Q. Are you suggesting there was one of the other cases - there are not all that number but are you suggesting that some of the other cases were dealt with in a similar way?

A. No, but what I am saying is that I do not know and that if you go and look at the data and find particular cases that are extreme ones, and study them with an intensity that you do not apply to all your other cases, and all the other controls, then that is also potentially biasing - a biased assessment.

Q. Dr. MacRae deals with, and discusses the question of, the Scottish case in his statement and the exclusion of that case, which he says was quite correct. Have you any basis whatever for suggesting that Dr. MacRae did not do a thorough job, if I can put it that way?

A. I think it is impossible for him to have looked at every case and every control. I do not know whether he looked at - you mention one local control for case 106 - there are, I think, seven area controls, a very large number of area controls, above the average for that particular case. I do not know whether he has gone through and ensured that they were all registered with the Cumbria FPC at the time.

Q. With respect, I find it incredible, Prof. Evans, that you attack Dr. MacRae and suggest that he is acting in some unscientific way in making a point, which although it has taken you a very long time to accept it, you now seem to agree is a valid point.

A. I am still not convinced it is as valid as Dr. MacRae seems to think it is and I also think that it is very, very dangerous, when you approach studies in this way, to try and find the cases that have high doses, and that is where you begin.

Q. But the position here is, and we have agreed with this, that you have to be very cautious about drawing conclusions from a single study. We agreed that yesterday?

A. Yes.

Q. You particularly have to be very cautious about drawing conclusions from a single study that rests upon a small number of cases?

A. I quite agree.

Q. You have to be particularly cautious, as we saw in relation to a comment in another study, if the inclusion or exclusion of a particularly high or low case would have a significant effect on the overall result?

A. Yes.

Q. What I cannot understand, and I give you an opportunity of explaining it to my Lord - perhaps my Lord does understand - where you have a high dose category, which on the Gardner Study, being the same high dose category for both the six month and total dose, comprises only four cases?

A. Yes.

Q. That if one finds that one of those cases, on the basis of the criteria which the authors of the study set for themselves, should not have been included in the study, then that is an important matter for anybody to point out, isn't it?

A. Yes, but as I say, it is very important to do that in an even-handed way and to look at all the cases and controls in the same way because there are particular pairs, or sets of data, where it is vulnerable to the inclusion of a case with no dose, because the controls have high doses. So it is very important that you examine all the controls in that way, and there is a danger, in examining the data, when you know what the results are. I think that to make a criticism of a study after the results are out is open to bias in a way that the criticism that could be made at the time the study was done might not have been made, and indeed one could argue, as Prof. Gardner himself did, that he was fearful that he might have been accused of bias for excluding that particular case.

Q. So he says, but having set his parameters, and if that case fell outside the parameters before he knew anything about it, he could not have been criticised, could he?

A. No.

Q. Are you aware of any other case which has been incorrectly included in a study?

A. No.

Q. You say over the page, on page 20:

> "Omission of case 106 would in any event have had a marginal effect: statistical significance would remain, and in particular the regression slope would remain similar."

A. Yes.

Q. I am not asking you about your re-analysis at the moment but I just wanted to ask you this, in anticipation: have you done any analysis through the computer to see what difference it makes if you exclude that case?

A. I have done at least one analysis in the past. I am not sure whether I did it on the most recent, on the agreed doses.

Q. I am merely saying that I shall be pursuing that at a later stage when we come to your re-analysis. So far as the Gardner Study, as carried out, was concerned, it had

a noticeable effect, didn't it, on the results as shown by Prof. Gardner in the documents annexed to his statement?

A. It will automatically have a noticeable effect on the statistical significance, yes.

Q. Indeed, and I shall be asking you about the wide confidence intervals and the statistical significance of some of the conclusions, but it is the fact that of the eight combinations, if you like, which were examined, namely leukaemia on the one hand, and leukaemia and NHL, and then within each of those area controls and local controls, and within each of those total dose and six month dose, so that one has eight in all, that of those eight, three of those categories would be deprived of statistical significance if one were to have excluded the Bristol case?

A. That, I think, is what Prof. Gardner says in his letter.

MR. JUSTICE FRENCH: I am sorry, I do not think I am confident I have got this right. Three of the characteristics, three of the eight ...?

MR. ROKISON: Three of the eight.

MR. JUSTICE FRENCH: Would be deprived of statistical significance if you omit Bristol?

MR. ROKISON: Yes, and one sees that - it is in bundle P4 if your Lordship want to see where that is shown ....

MR. JUSTICE FRENCH: I think the answer is good enough.

MR. ROKISON: Again, so that it is on the transcript, if your Lordship wants to look at it, it is bundle P4, pages 25 and 26, and it is stated by Prof. Gardner on page 19. He puts it in a slightly different way. He says that five out of the eight remain statistically significant. Obviously different people will look at that in a different way.

MR. JUSTICE FRENCH: Yes, like whether your glass is half full or half empty.

MR. ROKISON: Indeed, my Lord, exactly:

Q. Leaving aside the particular instance of the Bristol case for a moment, that does demonstrate, does it not, the comparative fragility of the study?

A. I would not have used "fragility" in that way.

Q. No, I know, because it is not really a scientific term, but would you say it demonstrates the lack of combined strength and power?

A. It demonstrates the small numbers involved, yes, very clearly.

Q. Its limited strength and power is itself a product of the small numbers, coupled with the relative risks. The fact that your lower confidence interval goes below one, the fact of that will be a reflection of the relative risk coupled with the number of cases that you are dealing with?
A. I think that Prof. Gardner in his statement makes it clear that the actual strength and relative risks remain rather similar, and what is counting here is the statistical significance that is affected disproportionately because of the small numbers, and I would agree that statistical significance is very vulnerable to a single case changing categories.

Q. What statistical significance reflects is the chances of this result occurring by chance?
A. Loosely, yes.

Q. I really can come back, if I may, now to your first and main report. That is Evans 1.

MR. ROKISON: Does your Lordship have still available P4?

MR. JUSTICE FRENCH: Yes.

MR. ROKISON: It might be convenient just to refer to P4, Prof. Gardner's statement in P4 and to the note which he appends to it, page 27:

Q. Although one may argue about whether the hypothesis, namely that there is an association between paternal preconception irradiation and leukaemia in the offspring, as to whether that was a hypothesis that was generated or tested by the Gardner study, but it is quite clear that, insofar as it was a hypothesis which was to be considered, albeit it was not something which had arisen from any other study, that there were a number of hypotheses which were being tested in this study, were there not?
A. Yes.

Q. Here there are set out 12?
A. No, those are 12 mechanisms, not hypotheses.

Q. Well, 12 possible causative links.

Q. MR. JUSTICE FRENCH: Do you accept that?
A. They are 12 possible mechanisms for the excess, yes.

Q. MR. ROKISON: One of them being, No. 4, that which we are concerned with here, "Parental occupational exposure of germ cells to radiation increases chance of leukaemia developing"?
A. Yes.

Q. That itself is a hypothesis which may in itself divide into two as to paternal or maternal?
A. Yes.

MR. ROKISON: One can put this away now, my Lord, unless your Lordship looks at the Gardner study in this document. It appears in more than one document, but if your Lordship has been looking and marking the Gardner study in P4....

MR. JUSTICE FRENCH: I have put a copy of Gardner, the two papers, in the front of Prof. Evans' bundle, so that is where personally I have it.

MR. ROKISON: I was going to look at that, my Lord, now:

Q. Although not set out in the same way and set out in a summary form, one finds at page 430, which is within the Methods paper, G 89, the second page of the Methods paper....

MR. JUSTICE FRENCH: Looking at page 30, before you embark, Mr. Rokison, I have made a note for myself: what is histiocytosis X?

THE WITNESS: I could not answer that, my Lord.

MR. ROKISON: I am terribly sorry, which document is your Lordship referring to?

MR. JUSTICE FRENCH: I am looking at page 430 of Gardner.

MR. ROKISON: Oh, yes, my Lord.

MR. JUSTICE FRENCH: It may not matter, it may matter, but at some stage I would like to know what the very last entry at the bottom is - histiocytosis. When I say the very bottom, I mean on Table 1.

MR. ROKISON: Below Non-Hodgkin's?

MR. JUSTICE FRENCH: Yes.

MR. ROKISON: My Lord, I am afraid I cannot help your Lordship on that.

MR. JUSTICE FRENCH: But I am sure somebody will appear who can at some stage. We need not bother about it now. It is only that I made a note to inquire.

MR. ROKISON: My Lord, those behind me will make a note to inquire and we will try and assist your Lordship on that.

MR. JUSTICE FRENCH: Thank you.

Q. MR. ROKISON: One can see in the left-hand column, under the four predetermined study aims, that what they do effectively in that list is to embrace within those

four categories the sort of possible causal mechanisms which we have been looking at in the other document?

A. Yes.

MR. JUSTICE FRENCH: But it is really pathways, is it not, rather than - or is it? I do not know.

MR. ROKISON: Yes, in some ways, it is pathways. For example, geographical distribution is not, in a sense, a pathway, although it may give a clue to a pathway.

MR. JUSTICE FRENCH: No, it is hard to categorise them all under one heading.

MR. ROKISON: Yes, it is, I quite agree, my Lord, and that is why I simply called them hypotheses.

MR. JUSTICE FRENCH: Yes.

MR. ROKISON: My Lord, my learned junior, Mr. Butcher, has come up fairly quick with an answer to your Lordship's question. I say an answer to your Lordship's question because it is referred to in the Draper paper, which is in P4 at tab 3, at page 34, but it does not, so far as I am concerned, my Lord - and your Lordship may be in the same boat in this respect - it really does not take the matter any further. What it says is that:

> "Langerhans cell histiocytosis (Histiocytosis X) is not included in the analyses as this group of diseases is not now regarded as neoplastic."

MR. JUSTICE FRENCH: So, for present purposes, the clever men think it is a non-neoplastic disease.

MR. ROKISON: Yes. There is a discussion going on as to whether it is concerned with the pancreas and the liver or what.

MR. JUSTICE FRENCH: If it is non-neoplastic, I can forget it.

MR. ROKISON: We are not concerned with it.

MR. JUSTICE FRENCH: And propose to do so unless I am told I must remember it again.

Q. MR. ROKISON: I think that we agreed about this already, that if you are testing a number of hypotheses or possible pathways or whatever, then obviously the more you test, the more likely you are to get a significant association by chance. You have agreed?

A. Yes. Gardner says there are two hypotheses.

Q. He may say that there two hypotheses but, with respect, that is not quite accurate, is it, because he was testing

a large number, which are summarised within numbers 1-4 and which were, as one sees when one looks at the Results paper, the subject of tables. For example, Table II on page 424, being the second page of the results table. What one finds set out there is "Numbers of cases and controls with relative risks for leukaemia and non-Hodgkin's lymphoma in children by some suspected risk factors," and they there set out a number of suspected risk factors and then they deal, in the next table, with family habit factors?

A. Yes.

Q. So that it is the case that those family habit factors, such as playing on the beach and so on, are being considered because they are a particular type of possible risk factor - eating shellfish, playing on the beach, and so on?

A. They are a particular type of risk factor that would be associated with a single positive risk that was behind that, that eating shellfish and playing on the beach and so on would imply that, in their minds from the description before, there is some radiation that is being absorbed from the sea in some senses.

Q. Yes, I see, but they are looking at....?

A. I think that you wish to make them all into separate hypotheses and neither I nor Gardner would have regarded those as each separate and independent hypotheses.

Q. But things like socioeconomic factors, maternal age, maternal x-rays, occupations, exposures to different things, chemicals, radiation....?

A. Yes, some of those are separate hypotheses.

Q. You are quite right. It may be a matter of, in a sense, classification as to how many hypotheses you come up with at the end, as to whether you say there are 10 or four or two?

A. Yes.

Q. But the fact that the authors of the paper were not merely testing one hypothesis is a factor which one should take into account in interpreting the results?

A. Yes.

Q. Even if, and I understand that you do not subscribe to the suggestion that one should actually make a mathematical adjustment?

A. I think that you may do, but you may not.

Q. You may do, you may not. Gardner did not?

A. No.

Q. And you have not, I think?

A. No.

Q. MR. JUSTICE FRENCH: What, made an adjustment?

A. Made any mathematical adjustment.

Q. MR. ROKISON: I think we have already discussed as a matter of theory the nature of the adjustment that one would make if one were to make one?
A. Yes.

Q. And the extent of that adjustment may depend on one's opinion as to the number of hypotheses one is testing?
A. And also to your view of epidemiology, yes.

Q. MR. JUSTICE FRENCH: When you say "make a mathematical adjustment," to what element in the expressed conclusion would you make an adjustment?
A. You can make an adjustment to the P value or, equivalently, the width of the confidence interval.

Q. If you make an alteration to the P value, that will automatically alter the confidence limit?
A. Yes.

Q. If you make an alteration to the confidence limits, will that also alter the P value?
A. Yes, they are inextricably intertwined.

Q. So, I mean, as a proposition, that is right?
A. Yes.

Q. Whether there is any need for me to understand the nature of the intertwining, no doubt, will appear. At the moment I do not understand the intertwining of the P value and the confidence limit. So the answer is, "One would have to make a mathematical adjustment to the P value." I think that is probably enough.

MR. ROKISON: May I just give your Lordship the reference again, without asking your Lordship to look at it again? The questions which were asked on the theory of this, before I came to deal with the Gardner study itself, are on Day 15, at pages 47-48.

MR. JUSTICE FRENCH: That is dealing with confidence limits and P values?

MR. ROKISON: What it is dealing with is the way in which you will, if you are going to do so, take account of the fact that you are testing for a number of hypotheses:

Q. Basically, I think your evidence was, Prof. Evans, that when you get to large numbers, there is a rather complicated way of doing it by something which I think is called a Bonferroni. Is that not right?
A. That is one of the rather naive ways of dealing with it.

Q. Well, I stand as being someone who is naive in these matters, though it is something, I think, which you yourself did mention in your evidence. I think you said that, where you are dealing with small numbers, then a

permissible approach is simply to say, "If I am testing for 10 hypotheses, then I will multiply my P value by 10"?

A. No, even at 10, that would not be the right thing to do. Even in the most crude way, you should only be multiplying it by 8.

Q. No, I think you said you are not quite multiplying by 10?
A. That is right. At two, then that might be reasonable.

Q. Can we just look a little further on in the Methods paper at page 430, and the next point I wanted to mention and to ask you about was the inclusion of non-Hodgkin's lymphoma?
A. Yes.

Q. Which you see is mentioned at the top of page 430 on the right, where they set out the reason why they have included non-Hodgkin's lymphomas, and they say the reason is because there is evidence of some relation with radiation. Just pausing there, are you aware of such evidence?
A. I think I stated that in Draper, where they are combined, there appears to be, but I think I would have to agree that, from my reading, there is only very rarely statistically significant evidence of a raising when considering non-Hodgkin's lymphoma on its own. I would have to bow to others in that.

Q. Very well. May I just ask you this, and if the answer is no, I am not going to take you to it. Have you read a review paper by Boyce in relation to the possible association between non-Hodgkin's lymphoma and radiation?
A. I recall seeing the paper, but I have no familiarity with it.

Q. Then I will leave it and deal with it with somebody else, thank you. The other justification given is because non-Hodgkin's lymphoma could have been confused with leukaemia during the early years of this study. That is a diagnosis problem, as I understand it?
A. Yes.

Q. You have explained why you thought it was a good idea to include Hodgkin's Disease, although it was not thought to be related to radiation, because it helps, in a way, to see whether there is a recall bias?
A. Yes.

Q. We have already looked to the question of the exclusion of some of those who were the subject of the cluster examined by the Black Committee, and I am not coming back to that. You will see lower down page 430 they make the point that they have included only cases in people born and diagnosed in West Cumbria and omitted six cases of leukaemia and eight of lymphoma in people born outside. So it appears that it is not only the two Seascale

diagnosed cases born outside who have been excluded but, taking the breadth of the study as being extended to embrace West Cumbria, they identified six cases of leukaemia and eight of lymphoma in people born outside, which were excluded because they narrowed the study, in the first instance, to those who were born there?

A. Yes.

Q. Just coming over the page to the selection of the two control groups - the area controls and the local controls - as you know, the epidemiologists to be called on behalf of the Defendants are of the view that it is perhaps more appropriate, when considering the hypothesis which we are considering for the purposes of this case, to look to the local controls rather than the area controls. Would you agree with that?

A. I think I have stated on more than one occasion in my evidence that I think it is better to look at both together, but if you were forced to look at only one then the local controls have certain advantages. There are also dangers inherent in looking at them alone.

Q. The point which is made by the authors of the paper in their Methods paper, in the second paragraph on page 431 on the left, is that the area controls were particularly relevant to the geographical analysis, which they mention in study aim 2, so that they, I think, particularly introduced area controls because of that aspect of their study?

A. Yes.

Q. Of course, in relation to the question of, for example, where one examines a hypothesis such as my Lord is examining, what we have called the Gardner hypothesis, if one finds that there is a larger relative risk if one is comparing with area controls and a smaller relative risk when one is comparing with the local controls, insofar as one is considering Seascale cases, would that be a matter which would, in a sense, illustrate some other Seascale factor?

A. I think you need to break that question down and I am not quite....

Q. What I have in mind is this, that supposing that you have - take Seascale cases?

A. Yes.

Q. If you find that, if you examine the hypothesis in relation to the local controls?

A. Yes.

Q. And you examine the hypothesis in relation to area controls?

A. Yes.

Q. And you find there is a greater relative risk if you relate it to area controls than local controls. This would suggest to you that, if there is any reason behind

the difference, it would be some Seascale factor, would it not?

A. No, I do not think so necessarily. Can I just clarify? You say Seascale factor as if you were meaning a geographical thing.

Q. Some factor associated with Seascale as opposed to being some factor applying more widely that might account for that difference?

A. It might suggest to you that there was something special about Seascale people. Not necessarily the fact that they lived in Seascale, but some special factor.

Q. Yes, that is what I had in mind. I agree it would only be a suggestion?

A. Yes.

Q. Particularly if the results were not very far apart?

A. Yes.

Q. Can I then ask you to go to the Results paper? I think that is all I wanted to ask you for the moment in relation to the Methods paper. I think you said in your evidence in chief - I can find the reference if you like, or those behind me can - but I think that its findings were not exactly as people had anticipated?

A. Yes.

Q. Did you mean that the hypothesis that we call the Gardner hypothesis was something which caused some surprise?

A. I think that there are two aspects to that. First of all, there are the findings, and the findings are that the association is with parental exposure, and you are pressing it to be that there is a specific hypothesis that Prof. Gardner suggested as one of the things and was one of the possibilities seen before, but I think that parental exposure and that mechanism was probably more surprising than the association itself.

Q. Than the association - by that, you mean....?

A. With parental exposure, and paternal exposure in this instance.

Q. MR. JUSTICE FRENCH: Yes, I was wondering whether one should write "paternal" for "parental"?

A. Paternal there, yes.

Q. MR. ROKISON: It was that which you say was surprising?

A. No, I think the hypothesis was surprising. I think the association with paternal dose is itself not a hypothesis.

Q. No, indeed.

Q. MR. JUSTICE FRENCH: What I have written is this: "The finding that it was connected with paternal exposure

was more surprising than that it was connected with radiation." I think I have compressed that too much?

A. I think that the hypothesis that it was genetic in some senses was more surprising than that the association was with paternal exposure, so I think it is the genetic aspect that was particularly surprising.

Q. Would you say that again? I will strike out what I read. Would you say it again?

A. I think the hypothesis that there was a genetic mechanism was more surprising than the finding of an association between paternal exposure and risk, of leukaemia obviously.

Q. MR. ROKISON: But, as the authors of the report are at pains to point out, what they are reporting as having observed by their study is an association?

A. Yes.

Q. And they are not themselves, in their paper, concluding that this reflects cause and effect?

A. No.

Q. Indeed, if one goes to the last paragraph of the study on page 428, at the bottom on the right, they make the qualification:

> "If the associations reported in this paper are causal they need to be explored further," and so on.

Then again, in their very last sentence:

> ".... if these results have causal significance then they are of much importance to radiological protection," and so on.

A. Yes.

Q. That shows that the authors are going no further than reporting the association which they observed?

A. Yes.

Q. Although it is true to say that there is some speculation as to what mechanisms might be responsible if there is cause and effect?

A. Yes.

Q. So what I do not quite understand for the moment is you have made the statement that its findings were not exactly as people had anticipated, and its findings were the associations which they found in their study?

A. Yes.

Q. With paternal preconception radiation?

A. They were not as anticipated, but you then wanted to say "very surprising" or "strikingly surprising".

Q. Not necessarily "striking", although we referred to how Prof. Greaves described it, but it was that association with paternal preconception irradiation which was not something which had been anticipated?
A. Not by many people, no.

Q. I will leave the Abstract for the moment, if I may. We will just look again at the form of the paper and one or two of their observations. They refer to their Methods paper and one sees that at the break on the right at page 423, about three-quarters of the way down, they say:

> "The analysis was carried out within the sets of cases and area or local controls...."

A. I think this is the Results paper, not....

Q. Yes, sorry, it is. That is what I was looking at now?
A. Sorry, and so you are referring to methods within the Results paper? I am sorry, I turned to....

Q. I am referring to where they summarise their methods within the Results paper, where they say - it is about three-quarters of the way down on the right-hand side:

> "The analysis was carried out within the sets of cases and area or local controls, and findings are presented as relative risks with confidence intervals."

Then they say how it was calculated using conditional logistic regression analysis, which produces estimates of odds ratios that approximate closely to relative risks, and you have described that to my Lord?
A. Yes.

Q. There is just one thing that I did not quite understand in your evidence. It is, as I understand your evidence, that Prof. Gardner is an eminent medical statistician and that Prof. Gardner has done as good a job as one could have done?
A. Yes.

Q. What I was wondering was why you reach that conclusion, bearing in mind the way in which he presents his results, when you yourself, when doing a re-working of his study, omitted confidence intervals because you say, as I understand it, that they have no scientific validity?
A. No, what I say is that is completely misunderstanding my evidence. If I had said that, that was in the context of calculating lots of confidence intervals as if that was going to tell you more than calculating the regression slopes.

Q. Oh, I see.
A. That is the point.

Q. Yes, I see. I had misunderstood it. It was perhaps because....?
A. Certainly I have written papers glorifying the use of confidence intervals, so....

Q. Confidence intervals are there because they tell you something about really the power of the conclusion to which they relate?
A. Yes.

Q. And, as you yourself said in your evidence, I think you gave an illustration, did you not, that if you have a relative risk of 30, with a confidence interval of, let us say, minus-2 and 100 - let us take a really extreme example?
A. You cannot have a negative relative risk.

Q. Not in this context, all right.
A. Okay, but some difference. If it was a difference in blood pressure between two groups, you could.

Q. Quite. Even in that case, let us find a confidence interval of 0.5 and 100?
A. Yes.

Q. With a relative risk of 30. That would be, in a sense, a less powerful conclusion, if I can use a non-scientific term, than a relative risk of 8 with confidence limits of 6 and 10?
A. Yes.

Q. Therefore, it is, where one is looking at relative risk, assuming that that is what one is wanting to show in the study?
A. Yes.

Q. But if one is looking at relative risk, it is useful - indeed, it is relevant and perhaps important - to show what the confidence intervals are for that relative risk?
A. Yes.

Q. We have seen, as they state in their Results paper as well as their Methods paper - and they state it at 424 - why they have presented NHL and leukaemia together?
A. Yes.

Q. I think in your evidence you said to my Lord that the question as to whether they ought to have taken NHL and leukaemia together and whether one can draw conclusions or what conclusions one can draw from the results in those circumstances, I think you said it is a fair point to make, but if we assume that leukaemia has an association with parental, paternal, irradiation, but NHL does not, on that assumption, then including NHL will dilute that association?
A. Yes.

Q. In your results?
A. Yes.

Q. But it is right, is it not, that the other side of the coin is that, if one makes that assumption, that leukaemia is caused by parental irradiation and NHL is not, it may be that it will dilute the association so far as leukaemia is concerned, but it may suggest to you, quite wrongly, that there is an association between NHL and leukaemia?
A. Yes.

Q. I mean NHL and irradiation?
A. NHL and irradiation.

Q. Would you agree that looking at the Gardner study ---

MR. JUSTICE FRENCH: Forgive me, I am sure the proposition is clear but I am afraid I have not grasped it.

MR. ROKISON: May I put it again, my Lord, because it is clearly of some importance?

MR. JUSTICE FRENCH: Yes, I can see that it may be.

Q. MR. ROKISON: You have said that it is a fair point to make, and with respect the point you made was a fair point to make, namely that if one assumes that leukaemia was caused by paternal pre-conception irradiation and NHL was not ---

MR. JUSTICE FRENCH: Perhaps I had better write it all down. "If one assumes that leukaemia ..."

MR. ROKISON: Was associated, is the way I put it, with paternal pre-conception irradiation, but NHL was not, then including NHL with leukaemia will dilute the association with leukaemia.

MR. JUSTICE FRENCH: That I have got. It is the next bit that I am finding elusive.

Q. MR. ROKISON: I put, and I think Prof. Evans agreed, that the other side of the coin is that on that same assumption, namely that leukaemia is associated with paternal pre-conception irradiation but NHL is not, your results may suggest to you that NHL is associated with parental pre-conception irradiation, when in truth it is not?
A. Yes.

Q. MR. JUSTICE FRENCH: Properly so regarded, does it suggest that?
A. Well it is a possibility, and that is what was put to me.

Q. I am just wondering on what the possibility is based. Is it based on a misunderstanding of the nature of the

exercise or is it based on some legitimate misconstruing of the evidence, or misconstruing of the results, to be more precise?

A. I think there would be a danger in over-interpreting the two combined.

Q. A danger of ....?

A. Of assuming that they were both associated strongly when you combine them.

Q. If you lump together chalk and cheese, then there is a risk that somebody looking at a heap and seeing a lot of cheese may think that the chalk is cheese-like?

A. That's right.

Q. But that is a simple error of observation?

A. Exactly.

Q. MR. ROKISON: It may be an error of observation, but the point is this, is it not, that if you are going to do a study in which you consider leukaemia and NHL together, which you may do because there are possible difficulties in the diagnosis of some of the earlier cases, the danger which you point out, which is as you call it a danger of interpretation, is drawing conclusions from your study and concluding that they necessarily apply both to NHL and leukaemia?

A. Yes.

Q. Because it may be that they do not actually apply to the one or to the other and that the collective results are effectively driven by the factor which is truly associated?

A. Yes.

MR. JUSTICE FRENCH: I still find it elusive, I am afraid. I am sure it is my fault.

MR. ROKISON: As I say, it is or may be in this case of some importance.

Q. Can I just ask you this, Prof. Evans: in reaching the conclusions which you reached as a statistician in your report and which you expressed, did you consider to what extent there was good evidence in the Gardner study or elsewhere that NHL was causally linked to paternal pre-conception irradiation?

A. I didn't look at NHL on its own in any of the analyses I did.

Q. MR. JUSTICE FRENCH: You made an assumption that the two diseases were sufficiently closely related?

A. Yes.

Q. But if told they are not at some stage, then you have to take them out of your calculation?

A. Yes.

Q. I do not see the difficulty. I can quite see that one may have a pre-conception which proves wrong?
A. Yes.

MR. JUSTICE FRENCH: I cannot see any greater inwardness to it than that. Mr. Rokison, if it is necessary for me to understand it, I am afraid you must have another go, if there is a deeper inwardness than that.

Q. MR. ROKISON: The point is simply this, Prof. Evans, is it not: that it may or may not be - and that is a matter which may be investigated hereafter - that leukaemia and NHL, speaking generally, and in particular a particular type or classification or category of NHL, are sufficiently similar for them to have similar aetiology?
A. Yes.

Q. That is a matter which has not yet been investigated. But if you carry out a study looking at leukaemia and NHL together, not because you decide that they are so similar that the same must apply to both, but you do it because it is simply difficult to distinguish or may be difficult to distinguish in some of the cases that you want to study, which it was, then if you come up with results for NHL and leukaemia together, you cannot necessarily draw conclusions from those results in relation to either leukaemia or NHL alone?
A. No.

MR. JUSTICE FRENCH: You have got to separate them out and do your sum again.

MR. ROKISON: Indeed.

MR. JUSTICE FRENCH: Perhaps I was grasping at the obvious. I thought it was more esoteric.

Q. MR. ROKISON: Your position is, as I understand it, that in expressing the conclusions that you have in your report, conclusions in relation to Dorothy Reay and Vivien Hope, you have simply assumed that the overall association in respect of leukaemia and NHL together applies to each?
A. I think at the end of my evidence I was asked specifically what my view was, and my view was that essentially leukaemia was more likely to be associated than non-Hodgkin's lymphoma, but that overall I was convinced that there was some association with non-Hodgkin's lymphoma, even though I have not specifically done each of the separate analyses.

Q. When you say that you were convinced that there was an association with non-Hodgkin's lymphoma, are you saying that you think that if the same exercise were done for non-Hodgkin's lymphoma on its own, it would produce a similar picture?

A. No, I think it would produce a weaker picture. My view is that it is not as strong an association but, on the balance of probabilities again, I think it is likely to be a genuine one.

Q. But you have not done the exercise and you do not know what the figures would be?
A. I haven't specifically in this re-analysis, but looking at Gardner's presentation and the other work, Draper's work and the other work, looking at them separately and combined, it is clear that the associations with leukaemia are always stronger, or in virtually every instance stronger than those with leukaemia and non-Hodgkin's combined.

Q. The fact that the associations with leukaemia are stronger than the associations with leukaemia and non-Hodgkin's combined shows at least that the association between NHL and parental pre-conception irradiation is weaker, is that right?
A. There is a tendency for it to be weaker, and, more importantly, because the numbers involved are smaller it will always have less power to determine that.

Q. With respect, that is not right, because if you are bringing them together, you will increase the power, so the fact that where you have leukaemia figures on its own, the association being stronger than leukaemia and NHL combined would run contrary to that, because you would expect, if the association were the same, that the picture for the two combined would be stronger because of the larger numbers, would you not?
A. No, you won't expect the association to be stronger, but you would expect the confidence interval to be narrower.

Q. The overall picture would be a stronger picture?
A. It may help to go to a specific point if we go to Table VI of Gardner's results paper on page 426.

Q. Yes, by all means.
A. If we look in Table VI at the results for leukaemia and total dose before conception, greater than 100 mSv ---

MR. JUSTICE FRENCH: Wait a minute, I want to make sure that I am following this. I have got Table VI.
A. We move down to the third block there, "Total dose before conception" and we look at the third category in that, which is the highest dose category ---

Q. 100 mSv?
A. Yes. We find there, for example, that for area controls the relative risk is 6.24, and if we were to look further down into the next table in the equivalent position for leukaemia and non-Hodgkin's lymphoma, we find that the relative risk is 6.42 and is actually fractionally greater, so that implies that in that set of data the association with non-Hodgkin's lymphoma is actually slightly stronger than that for leukaemia.

Q. MR. ROKISON: Let us just analyse that a little further. How many cases have you got for leukaemia in that highest dose category in area or local controls?
A. Four.

Q. How many cases have you got for leukaemia and non-Hodgkin's combined?
A. You have got four; there are no cases.

Q. They are the same, are they not?
A. Yes.

Q. So you do not have any NHL cases at all in that top category?
A. But you don't have any NHL controls either.

Q. Never mind about that. If you were to do the exercise - we have not done the exercise completely but you have taken this example - if you were to do a similar exercise with NHL alone, you would find that in your top category you had no cases?
A. Yes, and no controls.

Q. You cannot draw any conclusions about an association from that, can you?
A. Not from categorising it, and that is why it would be more sensible to look at slopes.

Q. It was you who went to this Table in order to make your point.
A. Yes, but what I am saying is that the pattern we have, if we look at the pattern elsewhere in Draper's study, you find similar sorts of things, that sometimes the strength of the association is as great and sometimes it isn't.

Q. The point is that the difference between the strength of the association, bearing in mind that you have no NHL cases in that high dose category at all, if you have no high dose cases, you have the same number of cases for leukaemia as you do for leukaemia and lymphoma, and because the cases have matched controls, you have the same controls as you are bound to do - no, you will not, will you? - but you have in this case the same number of controls as well, do you not?
A. Yes.

Q. So that in arriving at your relative risk, you are looking at the same cases and the same controls?
A. In the highest dose, but you are also comparing that by implication with the zero dose.

Q. Exactly.
A. And that is where the difference lies.

Q. Exactly, and the difference lies because you are comparing them with the cases and controls of no dose at all?
A. I agree that my picking on that particular thing was not the best thing to make my point, but the general pattern

that one sees is that the strength of the association with non-Hodgkin's lymphoma is rather less; but there are occasions when it is stronger.

Q. This is one that you have pointed out, but it does not arise from the fact that there is any NHL case in the category that is being considered?
A. In having considered categories, yes.

Q. But they are the same cases? The fact is that there is no NHL case which is the subject of the Gardner study which is above 100 mSv?
A. Yes.

Q. If one just goes down and looks at the second one, the category of 50-99, it is true that there is, it appears, an NHL case?

MR. JUSTICE FRENCH: Sorry, where are we looking now?

MR. ROKISON: At Table VI, my Lord, there is an NHL case, because combined there are two, and if you look only at leukaemia, there is one. Is your Lordship following me?

MR. JUSTICE FRENCH: I am afraid I am not.

MR. ROKISON: My Lord, look at Table VI on page 426 and look first of all at leukaemia, which is the top half of it, and if you look just over half-way down that, you will see "Total dose before conception".

MR. JUSTICE FRENCH: Yes.

MR. ROKISON: If you look to 50-99 mSv, you will find there "Cases 1". Does your Lordship see that?

MR. JUSTICE FRENCH: Yes, I have got that.

MR. ROKISON: It is obviously the same number when compared with area or local controls. If you look into the lower table which is leukaemia and non-Hodgkin's lymphoma, one finds in the parallel position "Cases 2".

MR. JUSTICE FRENCH: Yes, 50-99, two cases.

MR. ROKISON: So that shows that you had one NHL case within that dose category.

MR. JUSTICE FRENCH: Yes, I follow.

MR. ROKISON: That is the point, my Lord.

Q. So there were two NHL cases who had a dose, one being in the lowest category and one being in the 50-99 category and that is all, and my suggestion to you would be that

almost whatever exercise you did in relation to that, if you only have two cases who have a dose and if you were to do the exercise of looking just at NHL, you really could not draw much conclusion from it?
A. No.

Q. Would you agree?
A. On that alone.

Q. Thank you. May I come to your own report, if I may? At paragraph 52, page 19, you say:

> "The major finding of the Gardner study was that there was a clear link between excess leukaemias and the children who had fathers working at Sellafield?

A. Yes.

Q. You go on to say:

> "It showed that the children of fathers working at Sellafield prior to the child's conception had approximately a twofold higher risk of developing leukaemia or NHL than control children".

Where you refer to a clear link, do you mean a statistically significant association?
A. Yes.

Q. If you look at the Gardner paper, that is the results paper, it is Table V, is it not, on page 425?
A. Yes.

Q. If you look at leukaemia alone, you find find that for leukaemia only the relative risk is 2.82 as against area controls?
A. Yes.

Q. But the confidence interval is 1.07 to 7.40, so it is marginally statistically significant?
A. It is statistically significant, yes.

Q. Just?
A. Just.

MR. JUSTICE FRENCH: I want to make sure that I am looking at the right bit. I have got Table V and I look at Sellafield, do I?

MR. ROKISON: Your Lordship does, that is absolutely right. All these tables are divided into first of all leukaemia and then leukaemia and NHL. If you
look at the leukaemia table, which is the top part of the Table, in each case there is area and local, and what you are doing is comparing the number of cases which come within whatever description it is and the number of controls. So if you look at the Sellafield area, that shows that there were nine cases and 29 area controls whose fathers had worked at Sellafield.

Q. That is right, is it not, Professor?
A. Yes.

Q. Similarly if you look at local cases, inevitably, as in all these, you get the same number of cases, so there were nine cases and 41 local controls who had worked at Sellafield, although there was an overlap between local and area controls, was there not?
A. Yes.

Q. Because of the way in which they were selected?
A. Yes.

MR. ROKISON: So they are not necessarily a different 41, my Lord. The 29 of area would include some of the local.

MR. JUSTICE FRENCH: Yes, I follow.

MR. ROKISON: But one does this separate exercise and what one finds is that for association with paternal occupation at Sellafield, the relative risk is 2.82, but it is just statistically significant because the lower 95% confidence interval is just over one.

MR. JUSTICE FRENCH: Yes, just over one, i.e. 1.07.

MR. ROKISON: Yes, my Lord.

Q. Prof. Evans, if you look and compare with the local controls, where you have a larger number of controls who fall within the category of working at Sellafield, you find that your relative risk is 2.03, which is not statistically significant?
A. No.

Q. It is not just marginal, it is quite a way from being statistically significant, is it not?
A. Yes.

Q. If you look at leukaemia and NHL together, you see the numbers there set out?
A. Yes.

Q. It is clear from that, is it not, that you only have one case of NHL with a father who worked at Sellafield?
A. Yes.

Q. That is the difference between the 10 and the 9, so there is only one NHL case whose father worked at Sellafield?
A. Yes.

MR. JUSTICE FRENCH: Combining NHL and leukaemia in Table V shows only one NHL father who worked at Sellafield?

MR. ROKISON: Yes, my Lord.

Q. It also shows that the relative risk, when compared with area controls and local controls, is in neither case statistically significant?
A. No.

Q. MR. JUSTICE FRENCH: No, that is right, or no that is wrong?
A. No, that is right.

Q. As being what the figures show for area and local, neither is statistically significant?
A. Yes.

Q. MR. ROKISON: Of course, you would very fairly rely upon the relative risk of 2.02 when compared with area controls, but if you compare the total cases with the larger number of local controls, you find that your relative risk is only 1.32 and your lower 95% confidence interval is as low as 0.51?
A. Yes.

Q. Which is quite a way from statistical significance?
A. Yes.

Q. Would you agree, therefore, that the way you put it in the first two sentences of paragraph 52 of your report is putting it a bit high if you were attempting fairly to summarise what is shown in Table V?
A. If it was only based on Table V, yes, but I am looking at the whole thing in regard to doses and so on.

Q. You are not at that point, are you? You go on to deal with doses. In those sentences, you are dealing with what you call the clear link between excess leukaemias and the children who had fathers working at Sellafield, and I suggest that it is not a very accurate summary of what the Gardner report actually tells us in that regard?
A. I think I would have to agree that if you interpret my words that precisely, it is overstating the case.

MR. ROKISON: That is very fair, thank you. My Lord, would that be a convenient time? I am going on to another topic.

MR. JUSTICE FRENCH: Yes.

MR. ROKISON: May I just say that your Lordship indicated that we might review the position to see if your Lordship were to be good enough to sit a little longer today, we would be able to finish this part of Prof. Evans' cross-examination. The answer is that we will not, my Lord.

MR. JUSTICE FRENCH: Not need to sit late?

MR. ROKISON: It is not just that we will not need to sit late.

MR. JUSTICE FRENCH: You mean we will not get anywhere near finishing?

MR. ROKISON: We will not get near finishing, I am afraid.

MR. JUSTICE FRENCH: I had a sneaking feeling that that might prove to be the case.

MR. ROKISON: So we will have to discuss between ourselves if we may, in the first instance, arrangements as to when the evidence on that aspect is to be completed. May we discuss it first and then discuss it with your Lordship?

MR. JUSTICE FRENCH: Of course, and you will let me know how it presents itself to you both at 2 o'clock.

MR. ROKISON: Thank you, my Lord.

(Luncheon Adjournment)

MR. ROKISON: My Lord, we have discussed the question of timing with Prof. Evans and although for my part I would have been prepared, subject to your Lordship's approval, to have split the balance of my cross-examination, had that been more convenient to Prof. Evans, I think he has decided that he would rather get it done at one session and therefore will be returning, subject to your Lord's approval, on Friday morning, with the hope that he will finish his evidence on Friday. We are confident that that can be done.

MR. JUSTICE FRENCH: Does that include the reserve bits?

MR. ROKISON: No. That will involve a little time. I am sorry, Prof. Evans is shaking his head.

PROF. EVANS: It isn't because I want to get it over with but it was clearly inconvenient to people for me to be here on Friday afternoon and then Monday afternoon because Monday morning and Friday morning are both inconvenient.

MR. ROKISON: I did say, and obviously I don't want to spend time now, but I certainly said to Prof. Evans that for my part, in order for him to be able to teach his students on Friday, that I would have been prepared to have continued my cross-examination on Friday afternoon and then on Monday afternoon if that had suited him.

MR. JUSTICE FRENCH: When you speak of finishing you mean only finishing the cross-examination and not the re-examination?

MR. ROKISON: No, my Lord, I don't. I mean finishing the cross-examination and the re-examination upon that cross-examination, as I understand it.

MR. JUSTICE FRENCH: With any luck we shall finish all that by close of play Friday?

MR. ROKISON: Yes, my Lord.

MR. JUSTICE FRENCH: You have considered the knock-on effect on Scott Davis?

MR. ROKISON: Obviously that is a matter that has been taken into consideration, my Lord:

Q. I was asking you about paragraph 52 of your first report, and I had asked you about the occupational association appearing from table 5. You then deal with the results in table 6?
A. Yes.

Q. I think in giving your evidence you said that in looking at a table such as this you would look to see whether there was evidence of a substantial risk, which I think you described as a relative risk of 2 or more?
A. Yes.

Q. Secondly, you had looked to see whether the relative risk tended to go up as the dose went up?
A. Yes.

Q. So far as the total preconception doses are concerned, you would agree that within each of the dose categories there are a fairly small number of cases?
A. Yes.

Q. It follows from that that the confidence limits are not very narrow?
A. Yes.

Q. In fact if one looks at the tables, total dose before conception, leukaemia alone, 1-49, you have got 3 cases. You have got a slightly elevated relative risk as compared with the area controls and the rather greater diminution in risk when you look to your local controls. However, in each case your confidence limits are very wide?
A. Yes.

Q. It could very easily embrace 1 somewhere in the middle ground, or thereabouts?
A. Yes.

Q. So far as 50-99 is concerned, one finds in both cases, area and local controls, there is an apparent diminution in risk, but also with wide confidence limits?
A. Yes.

Q. If one compares very quickly with leukaemia and NHL, as we have already seen, you have 1 NHL case in the 1-49 category and 1 NHL case in the 50-99?
A. Yes.

Q. One finds that the relative risks in relation to each of those, whether area or local controls, is somewhere spread around the 1?
A. Yes.

Q. As indeed will be your fairly wide confidence intervals?
A. Yes.

Q. If one had stopped there it would tell you really very little? One might almost say it would tell you virtually nothing?
A. Yes.

Q. Where, and this is the point...

MR. JUSTICE FRENCH: This is table 6?

MR. ROKISON: Table 6, my Lord. As I say, if you had stopped there...

MR. JUSTICE FRENCH: Yes, Table 6 by itself would tell us virtually nothing?

MR. ROKISON: No, my Lord. That would be putting it too high and not what I was putting to Prof. Evans.

MR. JUSTICE FRENCH: Tell me how I should correct that?

MR. ROKISON: My Lord, yes. If one looks at the total dose before conception, either for leukaemia or leukaemia and NHL...

MR. JUSTICE FRENCH: If one looks at total preconception, whether for leukaemia or leukaemia plus NHL, it tells us virtually nothing?

MR. ROKISON: No, my Lord. If one looks at the first two categories of dose, that is, 1-49 and 50-99, it tells one virtually nothing because the relative risk is spread around and the confidence limits, because of small numbers, are very wide.

MR. JUSTICE FRENCH: Yes, I have got it.

Q. MR. ROKISON: If one looks at the greater than 100 mSv figure, it is that, in relation to total dose, which you point to in paragraph 52?
A. Yes.

Q. One can see that one has an elevated relative risk of 6 to 6.5 against area, just short of 8.5 as against local, taking either leukaemia and leukaemia and NHL together,

with again wide confidence limits but confidence limits where the lower level is over 1?

A. Yes.

Q. However, they are confidence limits where the lower level is done - well, it is about 1.5?

A. Yes.

Q. Which, because of the wide confidence limits and small numbers, is, I suggest, not a very strong association?

A. I would say that there is evidence of what may be a strong association.

Q. I would not quarrel with that. I would not quarrel with your saying there is evidence of what may be a strong association. What I would simply say is that looking at those figures, you cannot look at that and say that that is a strong association?

A. No.

Q. I know that you subsequently carried out your regression slope analysis and that is a matter about which I am going to ask you in due course but not at the moment. Prof. Gardner did not, and without doing a regression slope analysis would you agree that simply looking at those categories there would appear to be no clear dose response relationship?

A. No, I disagree.

Q. You disagree?

A. Yes.

Q. Prof. Howe will say, and no doubt others as well, that when they look for a dose response relationship what they look for is a tendency for the relative risk to rise with the dose?

A. Yes.

Q. That if they see over - if one assumes that the hypothesis one is testing is a hypothesis which has a linear relationship, then if what one finds is, for example, in a series 1, 1 and 10, or if one assumes a zero dose gives you 1, where you get 1, 1, 1 and 10, or 1, 1, 1 and 7, or whatever it might be, that they would not regard that as being a dose response relationship which would lend support to a causation theory?

A. If the confidence limits around those 1s for the intermediate categories was very narrow, then I would agree with you. When the confidence limits are so wide, then you would expect a test for trend in the table to nevertheless show a trend.

Q. You may expect it to show a trend, but to the extent to which it does show a trend of course it will be driven by the high dose category, will it not?

A. Yes.

Q. Whether you do a score test for trend or whether you do a regression slope analysis, your slope, insofar as you get a slope, will in those circumstances be driven by your high dose category, won't it?
A. Not the high dose category when you then do it...

Q. High dose cases within that category?
A. High dose cases overall, and within all the categories. The question would be whether the higher the dose the higher the risk.

Q. But you may find, and I anticipate more detailed questioning at a later stage in relation to the regression slope, that where you are doing a regression slope you may find that your slope may be to a large extent dictated by, for example, one very high dose case?
A. I think again if you now go back to the categories, I think that the test for trend - for example, Prof. Peter Smith, who I think was one of your experts, or an adviser to BNFL, in his comments he did a chi-square test for trend on the preconceptional total doses in table 2 of one of his papers. It is not driven by a single case, no.

Q. Forgive me, a test for trend such as that which Prof. Gardner carried out, is a test for trend across the categories, is that right?
A. Yes.

Q. To that extent the trend with these sort of figures would largely be dictated by the high dose category?
A. Yes.

Q. Whereas in a regression slope analysis, your slope may be dictated by one or more very high dose cases?
A. Less likely in a logistic regression than in other regressions, but nevertheless it is conceivable that a single case could...

Q. Could effectively be what is producing the slope?
A. It could be.

Q. That danger - I will come back to it with you, if I may - that danger is obviously all the more if you only have a few cases in your study. Obviously if you have a large number of cases in your study...
A. Yes, I am presuming it is a small number...

Q. As here?
A. Yes. In a very large study a single case is much less likely to affect it.

Q. If one is carrying out, and I think we have in a sense covered this, but if one is carrying out a study of categories, as has been done here, then you agree that by simply showing a relative risk, and I think you yourself have made the point, without looking to see what the confidence intervals are you may get a very - well, if not misleading, certainly a partial picture?

A. Yes. It is possible, of course, to have a significant trend when all of the confidence intervals overlapped 1.

A

Q. I can see that that is possible, but what I was asking you is, and I think you made the point in relation to the fact that when I put to you that if you have 1, 1, 1, 10, it would not be a dose response relationship, your answer was, "Well, it may reflect a dose response relationship because of the width of the confidence intervals around 1"?

B A. Yes.

Q. Therefore, what I was putting to you is that if you are depicting a relative risk by reference to categories, then if you simply look at the relative risk it may mislead you?

A. Yes.

C Q. So you are not suggesting, you are very far from suggesting that in doing his analysis in this way with relative risks and confidence intervals, that Prof. Gardner was somehow not doing it as well as he ought?

A. No.

D Q. What I don't quite understand is why, in those circumstances, when you did your category tables - I know you did a regression slope analysis as well - but when you did your category tables and presented them in your latest report, why it was you presented the categories without giving the confidence intervals?

A. Simply because I did not think that those particular categories were the best way of understanding any kind of dose response relationship. I gave the categories in

E order to be comparable with Gardner.

Q. But without the confidence intervals you are not comparable with Gardner, are you?

A. Well, I think I was more interested in the numbers and the confidence intervals were... In fact I did give confidence intervals for the highest dose category in my

F report. I certainly did in my second report...

Q. Yes, table 9.

A. In my third report I say that that is still relevant.

Q. Of course, what may be more important if one is looking for whether or not there is any dose response relationship, may be, as you say, the confidence

G intervals in the lower categories?

A. Yes, but I don't think that looking at the data in categories is the best way of looking for a trend and that is why I don't think that emphasising the categories and even the confidence intervals around them is the best thing to do if you are then going to do a regression analysis.

H

Q. The odd thing is, with the admiration which you have expressed not only for Prof. Gardner as a medical statistician, but also for the exercise which he did here, which you describe as being the best that he could do, he has done it in categories?
A. Yes.

Q. Do you know, and I don't think it is explained in the methods paper, why he chose the categories he did?
A. No.

Q. In particular why he stopped at 100?
A. No, but certainly if he extended it beyond, the numbers would become vanishingly small.

Q. Well, the numbers may become smaller to the extent that one may lose statistical significance?
A. Yes.

Q. On the other hand have you yourself done the exercise to see what happens if you split the "above 100" category into 100-149 and 150 and above?
A. No. That is exactly the sort of thing that I regard as one of the infinite ways of looking at the data.

Q. Quite. It would be as legitimate to do that as it would to stop at 100, presumably?
A. No. I think it is perfectly reasonable to stop at 100. People have that as a round number. I have a feeling, I may be incorrect on that, that that was one of the doses that has also been reported in other studies that people have categorised at that level. That is my recollection.

Q. There is no magic in it? If one has cases which have doses which are substantially above 100, that provided one doesn't carry it to the extreme where one finds that one essentially cannot get any result because one hasn't got a comparison between cases and controls that means anything, but subject to that there is no particular reason for stopping at 100, is there?
A. No. Had we had twelve fingers we would probably have stopped at 144.

Q. Would it surprise you if one were to find that if you take the category from 100-149, you find an elevated relative risk, but that at 150-plus you find that that has dropped substantially?
A. No, it wouldn't surprise me. I am sure I could find a set of categories that would appear to exaggerate the risk in some particular set of categories.

Q. Indeed. Perhaps taking 100 might?
A. No. If I had taken 95, for example, on the Gardner data that would undoubtedly have shown them.

Q. Yes. I am not suggesting that the categories were chosen in order to present something particularly. I am

merely saying, and perhaps it is an illustration of the point that you have made, that the categories are arbitrary and that one cannot, merely from looking at those categories which have been fixed in an arbitrary way, given the small numbers that you have, really draw any very firm conclusion about dose response?

A. What you are saying is if you categorise the data you can say nothing about dose response?

Q. No, not nothing about dose response. What I am saying is this: you have said yourself if you look at 1-49 and 50-99 that effectively tells you nothing?

A. Yes, on their own.

Q. Because of the wide confidence intervals, because of the spread of the figures around 1?

A. Yes.

Q. You, and, indeed, the authors of the report and those who have considered it since, obviously concentrate on the figures in the high dose category. They concentrate on that because it is only in the high dose category that one finds an elevated risk, an association shown?

A. Yes.

Q. Which is statistically significant?

A. Yes.

Q. The arbitrary nature of the exercise may be such that if you were to sub-divide that category further, you would find that although you may get a blip at a certain stage which happens to relate to one case which happens to have the right dose to give that blip, it could then fall away again?

A. Yes.

Q. In which case you would look at that and say, "Well, it doesn't seem to me that that shows me a dose response relationship"?

A. No, because the confidence interval now will be so wide and going up to such large values that you will look at the pattern overall still and the lower, what would now become an intermediate category of 100-149, may be the one that makes you think there is some sort of relationship.

Q. Well, it may make you think that there may be, but it would not show it?

A. You are telling me that if you sub-divide it into 100-149 that that has also a reduced relative risk, and the 149-upwards?

Q. No, that is not what I said. I said quite the reverse. What I said was that if you do divide it, and I can produce the figures to you...

A. Yes, it is a pity these aren't in the report I have seen so that I could reasonably comment.

Q. Indeed, I quite appreciate that and I was in a sense going to... I am not asking you in detail about figures at the moment. You will see these figures before you come back to answer questions in relation to your figures. I was merely putting to you by way of illustration that if it were the case - and my understanding is that it is the case - but if it were the case that if you divided up your greater than 100 into 100-149 and 150 and above, although you would get an elevated relative risk in relation to the category of 100-149, that that would then fall away again substantially in your highest dose category so that you would not, if you categorised it in that way, produce your highest dose, or your highest relative risk in your highest dose category? Do you follow?

A. I follow that, but to me that still isn't necessarily evidence that there isn't a trend.

Q. I agree.

MR. JUSTICE FRENCH: Forgive me, Mr. Rokison. Are you saying that the regression slope levels off or falls away?

MR. ROKISON: No, my Lord, it has nothing to do with the regression slope. One has to be very careful about this. I am not asking Prof. Evans about his regression slope.

MR. JUSTICE FRENCH: Let's forget the regression slope. You are talking about the dose response relationship falling away. At this stage can I pose the question: are you speaking of falling away in the sense that it reduces or are you speaking of falling away in the sense that it becomes less?

MR. ROKISON: No, it reduces.

Q. MR. JUSTICE FRENCH: Well, that is what is being put, can you give any answer to that?

A. I would say that that information on its own is not sufficient for me to say there is no evidence of a trend.

MR. JUSTICE FRENCH: The fact for doses of 1-149 and above?

MR. ROKISON: No, doses from... It is doses in excess of 150.

MR. JUSTICE FRENCH: The fact that for doses in excess of 150 mSv...

MR. ROKISON: The relative risk may be lower than that for 100-149, does not necessarily show that there is no dose response relationship.

THE WITNESS: That is it exactly.

MR. ROKISON: Does not necessarily show there is no dose response relationship, and we would agree:

A

Q. It follows from that, and I think you agree with me, Prof. Evans, that if you happen to choose categories arbitrarily which do show that your highest dose category has the highest relative risk, that doesn't necessarily show that there is a dose response relationship?

A. It doesn't necessarily show. All of it depends on the confidence intervals if you are going to do an analysis by categories.

B

Q. What your confidence intervals will show you, if you are going to do an analysis by categories, is the confidence that you can have in the relative risk shown for that category? That is what it shows you?

A. It does.

C

Q. What it doesn't show you is whether there is a dose response relationship?

A. No.

Q. It shows you no more than that the highest category you happen to have chosen arbitrarily gives you the highest relative risk and that that appears to show you a statistically significant association? It tells you no more than that, does it?

D

A. When you say "no more than"... I think I would find it very difficult to envisage a set of data in which the relative risks went 1, 1, 1 and the highly elevated number - all right, not necessarily particularly highly elevated but something like 6 or 8, something of that kind - where that was statistically significant and where when you did the proper trend analysis you would fail to find a trend. I cannot envisage a situation where that would be so.

E

Q. If you find something that goes, for example, 1, 1, 1, 8, 2, it may or may not be that there is an association. If there is an association then it may show a trend but what one cannot say is that, "Well, I look at that and see a trend and therefore that assists me in concluding that there is a true association"?

F

A. No, but I would carry out the proper analysis for a trend rather than all these hypothetical analyses.

Q. I ask you these questions - I appreciate your saying that you think the right thing to do here is to do a regression slope analysis on each individual case. I appreciate that and I will deal with it in due course, but at the moment what I am doing is looking at the Gardner report and what Gardner did and what conclusions one can draw from the Gardner report. We are doing it in stages as you indeed produced your evidence in stages.

G

A. Yes.

H

Q. All I am saying is that looking at the information on the categories one cannot say from this that there is or there is not a dose response relationship?

A. Yes, you can. You can do an unmatched analysis just by sitting down with your calculator and doing it.

Q. Again, supposing that...
A. Prof. Duncan Thomas did do such an analysis based on the group data which he provided in his first report.

Q. If you then divide your top category into different categories and it showed that the relative risk appears to go up and then goes down again, would that influence that in any way?
A. Well, if you had the data you would then be able to do that analysis and see whether there was a trend there and there may well be.

Q. There may be or there may not?
A. I think the odds are that there will be, given what you have described. However, if, for example, the relative risk went 1, 1, 8, 0.2, then that would mean it was much less likely there was trend, 0.2 being substantially less than 1.

Q. It will depend on where you set your categories and what the numbers within each category show you?
A. It would indeed.

Q. I don't think we can pursue that any further at the moment.

Q. MR. JUSTICE FRENCH: Am I right in thinking, Prof. Evans, that your last answer is really taking us back to where we were yesterday morning? Is that right or wrong, or is this new ground?
A. No, I don't think this is new ground.

MR. ROKISON: I am not quite sure which point your Lordship has in mind?

MR. JUSTICE FRENCH: The argument about choosing your points to demonstrate that you are less likely to die of heart disease in your eighties than you are in your seventies if you take the right point. I mean, is this a discussion of a different nature from that?

MR. ROKISON: It is only this, my Lord: I have canvassed with Prof. Evans a number of theoretical points and what I am now seeking to do in relation to the conclusions which he draws from the Gardner report is to apply those to the figures which one finds in the Gardner report.

MR. JUSTICE FRENCH: I entirely follow that. I saw that coming, with great respect. What I am wondering is whether I am in, as people say nowadays, the right ballpark?

MR. ROKISON: Yes, I think your Lordship is. Not much of a ballpark, but your Lordship is in it!

Q. Now you say that these findings which are depicted in tables 5 and 6 have two main strengths. You say they are consistent with the findings of Black and COMARE that leukaemia rates are raised in the vicinity of nuclear plants. Is that right?
A. Yes.

Q. Why does it tell you that?

MR. JUSTICE FRENCH: Where are we now?

MR. ROKISON: We are at the bottom of page 19 of Evans 1, paragraph 53:

Q. Gardner was not looking to see whether there was an excess or not, and it does not show you.... Those figures do not show you whether there is an excess or not, do they?
A. Table 4 shows that the risk falls with increasing distance from the plant.

Q. Oh, I see, forgive me. I thought you were referring to the findings which you had emphasised in paragraph 52.
A. The Gardner study.

Q. It is my misunderstanding, Prof. Evans. I had thought that where you were referring to the findings having two main strengths, that you were referring to the findings which you had summarised in the paragraph above. That is why I could not quite understand this point. You are referring to something different in 53A. What you are referring to is table 4?
A. I prefer to take papers, if possible, as a whole rather than piecemeal in the way that you do.

Q. That is unfair and, with respect, unjustified, because you set out in paragraph 52 what you rely on as being "the findings" and then you say that "the findings" have two main strengths. It would take somebody with a great imagination to realise you were not referring to those findings but some others. Now we have clarified the point, Prof. Evans, what you are relying upon in paragraph 53A is table 4, is it?
A. Looking at something more than that, in some senses it... You need to look at the conclusions here in Gardner, page 423, the abstract:

> "The raised incidence of leukaemia, particularly, and non-Hodgkin's lymphoma among children near Sellafield was associated with paternal employment and recorded external dose of whole body penetrating radiation during work at the plant before conception. The association can explain statistically the observed geographical excess."

The observed geographical excess is something that he discusses as having been raised during the Black Report.

Q. Of course, we understand and that has been found already. We know there is an excess, it was identified by Yorkshire Television, it was highlighted, if you like, in Black, and the Gardner Study was set up, in part, to try to find out whether one could find the cause of that excess?
A. Yes.

Q. We agree about that. What I simply do not understand is why you are saying the findings are consistent with that excess? We know that. That is the starting point, is the excess. That is something that has been established.
A. That sentence says:

> "They are consistent with the findings ... but that the given radiation emissions into the environment are not a sufficient explanation."

I cannot understand how 53a is at all controversial.

Q. Fair enough. If all you are saying there is that one of the strengths of this study is that it shows that environmental emissions do not appear to be the cause of the excess ....
A. Not a sufficient cause.

Q. Not a sufficient cause of the excess, then I agree, there is no controversy between us, and we can move on. The second strength of it, you say, is that there is evidence of a dose response relationship, and we have just been discussing that.
A. Yes.

Q. So far as the six month dose is concerned, I think it is fair to say that, as Prof. Gardner himself comments at the bottom of page 428, on the right:

> "... there is a more convincing trend of increasing relative risks of leukaemia for paternal radiation dose during the six months preceding conception than for total exposure."

Would you agree that what he has in mind is, in a sense, the point that I put to you, that as far as total doses are concerned you only effectively get an elevated risk in your last, in your highest dose category, but not in intermediate categories?
A. Yes.

Q. Whereas in relation to the six months dose you get broadly an increase in each of the dose categories?
A. Yes. I would not pay enormous attention to that, as you know.

Q. No, and would one of the reasons why you would not pay enormous attention to that really be for the same reason as that which we have looked at in relation to the total dose, that the confidence intervals which you have in

relation to the two lower of the three categories are very wide, and the lower confidence level is well below one?

A. That is part of the reason, yes.

Q. The other is that you do not think that doing it by categories is the best way to do it?

A. Yes.

Q. Page 428 of the Gardner Report - I think you have been asked about this passage but not the point I wanted to ask you about - on the left-hand side about a third of the way down that page, he says this:

> "These findings ...."

- that is, in his study -

> "... support the hypothesis, incorporated as part of this study, that exposure of fathers to ionising radiation before conception is related to the development of leukaemia in their offspring. The observed finding (the first of its kind with human data), however, is stronger than could have been expected from past knowledge, although relevant studies have largely not been undertaken."

May I just ask this: what did you understand him to mean by that passage, that it "is stronger than could have been expected from past knowledge"?

A. I think he means the amount that the relative risk is raised in the highest dose category, essentially.

Q. I see, for example, by comparison with the A-bomb data, or by any other studies which may have been done in human populations?

A. Yes.

Q. At paragraph 56 you deal briefly with other occupations and I think that one can go through that pretty quickly. It is, however, the fact, isn't it, that Table V shows that it is not only employment at Sellafield which may give rise to an elevated relative risk?

A. No.

Q. There are other employments which also may give rise to an elevated risk, in the cases and controls which were being studied?

A. Yes.

Q. Iron and steel is one in particular where one has a significant elevated relative risk both in relation to ....

A. You said a "significant elevated relative risk"?

Q. Forgive me. It is statistically significant for leukaemia and non-Hodgkin's lymphoma, is it not, when looking, for example, at the local controls?

A. Not "for example" but only in the local controls.

Q. Looking at the local controls, and the relative risk is higher than it is for working at Sellafield?
A. Yes. Every occupation is compatible with a raised relative risk in that table.

Q. Every occupation is compatible with a raised relative risk in that table and it is only Sellafield area, leukaemia only, and iron and steel, leukaemia and non-Hodgkin's lymphoma, local, that are not statistically compatible with no elevated risk?
A. Yes.

Q. So it does not show you very much?
A. No.

Q. Certainly not a major finding?
A. No, I agree.

Q. In paragraph 58, you have already said, and we agree about that, that there is nothing in this study where they specifically deal with aspects of environmental exposure which gives you any significant results, and it is for that reason that you say that it is consistent with Black and COMARE, in that it shows emissions into the environment are not a sufficient explanation?
A. Yes. They do not consider environmental doses at all in the paper.

Q. Not as such, that is right, but what they do is consider a number of habits and so on, which might be expected to increase one's environmental dose?
A. Yes.

Q. That is what you mean, I think?
A. Yes.

Q. In paragraph 58 what you appear to be saying is that because you have an association between occupation, and perhaps one can bring in there preconception irradiation and leukaemia, that you appear to be saying that argues against there being some other cause. Is that right?
A. What I think I say in my last sentence on page 21 is:

> "However, this in itself does not negate other pathways: it simply makes recourse to them unnecessary to explain the excess."

I do not think I am saying any more than that.

Q. But that rather begs two questions, doesn't it: (1) it begs the question as to whether the association that you have found does explain the excess, isn't that right?
A. I do not think I necessarily assume that. I say if that is correct then you do not need any other explanation.

Q. Of course. If the answer is that you have shown the cause then you do not need to look for anything else, that is obvious, but if all that you have done is to come up with an association, we have agreed a number of times that merely to find an association does not necessarily reflect cause and effect - we agree about that?
A. We do.

Q. So that the mere fact that you have found an association does not necessarily mean you do not need to look elsewhere?
A. I agree.

Q. Good - if you were not saying that I had misunderstood you. That would be particularly so if, given that there is a Seascale excess, that association does not explain why there is an excess in Seascale?
A. I think what again is slightly odd is it turns out that we now know - it says -

> "... Gardner was unable to trace the workforce file of the fifth".

and we now know that all five of the Seascale cases had fathers who had worked and had substantial doses, that all the remaining Seascale cases are not there at all, so among those who were unexposed at the plant, they did not get leukaemia.

Q. May I ask the question again and then we will look to the facts? I think the question I was asking you was this: you said that an association does not necessarily prove cause and effect; you said that the mere fact that you have found an association does not necessarily mean that you need not look elsewhere to explain the excess.
A. I agree.

Q. And I had suggested that would be particularly so if the association which you had found did not explain why it was that the excess was in Seascale - I choose my words somewhat carefully - it does not explain why the excess was in Seascale. If that is so, if it be the case, and we can look to see whether it is, but if it be the case that it does not explain why the excess was in Seascale, then all the more reason why it is not justified to say, "Oh well, we don't need to look elsewhere". Do you agree?
A. Yes.

Q. I am going to come later this afternoon, I hope, to ....
A. I do not think it is only based on that. I think it is based on other things, because what it counts is: are there people who have been equally exposed elsewhere in whom there is not only no evidence of an excess but a confidence interval that would exclude any possible raised relative risk.

Q. Certainly, and I am going to take you to the Louise Parker paper and to Dr. Wakeford's statement so that we can have another look at that to see what it tells us, when we have finished looking at the Gardner Study. You then draw your conclusions from the Gardner paper and you very fairly make the point, which of course we would entirely agree with, that the results are heavily dependent on a small number of cases and must be treated with caution. Again, I respectfully suggest to you that you are over-stating the case in the earlier part of that sentence, where you say:

> "The radiation dosimetry findings are most dramatic and highly statistically significant ...."

because we have looked at them and one finds that even in the low dose categories that your lower end of your confidence interval is around about one and a half, and I would suggest to you that that would not fairly be described as "highly statistically significant". Would you agree?

A. I think that we usually tend to say "highly statistically significant" is probably likely to be a P value of 0.001 and my own assessment of the dose response relationships was that it was likely to be of that sort of order of magnitude, and so I was not again basing it on individual categorical data.

Q. I am surprised by that. I can well see that subsequently, when you were carrying out your further exercise, you did your regression slope analysis, and it may have been that you had in mind that it would be a good thing to do, but why I express surprise is that you appear to - you are referring to the job that Prof. Gardner has done. What you are saying here is, if we look at it in this paragraph:

> "I consider that Professor Gardner has done as good a job as possible ...."

and you go on in the next sentence and say:

> "The radiation dosimetry findings are most dramatic ...."

You are there surely referring to the radiation dosimetry findings which he sets out in his study?

A. Yes.

Q. And you say:

> "... they are highly statistically significant ...."

A. But it is possible to do additional analyses of your own on those.

Q. It may be, Prof. Evans ....

MR. JUSTICE FRENCH: Forgive me, can I get the answer?

A

Q. Do you stand by the expression, "highly statistically significant"?
A. I think I could understand that you could regard that as a fractional over-statement. It is somewhere between "noticeably" and "highly", shall we say. In my own mind, I would have said, "Are those compatible with trend values that have P values that are 0.00-something".

B

Q. "Highly statistically significant" may be a slight over-statement?
A. I think I would have to agree that is a slight over-statement.

Q. MR. ROKISON: It may be that you had done your own different analyses on these figures, Prof. Evans, and had

C

reached a conclusion as to the statistical significance, but may I just press you on it in this way, that if one were simply to look at the Gardner figures as set out in these tables, and in particular Table VI where they deal with dosimetry, that it is not just that it might be a slight over-statement to say those figures are highly statistically significant. The position is that as far as the dosimetry findings are concerned, it is only the

D

highest dose categories that have any statistical significance at all, and that in those dose categories the lowest confidence limit, as I say, is around one and a half, and so to say that those findings are highly statistically significant is a gross over-statement, if you are looking at this data only?
A. Only looking at ...?

E

Q. If you are only looking at the Gardner Study and the way in which the dosimetry findings are there presented.

MR. JUSTICE FRENCH: Table VI?

MR. ROKISON: Table VI.

F

Q. MR. JUSTICE FRENCH: If one looks only at Table VI, would you regard the statement, "highly statistically significant" as a gross over-statement?
A. I would regard it as an over-statement, yes.

Q. What would you substitute for it?
A. The radiation dosimetry findings are dramatic and statistically significant.

G

Q. MR. ROKISON: In the highest dose category?
A. Again, I do not look at the table and the confidence intervals on its own. I look at the pattern, and I will do in some instances, and particularly in looking at that, I will do my own trend analysis, and so it is based on the data that are shown in Table VI but not the sums

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that are there presented.

Q. MR. JUSTICE FRENCH: If you do your own analysis on the data there presented, do you then stick by or do you amend the statement, "highly ...."?
A. I would still have to amend that. I think that was an over-statement but I would want to take it in the context of what I then go on to say.

Q. "Even doing my own analysis I would still regard the adverb 'highly' as an over-statement"?
A. Yes.

Q. Then you wanted to add something?
A. I would want to take it in the context of the next phrase of that because I have said:

> "... even though the results are heavily dependent on a small number of cases and must be treated with caution."

Q. This is really mitigating, or balancing, the use of the word "highly"?
A. Yes. I think that reading that sentence as a whole I do not think it is an over-statement.

Q. I want to take "highly" as being balanced by what follows, yes?
A. Yes.

Q. MR. ROKISON: Of course, that caution that you express there, with which, as I say, we wholly agree, would be even greater, bearing in mind that the only statistically significant association is in the high dose category, bearing in mind that high dose category relies upon four cases only, and bearing in mind that we have, I think, now agreed that applying the strict parameters which were set before the study started, it should be three cases rather than four.
A. I am not sure that I have still agreed with you on that. If we assume that is so, yes.

Q. That means you are even more cautious, bearing in mind that the only statistically significant figures as presented by Gardner are in the highest dose category?
A. Yes.

Q. Which depend on only four cases, and if we are right on the Bristol case it should be three?
A. But if we take into account one of the other cases that was not traced then it should be back to four.

Q. The re-analysis figures are somewhat different and they include 39 other workers. I will deal with those and with your analysis of those in due course, if I may. At the moment what I am doing is simply testing your evidence in relation to the Gardner paper, and as I understand it, it is right that you say that the caution which you express would indeed be emphasised, bearing in mind (1) the only statistically significant figures are

the high dose figures, (2) that those depend upon only four cases, and (3), that if we are right on the Bristol case, it should be only three?

A. Yes.

Q. Of course, we have seen from Prof. Gardner's own note, appended to his statement in the P4 bundle, that that statistical significance in the high dose categories, if you do exclude the Bristol case, no longer exists for three out of the eight high dose categories one takes?

A. Yes.

Q. So far as the six month dose is concerned, there is no statistical significance if you take leukaemia and NHL together in any category - page 26 of P4.

A. Yes.

Q. We have discussed the question, and you deal with it again at paragraph 60, where you say:

> "The study goes a long way to explain the Black findings ...."

and this is a question we have got to come back to, as to whether it does explain actually why the excess was in Seascale, but in considering this question, as to whether it does explain the Seascale excess, did you have in mind that the highest dose case was not a Seascale case?

A. I do not think that was either here or there.

Q. If you are considering whether the hypothesis explains (1) why there is an excess in Seascale, and (2), which is perhaps another side of the coin, why there is not an excess somewhere else, and you reach a conclusion that this study explains to your satisfaction why there is an excess in Seascale, if that study is driven, and if your regression slope, for example, would be driven, by one very high dose case which does not happen to be a Seascale case at all, then that conclusion must be revised, must it not?

A. No, I do not think so because the Seascale cases that we know about have such high doses.

Q. So you say, but if it were to be the case that one very high dose case, being a non-Seascale case, effectively significantly influences your regression slope, then you would, would you not, have to think again at least as to whether this hypothesis does in truth explain the Seascale excess?

A. If elimination of that one very high dose case caused the regression slope now to be less than one, as you might say, or less than zero to be a negative slope, yes I would.

Q. Supposing that the removal of that high dose case, being a non-Seascale case, effectively removes the statistical significance of your slope, in other words so that it has a P value which does not come within statistical significance, what would you say then?

A. I do not think that necessarily means that is not an explanation but it certainly weakens the case.

Q. I wonder whether, and it is up to you, I shall be putting it to you in due course, but it may be that before we meet again to look at your regression slope and so on, you might consider that point and see what the effect on your regression slope would be if you were to remove the high dose non-Seascale case, namely Reay?

A. Yes, I am sure that it may make things such that statistical significance disappears.

Q. Yes. I will come back to the point at paragraph 60, which is really this point about whether it explains the Seascale excess. 61, I can leave, there is really no issue between us, I think, on that. 62, you just mention what Gardner puts forward as a possible explanation if this is causative?

A. Yes.

Q. I think that you very fairly say that although the overall hypothesis given is plausible the mechanisms involved are outside your competence?

A. Yes.

Q. And I do not want to ask you about them. Looking at the detail of it, would I be right in thinking that it would not really be within your competence to say to what extent it was plausible?

A. You would be right, yes.

Q. Subject to the comment that I think you made earlier, that medical men can always find some plausible link if they have to?

A. Yes, or the inverse.

Q. Or the reverse, yes.

Q. MR. JUSTICE FRENCH: If one substituted "looks plausible" for "is plausible", perhaps you would still stand by that?

A. I think so, yes.

Q. MR. ROKISON: And you mention another possible hypothesis, which I think is itself mentioned by Gardner, but so far as we are aware nobody is developing that case in this litigation.

A. I do not know the details of what the case is but I would certainly think that is a very real possibility as far as I am concerned.

Q. Yes, but it depends upon the extent to which radionuclides, bearing in mind the precautions that were taken in relation to changing rooms and so on and so forth, would be attached to the father's clothing when he came home, and I think you can rest assured that nobody is putting forward any positive case based on that hypothesis.

Before we leave the study, let us try and step back and look at it a bit and see where we have got to. You very properly, if I might respectfully say so, voluntarily expressed the caution that one should draw, before drawing conclusions as to causation from one study?

A. Yes. You suddenly interject the word "voluntarily".

Q. I think you have expressed it yourself.

A. Yes, I expressed it myself. You seem to imply in your question that I have a vested interest or a fixed position on it.

Q. No, I do not at all, but I may imply from my question that some of your concessions one has had to squeeze out of you, but that is a matter of comment. In saying "voluntarily" I was really suggesting that was something which you did not seem to need much persuasion to accept?

A. No.

MR. JUSTICE FRENCH: I think it is best if we remember the heat and light regression slope!

MR. ROKISON: Yes, indeed. There is no bad feeling, my Lord, as far as either of us are concerned, I am sure.

THE WITNESS: No comment, my Lord! (Laughter)

MR. ROKISON: Touché.

Q. First of all, we agree one has to be cautious about drawing conclusions of causation from one study?

A. Yes.

Q. And I think you agree with me that from a scientific point of view rarely if ever is that done?

A. Yes.

Q. Next, one has to bear in mind that some of the parameters of the Gardner Study at least, as far as the design of it is concerned, were dictated by the Black Report and the Yorkshire Television programme which had preceded it?

A. Yes.

Q. One in particular would be the age that was taken for the study, that is the age of the children and young people, which we have seen from a number of other studies, and indeed it is emphasised by Black, that it would have been, ideally, more appropriate to take a different age group, or a different age analysis?

A. Yes.

Q. Next, that NHL and leukaemia were looked at together and we have discussed that, that unless the position is that their aetiology is such that one should really draw no distinction between them, then lumping them together may, in the way in which we have discussed, give a misleading picture?

A. You said that their aetiology was ....

Q. I said unless their aetiology was such that there was really no distinction between them, so that one could lump them together biologically and say, well, they are effectively the same disease which would be likely to be caused in the same way therefore we can lump them together, but if that is not the case then to lump them together may present a misleading picture?
A. I think I disagree with you there because you have said that unless their aetiology is identical and that they can be regarded as the same disease ....

Q. No, I said such that they can ....
A. I disagree with that because you can have the same aetiology for very different diseases in the sense that you can have, I am afraid, tobacco smoking as a risk factor for both lung cancer and heart disease, which are very different diseases, but nevertheless it might therefore be reasonable to look at all mortality lumped together, and so I think that ....

Q. Well it might, but on the other hand - I know nothing about this and I ask you only to clarify - but the mere fact that there may be a recognised association between tobacco smoking and lung cancer on the one hand, and heart disease on the other, does not mean to say that the relative risks would be the same in respect of those.
A. No.

Q. Of course, where you are drawing conclusions in relation to relative risks, which you are here, then there is a danger in lumping together NHL and leukaemia, unless effectively one can say they are really one and the same disease?
A. Unless you have some belief that they have a similar relative risk.

Q. Indeed, similar aetiology and similar relative risk?
A. Yes, that I would be happy with.

Q. MR. JUSTICE FRENCH: Or unless you can postulate that one change in the structure of the body, speaking very loosely, can have two different results?
A. Yes.

MR. JUSTICE FRENCH: If one mutation can have two different results then why should you not lump them together?

MR. ROKISON: This is a biological question.

MR. JUSTICE FRENCH: Of course it is but you are giving a hypothetical question and I am trying to narrow it down.

MR. ROKISON: What I am doing is trying to summarise and bring together the various matters which should cause one to look at the Gardner Study with some caution.

MR. JUSTICE FRENCH: I follow that entirely, Mr. Rokison, but as I recall Prof. Evans' evidence this bit of your summary does not emerge, at least with any clarity, that if they are two different diseases you cannot properly lump them together. I was understanding him to say that which, no doubt quite inadequately I was trying to express and repeat, that if you can regard the two diseases, if they be two diseases and one suspects they will turn out to be two diseases, if they be two diseases but the same trigger may cause them both in different people, then I understand the witness to be saying it would be legitimate statistically to join them together. I may be wrong about that.

MR. ROKISON: I think your Lordship is wrong because I think the witness added that they must have the same relative risk.

MR. JUSTICE FRENCH: Let us come on to relative risk in a moment.

MR. ROKISON: No, my Lord, with respect, it is part of the same question. The question is the extent to which you should look at the study with greater caution because it has lumped NHL and leukaemia together and, as I understand it, and I will ask Prof. Evans again in order to clarify:

Q. As I understand it, never mind the reason why they did lump them together, which we have looked at, which was because of possible difficulties in diagnosis in the early years, but unless the aetiology is essentially the same and the relative risk would be essentially the same, then, by lumping them together, you may present a distorted picture for one or the other?
A. A distorted picture of the exact value of the relative risk in the sense that you are doing.

Q. Yes?
A. But we are going on and adding something, and what his Lordship said about lumping them together does not mean that you should, therefore, treat the study with caution as a study. If you then use it for a precise estimate of relative risk - right - then you should be a little careful. I would agree with you on that.

Q. Or, indeed, let us remove the word "precise" for the moment. If you were to use the study for an estimate of relative risk, you should be cautious?
A. Yes.

MR. JUSTICE FRENCH: I understand, Mr. Rokison, with respect, and accept your qualification based on relative risk. I can quite see that the relative risk of the mutation causing A may be different from a virtually identical mutation causing disease B. I quite follow that, but, having accepted that, can I now get the answer recorded?

MR. ROKISON: Certainly, my Lord, yes.

Q. MR. JUSTICE FRENCH: How would you like to express it, Professor?
A. When combining two different diseases.....

Q. Shall I start writing?
A. Yes, I think so - and using a single study, caution should be exercised when applying the overall relative risk and assuming it to be equal for the two diseases.

MR. JUSTICE FRENCH: Yes, thank you.

Q. MR. ROKISON: Would you agree with this, that unless the aetiology of the diseases is the same?
A. Unless radiation were a risk factor for both of them. They do not have to have entirely the same aetiology.

Q. Of course. On the assumption that paternal preconception radiation exposure is a potential cause of each?
A. Yes.

Q. Then I accept the answer you have just given. Then it is a question of looking to see whether they have, or may have, different relative risk?
A. Yes.

Q. But in seeking to answer the question, is there an association even, let alone a causal connection - is there an association - between paternal preconception radiation exposure and, for example, NHL, one cannot answer that question by reference to an association which is produced by looking at leukaemia and NHL together. There may or may not, in those circumstances, be an association between parental preconception irradiation and NHL alone?
A. I agree with that.

MR. JUSTICE FRENCH: The question, is there an association between paternal irradiation and NHL, cannot be answered by lumping NHL with leukaemia.

MR. ROKISON: Effectively, yes. The way I put it was that it cannot be answered by looking at an association between paternal preconception irradiation and leukaemia and NHL together.

MR. JUSTICE FRENCH: Cannot be answered by - repeat it, would you, please?

MR. ROKISON: It cannot be answered by reference to an association between paternal preconception irradiation and leukaemia and NHL together.

THE WITNESS: Unless there were other information. You have excluded the possibility that there is other information.

Q. I agree. Obviously, if there is other information which tells you you can, depending on what the information is, then you may be entitled to?
A. Yes.

MR. JUSTICE FRENCH: Cannot be answered by reference to an association between paternal preconception irradiation and....?

MR. ROKISON: Leukaemia and NHL together.

MR. JUSTICE FRENCH: Thank you.

Q. MR. ROKISON: I am at the moment looking at the design of the study, what it was seeking to do. We have already mentioned that, by limiting it in the first instance, as they have done, to children born in West Cumbria, then they are, I think, in my Lord's words, excluding some of the relevant data if they are looking for the cause of the Seascale excess?
A. Yes.

Q. Another aspect of the design is that, in testing, as they had to do, a number of hypotheses - and whether it is 10, 4 or 2 may depend on how you view it - but in testing a number of hypotheses, some account may have to be taken in assessing your confidence limits or P values?
A. May have to be taken, yes.

Q. Yes, and that, if the right view is that they were testing, say, 10 hypotheses, then, generally, with low numbers, one would multiply the P value by somewhat less than 10. Would that be right?
A. If they were independent hypotheses.

Q. MR. JUSTICE FRENCH: If there were, say, 10 hypotheses....?
A. 10 independent hypotheses.

Q. Yes, I was going to put the qualification. If there were, say, 10 hypotheses, one would have to multiply the confidence limits....

MR. ROKISON: Yes, it is the P value or confidence limits, depending on which way you are looking at it.

MR. JUSTICE FRENCH: Which way you are looking at the sample. By, say, 10.

MR. ROKISON: I think it is fair to say that it is somewhat less than 10. It is not quite as high as the number of hypotheses.

MR. JUSTICE FRENCH: Say 8.

Q. MR. ROKISON: Yes, that is fair, is it not?
A. Yes.

MR. JUSTICE FRENCH: That is what we had earlier, anyway, but that depends on them being truly independent hypotheses.

MR. ROKISON: Yes:

Q. One other point in relation to the design of the study, which I have not touched upon, but are you aware of the logic or relevance of considering a dose during the six months before conception?
A. Am I aware of the logic of....?

Q. What is special about six months, do you know?
A. I believe there is something or other about sperm turnover time.

Q. Oh, I see, because there would not be much point in taking any period such as six months as opposed to the total preconception unless it related to some relevant biological occurrence, would it?
A. Six months as opposed to seven or eight or nine or five or....

Q. Or a year or two years or anything?
A. Yes, you would normally expect there to be a biological reason behind your choice.

Q. Quite. The odd thing is, I think, that it is nowhere explained in the Methods paper or in the Results paper as to why the six month period was chosen. The other, and perhaps major, factor which should lead to caution, and this may relate, in part, to the results because they may not have known in advance, but you have to be extremely cautious in drawing conclusions from a study which has such small numbers?
A. Yes.

Q. So far as the methodology is concerned as opposed to the design then, one has the factor of whether or not the high dose category, for the purposes of the Gardner study, should have been four cases or, as we say, three. That is the Bristol case point?
A. Yes, I still do not understand what you are asking.

Q. I am attempting to summarise by listing the factors that one has to take into account. In relation to the way in which they carried out their design, there is the question which arises as to whether the Bristol case should or should not have been included?
A. That question arises.

Q. And we have dealt with that exhaustively?
A. Yes.

Q. And exhaustingly, so we can leave it. So far as the results are concerned, I think, in the end, you suggested that the occupational table told us very little?
A. On its own, yes.

Q. So far as the dose table is concerned, the dose categories are arbitrary?
A. Yes.

Q. On those that were chosen, for the lower two of the three categories, there is no statistically significant difference apparent?
A. No.

Q. That, so far as the Gardner presentation is concerned - I leave aside any other work which you may have done by way of regression slope analysis - but, so far as the Gardner presentation is concerned, the only significant results are associations within the highest dose category?
A. Yes.

Q. That category contains only four cases, none of which are NHL cases?
A. Yes.

Q. If we are right on the Bristol case, it should be three?
A. Yes.

Q. The statistical significance even in those high dose categories is, at the highest, only about 1½ at the lower confidence level?
A. Yes, that is not the statistical significance....

Q. No, forgive me. It is the lower confidence level relating to the relative risk?
A. Is only about 1½.

Q. Only about 1½ at the highest level?
A. No, it is about 1½ at the lowest level of confidence interval. It is about 1.3, 1.4, 1.5.

Q. Yes, it goes up, the highest is 1.69?
A. Yes.

Q. And it goes down as far as 1.13?
A. Those are the lowest levels, not the highest levels.

Q. Yes, on the lowest confidence level, correct. Again, if we are right about the Bristol case, three out of the eight categories looked at, there is no statistical significance, even in the highest dose categories?
A. Yes.

Q. Bearing all those matters in mind, as no doubt you have them all in mind, though it is quite difficult to have them all in mind at once, but bearing all those in mind, would you not agree that it would be rash to draw any conclusions as to cause and effect from the Gardner study?
A. No, I do not think that it would be rash to draw any conclusions. It would depend on the strength of your conclusion. If you mean conclusive, positive proof of something, then I would have to agree with you, yes.

Q. I do not mean conclusive, positive proof. I suggest it would be rash for any epidemiologist to draw any conclusions as to cause and effect from that study?
A. To draw any conclusions from that study alone?

Q. Yes, other than to say, "It is interesting. It requires further investigation"?
A. I would go a little further than that, but I would agree with you, you cannot draw strong conclusions from it on its own, yes.

Q. I want to press you on this a little bit because you introduce the word "strong". I want to make it quite clear what I am putting to you and to see whether you agree with it or not. I would suggest to you that it would be rash for any epidemiologist to draw any conclusions as to cause and effect from the Gardner study, bearing in mind all the factors I have summarised to you. Do you agree?
A. No.

Q. And I suggest to you that the highest that any epidemiologist should go, in the light of the Gardner study, is to say, "Well, here we have an association. It is a matter which merits further investigation"?
A. I agree that that is true.

Q. And I suggest that that is as far as one could responsibly go, looking at the Gardner study?
A. I do not know what you put on your meaning as "as far as one could responsibly go".

Q. What I mean is that, as I say, if one went any further than that, if one drew any conclusions other than that, one would be drawing conclusions which, as a responsible epidemiologist, one should not draw?
A. I think you are saying any conclusions and I think that I would need to have a list of the possible sorts of conclusions that you could draw and could not draw. For example, you could not draw the conclusion from the Gardner study that radiation has no relevance at all in this.

Q. I agree.
A. If you had found that, for example - what shall we say - that maternal x-rays explained everything and that was so. So when you say you cannot draw any conclusions, you are pushing me just too far.

Q. I agree and I take the point. Let me be more specific, that one cannot conclude or one should not responsibly, bearing in mind all the factors that I have put to you, conclude from the Gardner study that there is a causal connection between paternal preconception irradiation and either leukaemia or NHL?
A. I would agree with that.

Q. MR. JUSTICE FRENCH: Is that speaking from the philosophical standpoint of a statistician - we had this discussion earlier - or is it speaking from some other standpoint?
A. That is speaking as a scientific, I hope, statistician.

Q. MR. ROKISON: Which is the only way in which, presumably, you can speak, is it not?
A. In the sense that I cannot speak as a medical person, but there will be occasions where my scientific conclusion that I will be able to stand here and say "I am absolutely sure of...." is going to be quite different to my saying "I think there is a strong possibility that...." or even "probability that...." So to say that I cannot draw conclusions on a probability basis is exactly what I do not want to say but, in terms of your remark about radiation specifically, I could not say that this study proves, that you can conclude from this study alone, that paternal exposure to radiation causes leukaemia and non-Hodgkin's lymphoma.

Q. Would I take it that, so far as NHL is concerned, bearing in mind that all one has within your dosimetry figures are two cases - one in the low dose category, one in the middle dose category and none in the high dose category - one really cannot draw any conclusions at all from the Gardner study?
A. I would have to agree.

Q. MR. JUSTICE FRENCH: As to NHL alone, one cannot draw any conclusion from the Gardner study on any philosophical basis?
A. On any philosophical basis.

MR. ROKISON: Forgive me, my Lord. I am not in the witness box, let alone being in the fortunate position of your Lordship, but I do not quite understand what your Lordship meant by "on any philosophical basis".

MR. JUSTICE FRENCH: I am harking back to what Prof. Evans said either yesterday or the day before - I cannot remember which - that, if he is speaking as a scientist, he is speaking from one philosophical basis. If he is speaking as somebody asked to express a view as to what the balance of probabilities are, he is speaking from another philosophical basis. That was what I intended by the question.

MR. ROKISON: I see. So, if I may respectfully ask through your Lordship, what your Lordship was intending was to make it clear that that answer was whatever philosophical basis one is adopting.

MR. JUSTICE FRENCH: That is right, on any philosophical basis, one cannot draw any conclusions from the Gardner study alone.

MR. ROKISON: Thank you very much:

Q. I now move to look at subsequent studies with you. Paragraph 66. Is there anything positive you seek to draw from this paper? You say that it "demonstrates the lack of a strong inherited effect." It is D 63. Perhaps we can just look at it quickly. If one looks at page 283, what is said is this:

> "Occupational and other exposures to radiation
>
> The risks of transplacental carcinogenesis arising from radiation .... have been discussed widely and included in the review by Preston-Martin.
>
> The carcinogenic risks of preconception irradiation for patients being treated for cancer were discussed above; there is at present no evidence that there is any risk. Other groups that have been or might be studied include radiologists, workers in the nuclear industry, patients undergoing diagnostic radiology, the atomic bomb survivors and those exposed to radiation as a result of accidents or fallout. Among these groups, the most comprehensive study is that of the atomic bomb survivors reported by Ishimaru et al. Those authors found no increase in the incidence of leukaemia among the children of exposed parents. Although there have been reports of positive associations between preconception irradiation (mainly diagnostic radiology), and childhood malignant disease, there appears at present to be no convincing evidence that such an association is causal.
>
> Unexplained reports of leukaemia clusters around nuclear installations in the UK have led to speculation about whether these could be explained by an increase in the risk of leukaemia among children of workers in these installations, but there is at present no published evidence to substantiate this."

Is there anything that we get from that study that you want to refer to, that you consider assists my Lord in this case?

A. No.

Q. I now want to look at the McKinney study with you, if I may, and it is that which you refer to in the next section of your report?

A. Yes.

Q. As I understand it, this is a study on which you particularly rely because my recollection is in your evidence that you pointed to this as being the one study that you were aware of in the United Kingdom which was positively consistent with the Gardner hypothesis?
A. It is the letter that followed.

Q. The study together with the letter, yes, and I was going to look with you at both of them. Can we, first of all, look at the McKinney study, please? M172. It is not all that long, but since you place a lot of reliance upon it, I think we must look at it in a little bit of detail.

MR. ROKISON: It will have to be looked at at some time, my Lord, and now seems to be as good a time as any.

MR. JUSTICE FRENCH: Yes.

Q. MR. ROKISON: Can we look at it in some detail? The Abstract says that the objective is to determine whether parental occupations and chemical and other specific exposures are risk factors for childhood leukaemia. It is a case-control study. Information on parents was obtained by home interview. Just pausing there, that is one of the, if one can say, shortcomings of the study, in the sense that information obtained by interview is not necessarily very reliable?
A. Not necessarily, no.

Q. I think you mention that?
A. Yes.

Q. And then what they did is they studied three areas. it was Copeland and South Lakeland (west Cumbria)?
A. Yes.

Q. Kingston upon Hull, Beverley, East Yorkshire, and Holderness - that is North Humberside - and Gateshead?
A. Yes.

Q. They studied 109 children, interestingly, aged 0-14?
A. Yes.

Q. But they also lumped together leukaemia and non-Hodgkin's lymphoma, and they studied them during the period 1974-88. They had two matched controls for each case, and:

> "Main outcome measures - Occupations of parents and specific exposure of parents before the children's conception, during gestation, and after birth. Other adults living with the children were included in the postnatal analysis.
>
> Results - Few risk factors were identified for mothers, although preconceptional association with

A

the food industry was significantly increased.... Significant associations were found between childhood leukaemia and reported preconceptional exposure of fathers to wood dust, radiation and benzene; ionising radiation alone gave an odds ratio of 2.35 (with confidence limits 0.92 to 6.22). Raised odds ratios were found for paternal exposure during gestation, but no independent postnatal effect was evident.

B

Conclusion - These results should be interpreted cautiously because of the small numbers, overlap with another study, and multiple exposure of some parents. It is important to distinguish periods of parental exposures; identified risk factors were almost exclusively restricted to the time before the child's birth."

C

They refer in their Introduction to, as you point out, an increase in the incidence of leukaemia at Gateshead before 1977?

A. Yes.

Q. I think you specifically mention that?

A. Yes.

D

Q. We will come back to it. They say:

"No causal link has yet been established, although occupational exposure of fathers to radiation has recently been suggested as the explanation for the localised excess at Seascale, west Cumbria."

E

That is a reference to Gardner?

A. Yes.

Q. They refer to emissions from the Capper Pass tin smelter. At Gateshead public attention has been directed towards local industrial incinerators, and so on. I do not think we need to look further at the Introduction, unless you think there is anything more that we ought to. Just

F

glancing through it, I think not. I think that we can come, if we may, to look at the results and one sees the results on page 683. Maternal exposures are first dealt with in Table II and you see the results there set out and there are statistically significant associations with some of them, in particular, catering, cleaning and hairdressing, food related. Those are the only ones that

G

are statistically significant, are they not?

A. Yes.

Q. But exposure to radiation....?

A. And wood dust, sorry.

Q. And wood dust, yes, you are quite right. It is just statistically significant. Radiation not so. Relative

H

risk only 1.12?

A. Yes.

Q. Although we have not looked at it, Gardner did, in fact, look at maternal preconception x-ray exposure?
A. Yes.

Q. And found nothing of significance?
A. No.

MR. ROKISON: It is a point that we had not noted in Gardner, my Lord, but it may be relevant to other studies which are being put before your Lordship:

Q. It becomes slightly more complex when one looks at paternal exposure in Table III?
A. Yes.

Q. And the reason why it becomes more complex is because the authors of this study have divided the relevant periods, or potentially relevant periods, into three categories. There is preconceptional, periconceptional, being at about the time of conception. Is that right?
A. I take it "peri" meaning "around".

Q. Yes, and gestational - that is the period between conception and birth - and postnatal being the final period. One sees there that, for exposure to radiation, there were 15 cases, there were 10 controls, and the odds ratio there was 3.23, an elevated risk, which is mentioned in the Abstract, with a confidence interval, 95%, of 1.36 to 7.72.

Q. If one looks at Table V - first of all can I just pause there? You have said in your report in summarising this:

> "A statistically significant relationship was found between the preconception exposure of fathers to ionising radiation and leukaemia incidence in their offspring".

Was it that association to which you were referring?
A. I have a feeling that there may be a mistake there - I don't know - because I certainly know that this paper shows that the effect is with radiation and not with ionising radiation on its own.

Q. Exactly.
A. I was not aware of that in there. I haven't looked at the Table yet, but my mind knows that it was ionising and non-ionising radiation combined that showed the statistically significant effect.

Q. Indeed. Of course, the Gardner hypothesis is a hypothesis which relates to ionising radiation?
A. Yes.

Q. Indeed the possible biological explanation is that of that ionising radiation causing some damage to the germ line cells?
A. Yes.

Q. MR. JUSTICE FRENCH: So that the last sentence of paragraph 67 is wrong?
A. Yes, "ionising" should be deleted there.

Q. Or "non-ionising" should be added.
A. Yes.

Q. MR. ROKISON: It is rather important, is it not, if one is seeking to derive comfort from this study as being the one study which is positively consistent with Gardner?
A. The important thing as far as I was concerned was the letter which was independent confirmation really.

Q. With respect, it was not independent. We can look at it. What it is doing is further clarifying some aspects of this study?
A. Yes.

Q. It is very, very important, it is not, that if you are relying on this study, which you purport to do in your report, not a letter, but you rely on this study, and this study as being the UK study which is the only one positively consistent with Gardner, and my suggestion to you is that in relying upon this study as being consistent, you had misread it and did not realise that it was not relating to ionising radiation alone but, upon analysis, much of the radiation was non-ionising radiation?
A. I honestly can't say whether I misread it or not at the time, but certainly I have at no point in my memory thought that this study only related to ionising radiation; it did split it, and I do recall that. I should have perhaps read my report a little more carefully, and I would have to agree that that is a mistake.

Q. You would agree that it is ionising radiation which is important if one is considering whether it supports the Gardner hypothesis?
A. Yes.

Q. MR. JUSTICE FRENCH: It may have no significance at all - I think I have answered my own question - but one sees the make-up of the radiation in Table V, which is 2, 3, 1, 2, reading down the number of cases, and you have got "certain ionising", "possible ionising", "likely ionising" and "non-ionising"?
A. Yes.

MR. JUSTICE FRENCH: Yes, I see.

MR. ROKISON: My Lord, it is very complicated the way in which this study works. If, as it appears, Prof. Evans made a mistake, as he very frankly admits, it is perhaps not surprising, because it is quite complicated, and perhaps we can have a look at it.

Q. If you go on to Table V, Table V is "Exposure of fathers to ionising and non-ionising radiation before children's birth reported at interview?"
A. Yes.

Q. May I explain to my Lord, if you will forgive me, and if I may be permitted to, what the problem is: that whereas in Table III they divide into preconceptional, periconceptional and gestational, and postnatal, three periods which are mutually exclusive, when they do it in Table V, they do not; what they deal with is they split it between preconceptional only, which is the first part of the table, and the second part of the table is preconception, periconception and gestation. In other words, those listed in the second half of the table were those who were exposed during all those periods, whereas the first part of it is those who were exposed only before conception, so it is very confusing? I see that you nod, but you agree that that is the way it is set out and that that does make it rather confusing?
A. I do agree.

Q. MR. JUSTICE FRENCH: We cannot be certain whether periconceptional includes preconceptional?

MR. ROKISON: No, periconceptional would not include preconceptional. I suppose it could, just.

MR. JUSTICE FRENCH: If one uses the word "peri" in its proper sense, it must.

MR. ROKISON: Exactly, I see that. That is right.

Q. May we look and see how it works? For the purposes of Table V, they divided the exposures by reference to a number of descriptions: there was "certain ionising" which was "Exposure confirmed by registration with National Registry for Radiation Workers or British Nuclear Fuels, or both"; then "possible ionising" was "Industrial radiographers unless indicated otherwise"; and then "unlikely ionising" and "non-ionising"?
A. Yes.

Q. One sees the same categories then used for the preconception, periconception and gestation periods, so that the number of cases which one therefore finds in Table III on the previous page for preconceptional would, of course, include both preconception only and those who were exposed during all three periods, so that is why your 15 cases there is the sum of the 7 and 8 in Table V, is that right, Prof. Evans?
A. I think you are correct. It is confusing, as you say.

Q. It is confusing, but that would follow, would it not?
A. Yes, I think so.

Q. That the preconception would include those who were exposed only during the preconception period and those who were exposed throughout?

A. Yes.

Q. They being mutually exclusive, you can add them together and that gives you your 15?
A. Yes.

Q. MR. JUSTICE FRENCH: You say that that gives us our 15. Where is our 15 on Table III?

MR. ROKISON: That is the radiation one, my Lord, the cases - 15.

MR. JUSTICE FRENCH: Then let me count down to "radiation". Yes, I have got it.

Q. MR. ROKISON: So that your association there is an association which depends on those 15 cases, and of those 15 cases, as one sees from Table V, there were only four of those cases who came within the "certain ionising" category?
A. Yes.

Q. A further five were "possible ionising", but the cases have nothing otherwise stated and therefore were industrial radiographers?
A. Yes.

Q. But they include within the 15 six who were either "unlikely ionising" or "non-ionising"?
A. Yes.

Q. So the position is that if one looks at all areas, of course all areas include Gateshead and Humberside, which is specifically picked out on the right?
A. Yes.

Q. As far as the "certain ionising" cases are concerned, one of them was a Gateshead and Humberside case, and therefore only one of them was in one of the other two areas?
A. Yes.

Q. Of the "certain ionising" in all categories, it included - as one sees, there is a double mark against that - the two subjects were included in the study by Gardner?
A. No, I think one of them was.

Q. It says "two"?
A. I am sorry, you are right. I am looking in the Table above, in the control.

Q. Never mind for the moment the control; we are just looking at the cases, which is perhaps of more immediate interest. So the result of that is that if you are looking at certain ionising radiation cases outside Gateshead and Humberside, there is only one case which could be in West Cumbria?
A. Yes.

Q. So there is one case that could be in West Cumbria and one case in Gateshead and Humberside, other than the two which are included in the Gardner study anyway?
A. Yes.

Q. MR. JUSTICE FRENCH: One case from West Cumbria?
A. No, not necessarily.

Q. MR. ROKISON: One case which may be West Cumbria. It could either be West Cumbria or it could be the East Yorkshire area?
A. Yes.

Q. MR. JUSTICE FRENCH: One case which may be West Cumbria, and did you say two from East Yorkshire and Humberside?

MR. ROKISON: No, one, my Lord; one from Gateshead and Humberside. The first one, my Lord, could have been either West Cumbria or East Yorkshire, and there is one case which is Gateshead and Humberside.

MR. JUSTICE FRENCH: Yes.

MR. ROKISON: Other than included in the Gardner study.

Q. As I say, we have seen that as far as the cases are concerned, the possible ionising cases are all radiographers. One of the cases, preconception only, was included in the Gardner study?
A. Yes.

Q. So that if we look at the way in which you express this - and I do not want to criticise the expression particularly but let us try and get it accurate - in paragraph 68, you say:

> "The quality of this study does not match that of either Gardner's or Urquhart's. For example, the study was based entirely on the results of interviews of case parents. Work records from employers were not obtained. This meant that there could be no assessment of a dose-response relationship"?

A. Yes.

Q. Of course, no dose, no assessment of dose-response relationship?
A. No.

Q. Without doses, it is perhaps of limited value, to put it no higher, as being supportive of the Gardner hypothesis?
A. Undoubtedly.

Q. It then says:

"In addition, the conclusions of the part of the study dealing with preconception exposure to radiation were based on only seven cases, some of which could have been those included in the Gardner study".

Having looked at it, I think we could more accurately say, could we not, that that was based on only - forgive me, it is four cases, is it not, of certain ionising, of which two were included in the Gardner study, and only one, so far as "certain" is concerned, could have been West Cumbria?

A. Yes, could have been Cumbria, in fact.

Q. Could have been Cumbria, yes.

A. Forgive me, I know it is not my job to, but I don't quite understand why you want to keep excluding Gateshead.

Q. Because Gateshead is a different area, and if there is a cluster in Gateshead, it is a different cluster?

A. You seem to want to look at things happening in Cumbria and yet because we know there is a cluster there, you say "Let's look at that", but you have said "We already know there is a cluster there, therefore it is not valid to look in that area", and the whole strength of this study is that it does look in other areas such as Gateshead.

Q. You say "the whole strength of it"; all right, we will bring in ---

A. You know, what strength it does have.

Q. We will bring in Gateshead if you like. The result of bringing in Gateshead is that so far as certain ionising radiation is concerned, there are a total of five cases, of which two were Gardner cases?

A. Yes.

Q. So that independently of Gardner, you have three cases?

A. Yes.

Q. No, you do not; I am talking nonsense. You do not, because all areas includes Gateshead and Humberside?

A. Yes.

Q. We are both talking nonsense, forgive me?

A. Yes, we have only got two. You are quite right, there are only two.

Q. Forgive me, I was right the first time. The position is that of the certain ionising cases within your 15, there are four cases of which two were Gardner cases, so that there are two non-Gardner cases of certain ionising?

A. Yes.

Q. And one of those is a Gateshead case and the other may be anywhere other than Gateshead?

A. Yes.

MR. ROKISON: My Lord, I am told that I have made a mistake, and I apologise for having done that. It may have lent a little confusion to the exercise. I apologise, and may I correct it? My mistake was in misreading the setting set out in the abstract. It appears that the three areas are, first of all, Copeland and South Lakeland, which is described as West Cumbria; secondly, Kingston-upon-Hull, Beverley, East Yorkshire and Holderness, which are together described as North Humberside; and Gateshead. That means that if a case as in Table V is shown as being all areas not being Gateshead or Humberside, it must be a Cumbria case.

MR. JUSTICE FRENCH: Yes, I see.

MR. ROKISON: My Lord, I am not going to finish and I do not know how long it is going to take to look at McKinney. It will take a little time together with the letter. I am confident that I will finish within half a day on Friday, and my learned friend has indicated that the other half of the day will be ample for him to re-examine. My Lord, would it be a convenient time for your Lordship to rise now?

MR. JUSTICE FRENCH: Yes.

MR. ROKISON: I think the witness is tired, and so am I.

MR. ROKISON: I think we all get a bit tired after a few days of this!

MR. LANGSTAFF: My Lord, before your Lordship rises, may I just mention a matter which causes us some concern? It is not a matter upon which I felt it appropriate to further interrupt the flow of Mr. Rokison's cross-examination.

It is this: a number of questions were put earlier on this afternoon to Prof. Evans which appeared to suggest not simply a hypothesis - "What if the dose bands in Gardner were 100 to 150, 150 to 200 ...?" - that line of questioning, but appeared to suggest that they were being put upon some definite basis upon instructions that my learned friend has as to the calculation and the details.

My Lord, I mention this because we have been served with no evidence that suggests that any witness will be called to put this forward from the Defendants' point of view. We have had no material, although there has been ample time to consider the Gardner study which this related to; it is not a question of the re-working. It is not a matter in relation to which, so far as I am aware, there has ever been any published criticism of the Gardner study, and despite the three reports from Dr. MacRae and the two from Dr. Wakeford of very recent origin, it is not a criticism which has ever been mentioned ---

MR. JUSTICE FRENCH: Did you say "agreed reports"?

MR. LANGSTAFF: The three reports. It is not a criticism which has ever been mentioned, my Lord, and I merely say this: that if my learned friend is going to take that line of cross-examination any further, we would expect to see the material which he proposes to call an expert to support and would expect to see it sooner rather than later.

MR. ROKISON: That is a very fair comment, my Lord. It is absolutely right. My learned friend is quite right, and I think I made it pretty clear that this exercise has been done. It is actually an exercise which has been done in relation to the new figures. We have not actually done it for the old figures. It will relate to the report which, as my learned friend knows, is currently being prepared but has not yet been finalised by Prof. Howe, who will be dealing with the latest figures. Amongst the exercises which it is my understanding he has done is this exercise to see what happens if you adjust the bands and so on, and it was on that basis that I put what was, in a sense, a hypothetical question of saying "Supposing it shows ... what conclusions would you draw"? However, my learned friend is absolutely right, and my present understanding is that we will be serving evidence to show that this is the case.

The position on evidence is quite simply this: we had Prof. Evans report as soon as my learned friends could produce it and we have been able to cross-examine on the first part of his evidence. It is not an easy job, it is very difficult, and it is not just a question, as my learned friend Mr. Hytner said, of number crunching - it really is not as simple as that - and the epidemiological aspect of these cases is of fundamental importance and it is taking time. I have not got the Howe report yet, any more than my learned friends have even produced the report from Prof. Thomas in which he apparently is going to re-calculate his various calculations on the basis of the new doses.

My learned friend is right. He may rest assured that we are intending to serve evidence. We are very conscious of the fact that it should be sooner rather than later, and we will get it to my learned friends as soon as we possibly can, so that Prof. Evans will have time to consider it before he returns to be cross-examined on that aspect of the case.

MR. LANGSTAFF: My Lord, I am pleased to hear what my learned friend has to say, though I remain particularly concerned that he appears now to be saying that when he was cross-examining Prof. Evans about the Gardner study, his information upon which he was putting his questions was not in relation to the Gardner study at all, as it purported to be, but in relation to Prof.

Evans' re-working, but there it is. I hear what he says, and plainly I can take it no further at the moment.

MR. JUSTICE FRENCH: Have you any tables even, Mr. Rokison, that you can show or lend?

MR. ROKISON: I have not even myself yet seen tables. That is one of the exercises which we hope to be going through tomorrow. I am afraid that I have been rather busy preparing and continuing from day to day to prepare this part of my cross-examination. I am sorry, my Lord. The answer to your Lordship is that I have not seen any tables yet.

MR. JUSTICE FRENCH: I do not think you need my help to take it any further. If I tried to put my shoulder to the wheel, it would not push it any further than you are pushing it.

MR. ROKISON: Thank you very much, my Lord.

(The Court adjourned until 10.30 a.m. on Friday, 4th December 1992)