COURT OF JUSTICE

1990 R No 860
1989 H No 3689

BENCH DIVISION

ROYAL COURTS OF JUSTICE
THE STRAND
LONDON

Thursday 26th November 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)

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THIRTEENTH DAY'S PROCEEDINGS

THURSDAY, 26th NOVEMBER, 1992

MR. ROKISON: My Lord, before my learned friends call Prof. Evans may I just tell your Lordship what the position is as far as the epidemiological evidence is concerned? My Lord, I have mentioned, of course, to my learned friends and there have been letters exchanged between solicitors, and I also mentioned to your Lordship, the possibility that we might be in some difficulty in dealing with all aspects of epidemiology straightaway.

The position was, as your Lordship knows, that the re-working of the Gardner Study, using the figures which had been agreed eventually been Dr. Strong and Drs. Dennis and Lambert, was an exercise which was completed some two weeks ago. My Lord, it is not, as my learned friends have suggested, just a number crunching exercise to draw one's conclusions from the computer programme once those numbers have been fed in; there is a deal of interpretation involved.

My Lord, the position is that it was not until, I think, Monday evening of this week that we received the third report of Prof. Evans in which he interpreted, effectively, the figures which had come out of the Gardner Study. Of course, we had done, I do not pretend otherwise, we have been doing work on the figures ourselves but the position is that our main epidemiological witnesses are Prof. MacMahon, who is in the United States recovering from a serious operation which he had about two weeks ago, Prof. Sir Richard Doll, and also Prof. Howe, who is in Canada, as I told your Lordship, and your Lordship was kind enough to allow me the time to see Prof. Howe as he was on his way from Lyon back to Toronto, and I have discussed it with him and he is doing further work.

I am not in a position to cross-examine Prof. Evans or any other of my learned friends' epidemiological witnesses in relation to the latest figures and what conclusions one should draw from them. My Lord, we are as anxious as the Plaintiffs that no time should be lost, and as anxious as your Lordship that no time should be lost and we can get on with it. My Lord, the position is that there is a large amount of epidemiological evidence, as your Lordship will have seen from the reports, which is concerned with other studies which have been carried out, both in the United Kingdom and throughout the world. Prof. Evans deals primarily, in his first report, with those studies and comments upon them, and then Dr. Scott Davis and Dr. Kopecky then deal with studies worldwide.

My Lord, it is our suggestion that in order not to waste time I cross-examine Prof. Evans to the extent to

which I am able, not going onto the reworked Gardner figures, and similarly that I can deal with Dr. Kopecky and Dr. Scott Davis, by which time I hope, by perhaps the beginning of the week after next, I will be in a position to complete my cross-examination of Prof. Evans. The result of that will be that hopefully there will be no time lost to anybody except the inconvenience, for which I apologise, of Prof. Evans having to return for further cross-examination.

My Lord, this is a matter that I have mentioned to my learned friends.

MR. JUSTICE FRENCH: You have alerted Mr. Hytner to that?

MR. ROKISON: Yes, my Lord, I have.

MR. JUSTICE FRENCH: Mr. Hytner, have you any observations?

MR. HYTNER: My Lord, it seems to me there are two separate issues. The first is whether Mr. Rokison is in a position to finish his cross-examination of Prof. Evans. The answer to that is he is not and that is an end of it. If he is not in a position to cross-examine there is no possible objection that I can put to the course he proposes.

The second question, which may be academic, is ought he to be in this position, ought he to have been put in this position? My Lord, all I can say is that I have been reviewing the correspondence and I merely content myself with saying we are slightly surprised. The correspondence in relation to this begins on 3rd November and on the 4th the Defendants were agreeing that they were undertaking the re-analysis. My Lord, there it is, they say they are not ready and it would be silly for us to raise any objection.

There are only two problems that arise. The first I have already mentioned to Mr. Rokison and he agrees with the point that I make that the fact that Prof. Evans will have to return cannot in reality result in his sanitisation from us during the whole of the intervening period. Mr. Rokison agrees with that, so that we will be seeing him, consulting him and getting advice from him during the period when he is strictly still under cross-examination.

MR. JUSTICE FRENCH: Yes. I think this situation was foreseen during an in-chambers discussion before the trial began and certainly, as far as I am concerned, I see no possible objection in these circumstances to your taking instructions from Prof. Evans as may be necessary. Mr. Rokison, I am sure you will confirm that?

DISCUSSION

MR. ROKISON: I have confirmed that to my learned friend already, my Lord.

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MR. HYTNER: The second thing which Mr. Rokison apparently does not appear at the moment to have taken on board is that, of course, it is not just Prof. Evans but when Prof. Davis goes into the witness box he may well be asked about Prof. Evans' re-analysis and if Prof. Evans has not yet been cross-examined on it various assumptions will have to be made in relation to Prof. Davis' evidence and he may have to then come back as well, we will have to see.

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MR. JUSTICE FRENCH: We will meet these problems when they arise.

MR. HYTNER: Yes. My Lord, that is simply something I alert your Lordship and Mr. Rokison to.

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MR. ROKISON: My Lord, there was one thing that I had omitted to mention although I have mentioned it to your Lordship earlier, and I note that it was mentioned to your Lordship when your Lordship last sat on this matter on Tuesday, and that is that I think primarily Dr. Scott Davis and Dr. Kopecky deal with the epidemiological studies carried out throughout the world and although they do, in part, refer to the Gardner Study they do not, I think, draw any quantitative conclusions in relation to it.

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My Lord, the position with Prof. Thomas is very different because Prof. Thomas is, as we read the first reports from the Plaintiffs, the witness on the Plaintiffs' side who, together with Prof. Evans, interprets the Gardner Study and draws conclusions from it in relation to causation - that is the Gardner Study itself. Those conclusions which he draws in his report are obviously based upon the figures and conclusions which are set out in the Gardner Study itself. As we read it that report of Prof. Thomas, if there is to be evidence from Prof. Thomas, must be substantially revised and we have already indicated to my learned friends, on more than one occasion, that if they are intending to rely on the evidence of Prof. Thomas we would like to know at the earliest stage what it is he is now going to say in relation to the Gardner Study and what the re-working of it throws up.

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MR. JUSTICE FRENCH: Not only the re-working but the re-working with the additional individuals added?

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MR. ROKISON: Certainly. That is what I meant by the re-working, forgive me, my Lord. I meant the complete picture, all that has now been done which involves adding individuals to the study as well as alterations of dose figures and we are anxious to know whether they are going to call Prof. Thomas and if so

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what he is going to say. It is part of the Plaintiffs' case on epidemiology and the whole object, as your Lordship knows, of having a sequential exchange as we had was that we should know what the Plaintiffs' case was before we would be expected to answer it, and we still do not know to what extent they are relying on Prof. Thomas.

MR. JUSTICE FRENCH: Yes. Can you help, Mr. Hytner?

MR. HYTNER: Wednesday, my Lord, is the estimated time of arrival.

MR. JUSTICE FRENCH: You will be calling Prof. Thomas?

MR. HYTNER: Yes, my Lord.

MR. JUSTICE FRENCH: And Wednesday is the ETA for his observations.

MR. HYTNER: For his observations, yes, my Lord.

MR. JUSTICE FRENCH: Mr. Langstaff, are you ready to call Prof. Evans?

MR. LANGSTAFF: I think your Lordship may have seen the statement from Prof. Gardner. My Lord, that was served under cover of a Civil Evidence Act Notice ....

MR. JUSTICE FRENCH: I have not seen Prof. Gardner's statement.

MR. LANGSTAFF: My Lord, that must be put right. I am told, my Lord, that there is a bundle of documents which contains those relevant to what is called the "Gardner Re-analysis". If your Lordship takes the blue folder - my learned friends have a copy - and your Lordship goes to divider 2, my Lord, the formal notice which relates to the Civil Evidence Act is not there included, but I understand from my learned friends that having considered their position they are now content that the statement should be put in.

MR. JUSTICE FRENCH: I have not seen this because on Tuesday it was not certain whether there would be opposition to it.

MR. LANGSTAFF: My Lord, so I understand.

MR. JUSTICE FRENCH: Now there is no opposition and it can be treated as evidence under the Evidence Act?

MR. LANGSTAFF: My Lord, yes. May I then read the statement and your Lordship may be assisted by recalling that Dr. MacRae in his various reports has made a number of criticisms of Prof. Gardner.

MR. JUSTICE FRENCH: Yes.

MR. LANGSTAFF: For the benefit of your Lordship's notes your Lordship will find that in Dr. MacRae's second report, at pages 7-11 he complains that Prof. Gardner's study was flawed because of the misclassification of some cases and because not every case was traced, what he called "incomplete tracing".

MR. JUSTICE FRENCH: I think there was also a complaint about the lad who was at university in Bristol?

MR. LANGSTAFF: My Lord, that was the next one I was going to mention. At page 11 he deals with the exclusion of those cases born outside the West Cumbria area ....

MR. JUSTICE FRENCH: One was excluded - the Edinburgh one was excluded and the Bristol one was not.

MR. LANGSTAFF: My Lord, yes. Your Lordship will recall the words that he used, at page 12:

> "Remarkably, there is no explanation put forward for this in the published report of the Study."

He said at page 18 that he was surprised that steps had not been taken to include such an explanation and at page 28 he talked about:

> "... a curious aspect of the decision to include Case C00106 ...."

- it might be more convenient, my Lord, to call that the Bristol case -

> "... is the lack of discussion of this decision either in the published papers on in Dr. Snee's thesis ...."

and obviously by those comments hinting, as they might be taken to do, to a direct criticism of Prof. Gardner himself, plainly called for an answer and your Lordship will see what Prof. Gardner said.

My Lord, there is a statement, not made to those instructing me but made to the Treasury Solicitor and made in response principally to that which was said by Dr. MacRae. If your Lordship turns to page 9 of the statement ....

MR. JUSTICE FRENCH: Page 21 of the bundle.

MR. LANGSTAFF: My Lord, yes. Your Lordship will see there, after Prof. Gardner's signature, in handwriting the circumstances under which the statement was taken:

> "This statement was made by Professor Martin Gardner to L. L. Blake ...."

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- my Lord, my understanding is that he is the Treasury Solicitor -

> "... on the 13th day of November 1992 at 2.20 in the afternoon at his home in Eastleigh Hants in the following circumstances: the statement was prepared in type beforehand and it was confirmed with
B Prof. Gardner that such was his statement and that he did not wish to change or add anything. Prof. Gardner stated to me that he would not wish through illness, to give oral evidence."

and it is signed by "A barrister in the employment of the Treasury Solicitor".

C My Lord, the statement of Prof. Gardner then, reading it, begins at page 1:

"I am Martin Gardner, professor of medical statistics in the Medical Research Council's Environmental Epidemiology Unit at the University of Southampton. I have been employed in the Unit since its inception in 1980. My formal qualifications comprise a
D BSc in Mathematics, a Diploma in Mathematical Statistics and a PhD in Statistics. I am joint author of the report of the West Cumbria case-control study of leukaemia and lymphoma published in the British Medical Journal in 1990.

I say as follows:

E In the matter of Reay & Hope v BNFL, the plaintiffs' solicitors require me to give evidence in relation to the second report of Dr. K. D. MacRae. As I am medically unfit to attend trial I would respectfully ask the Court to accept this as my statement to be served under the Civil Evidence Act. Dr. Hazel Inskip ...."

F - my Lord, she is an employee also of the MRC and collaborated with Prof. Gardner on the same report -

> "... has already commented on Dr. MacRae's report at the request of the plaintiffs' solicitors in a letter dated 8th October 1992, a copy of which is appended hereto. I concur entirely with the points made in her letter but will amplify them here and
G add others."

My Lord, that letter appears immediately after page 9 of the report and I should perhaps read it since Prof. Gardner has adopted it. It is a letter of 8th October, 1992, addressed to Ms. Downs of Leigh, Day and Co., the Plaintiffs' solicitors:

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MR LANGSTAFF

"I am now in a position to reply to your letter of 17th September in which you asked me to comment on Dr. MacRae's report. I discussed an earlier draft of this letter with some of the authors of the paper and their comments are included. I have not however been able to contact them this week so they have not seen this final version of the letter. Since I know that you want a reply as quickly as possible I thought I should do what I can and send it off to you.

There appear to be three main aspects of the study upon which Dr. MacRae comments and I will discuss them in turn.

1. Misclassification of cases and controls

That untraced cases and controls were omitted from the analysis is a standard procedure for dealing with missing data. The 21 cases and controls who were misclassified as being amongst the 891 'negatively linked' to the BNFL workforce file, arose partly because the information on the original BNFL workforce tape sent to this Unit was incomplete. It is only since a revised tape has been received in the Unit, and further tracing of our own, that the misclassifications have been identified.

2. The exclusion of leukaemia and lymphoma cases born outside West Cumbria

Although not included in the first analysis, it is still the intention to examine those cases born outside West Cumbria. The main reason for excluding them from the published paper was that the birth and schools cohort studies had shown that the risk appeared to be confined to those born in the area."

- your Lordship will recall that is a reference to the 1987 studies of Prof. Gardner and I shall be asking Prof. Evans in due course about those studies -

"These cases were also considered to be more relevant to the assessment of X-rays, mother's age, social class etc., than to the Sellafield environment or employment. For the examination of paternal radiation exposure it would have been necessary to obtain information from other nuclear establishments should the fathers of cases or controls have been working there prior to the birth of their children. Since the UKAEA was not prepared to release such information unless each individual concerned gave consent, the inclusion of these sets of children in the analysis of pre-conception occupational radiation exposure would have been impossible.

3. The inclusion of a case diagnosed outside West Cumbria.

The intention at the outset of the case-control study was to include all cases diagnosed while resident in West Cumbria, and the starting point was the cases in the Black report. Each potential case was reviewed and assessed for its eligibility for inclusion. As in many studies, there were borderline situations where eligibility was not clear-cut because differing amounts of information about individuals were available during the 1950 to 1985 study period. Some subjects spent time in other parts of the country, and each such case had to be assessed on its individual merits. It appears that in making the assessment, the duration of time spent away from West Cumbria was taken into account. The important point however, is that the decisions were made before information was sought about risk factors and, thus, they should not be expected to produce bias. There would be a greater concern about bias if cases were selectively included in or excluded from the analysis in the light of knowledge about their various risk factors.

From the information available at the time that case C00106 was assessed ..."

- my Lord, that is the Bristol case -

"... his permanent address was given as being in West Cumbria (on the death certificate) and he appeared to have been away from home for only a short time (on the basis of his age and FPC registration).

I hope that this information clarifies the position for you. I am sending a copy of this letter to Freshfields to keep them informed."

My Lord, then returning to page 1 of Prof. Gardner's statement, having adopted those points made by Dr. Inskip he continues:

"1. Misclassification of cases and controls (MacRae, page 7)

Sometimes minimal identification data (surname, initials and date of birth) for linkage of fathers of cases and controls were not available on our West Cumbria study file. In such instances these cases and controls had to be omitted from the analysis of Sellafield paternal employment. To have included them as 'negative links' to the Sellafield workforce file could have created a bias. Around 10% of the cases of leukaemia and non-Hodgkin's lymphoma (8 out of 74) and of their controls (76 out of 790) had to be excluded for this reason.

A matched case-control study was considered to be the appropriate way of conducting the West Cumbria study. Inherent in this methodology is that when information on a factor is unknown for a case then the entire matched set

of controls has also to be excluded from the analysis of that factor. In this study the exclusion of controls where the father had been satisfactorily identified, but the fathers of the matched case had not, represented about another 10% exclusions (68 out of the remaining 714 controls). These exclusions were essential in order to conduct the analysis correctly using the appropriate statistical methods. The reason why the overall loss of controls at about 20% (144 out of 790) is greater than for cases is because of the two explanations given for their exclusion.

There was misclassification of only 2.4% of the fathers of cases and controls (21 out of 891) who were 'negatively linked' to the Sellafield workforce file initially made available to us. This occurred partly because the information on our own original file was incomplete, but more so because individuals were missing from the Sellafield workforce computer tape. Of the 21 misclassifications three fathers were identified after we had obtained further tracing information for our database. Sixteen of the remaining 18 fathers were not on the original computer tape from British Nuclear Fuels and were 'positively linked' only after we had been provided with a revised tape about one year after the publication of our paper. Both of the other misclassified fathers were on the original Sellafield tape - but one without initials and the other with a different surname spelling and date of birth than on our file.

2. <u>The exclusion of leukaemia and lymphoma cases born outside West Cumbria (MacRae, page 11)</u>

The case-control study was planned during the mid 1980s with the aim of including all children diagnosed with leukaemia or lymphoma in West Cumbria. The results of the Seascale birth and schools cohort studies reported in 1987 showed that the risk appeared to be confined to children born there and so these cases were of primary interest. The published analysis, therefore, focused on those both born and diagnosed in West Cumbria. It has always been the intention to present findings for the six cases of leukaemia and eight cases of lymphoma born elsewhere. These cases, however, are more relevant to the assessment of such factors as X-rays or mother's age than to the Sellafield geographical and occupational environment before birth or at a young age.

To enable the examination of father's occupational radiation exposure for cases and controls born outside West Cumbria, it would have been necessary to obtain information from nuclear establishments in the geographical area where the father had lived before the birth of his child. Dr. Brian Wade of the United Kingdom Atomic Energy Authority informed me in a letter dated 22nd May 1987 that 'I can release occupational radiation

exposure data to you only if the individual concerned gives consent'. To make suitable contact to request permission would have been, for reasons such as lack of knowledge of fathers' current addresses or their death, substantially not possible. Thus we were unable to obtain occupational radiation data for fathers of children born outside the area.

Dr. MacRae (page 17) comments particularly on the omission from our analysis of two cases of leukaemia and one case of non-Hodgkin's lymphoma diagnosed while resident in Seascale but born outside West Cumbria. These three cases are among the 14 mentioned earlier for which we will be presenting results subsequently. On the birth certificate of one of the three cases, the father was recorded as working at the Atomic Energy Research Establishment. The father moved to work at Sellafield after the child's birth and so a transfer radiation dose record was available for him, but with no information on our field from British Nuclear Fuels as to whether exposure had occurred before or after the child's conception. It would not have been possible to obtain radiation data in a similar way for fathers of the birth-area matched controls, even though some were known to have worked for the United Kingdom Energy Authority from their children's birth certificates, since the fathers were not on the Sellafield workforce computer tape. Thus, even if we had included cases born outside West Cumbria in the published paper, it would have been necessary to exclude this case and corresponding controls from the analysis of paternal radiation exposure. For the other two cases there was no mention of employment at nuclear establishments on their child's birth certificate.

3. <u>The inclusion of a case diagnosed outside West Cumbria (MacRae, page 22)</u>

Decisions about inclusion of cases in the study were made at an early stage using information then available. Different amounts of information from a variety of sources were available for each case and they were assessed individually. Decisions regarding the inclusion or exclusion of any particular case were made independently, without reference to the exposure factors of interest. In fact, this assessment was made well before we tried to link the fathers to the Sellafield workforce file, and thus before we had any details of occupational radiation doses. At the time, my study team and I used the discretion and judgment that we must necessarily exercise as scientists to interpret the available information.

Dr. MacRae argues that case number C00106 should not have been included in the analysis. This case, as others, was assessed for inclusion at an early point in the conduct of the study. The case was born in Seascale

and appeared in the Black report. The residential address on the death certificate was given as in Seascale. No hospital notes were available, although the case had registered with a general practitioner in Bristol two months before diagnosis. Nonetheless, we felt that lifetime residence had effectively been in Seascale and that the factors which contributed to the development of leukaemia must have occurred while living there. We also felt that we would be more open to criticism for excluding, rather than including, such a case.

Case C00213, in contrast, had been registered with a general practitioner in Dorset for six years and then in Edinburgh for three years prior to diagnosis. With such a history it would be much more likely that exposure to factors of interest outside West Cumbria would be relevant. These two cases (C00106 and C00213) were considered to be quite different.

4. Statistical significance (MacRae, page 27)

Dr. MacRae states that "If Case C00106 had been excluded from the West Cumbria Study then the 'statistical significance of these raised relative risks would not have appeared.' Specifically and only to examine Dr. MacRae's claim, we have re-analysed the data in relation to father's occupational radiation exposure excluding this case. Although the relative risks for the highest dose categories are consequently lowered, the majority in fact remain statistically significant with 95% confidence intervals which exclude unity. Our interpretation of the results would hardly change from that published.

The table shows the detailed analysis from the published report and from the letter to the British Medical Journal (19th September 1992, page 715). The corresponding results based on the data excluding Case C000106 and his matched controls are also shown. Both the published letter and the table are appended hereto."

My Lord, it is probably convenient to look now before dealing with what Prof. Gardner regards as the salient points, at those documents. They are at the end of the report.

MR. JUSTICE FRENCH: "The end of the report"? Where should I be looking?

MR. LANGSTAFF: My Lord, immediately after the letter from Inskip.

MR. ROKISON: Page 24, my Lord.

MR. LANGSTAFF: Your Lordship will see here the article to which reference is made from the British

Medical Journal of the 19th of September, 1992. It is a letter which speaks for itself. It is from Prof. Gardner to the British Medical Journal:

> "Editor,
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> My colleagues and I have found a few small numerical mistakes in tables II and VI of our case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria published in the BMJ in 1990. These tables related to risks of leukaemia and non-Hodgkin's lymphoma in children with reference to mother's and father's ages at their child's birth and to father's employment and radiation dose during employment at the Sellafield nuclear plant. Tables 1 and II here show the amended results.
>
> The original calculation of parental age was either one year lower or higher than it should have been depending on whether the parent's birthday was earlier or later in the year than that of the child. The new relative risks in Table I are similar to, but generally larger than, the previously published figures. We have revised the estimates of radiation dose to take account of men whose periods of employment in the year of, or before, their child's conception did not cover complete calendar years. No cases and only a few controls were reclassified, and the new relative risks in table II are in general similar to, or a little higher than, the earlier figures.
>
> We regret the changes but believe they do not alter our interpretation of the study."

My Lord, that was correcting the error that had occurred by reason of the relative dates of birth.

MR. JUSTICE FRENCH: Yes, the 19th of September?

MR. LANGSTAFF: My Lord, yes, the 19th of September of this year. Your Lordship will see on the right hand side of that page, tables I and II, which replicate tables from the Gardner report of 1990, and set out the slightly revised relative risks.

My Lord, that stands by way of comparison with the documents set out at pages 25 and 26.

MR. JUSTICE FRENCH: Though they are not side by side, one compares 24 with 25 and 26?

MR. LANGSTAFF: My Lord, yes. Your Lordship will see that the comparison is made all the easier because one can read across the columns from left to right. Under the first of the tables on page 25.

MR. JUSTICE FRENCH: I see, they are set out side by side on those two pages.

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MR. LANGSTAFF: Your Lordship will see the relative risk: "Published paper", "Published letter", "Published paper without Case C000106" and the "Published letter without Case C00106". My Lord, it is probably the letter one should take since it is the corrected version of the data. Your Lordship will see the relative risk drops in the highest dose category, that is, exposure to more than 100 mSv. lifetime dose prior to conception, from the relative risk of 6.3 to one of 4.59. The 95% confidence interval there being .99 - 22.29. For the six months' preconception dose, from 7.38 to 5.43. The 95% confidence interval running from 1.14 to 25.89.

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My Lord, that is the area controls.

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When one looks at the local controls at the bottom of the page, and taking again the highest risk category, your Lordship will see that for a dose in excess of 100 mSv lifetime dose prior to conception, the published letter was 8.38, a relative risk of 8.38. Without Case C00106 the relative risk was 7.58. Your Lordship will see the confidence intervals there going from 1.14 at the lowest to 50.21 at the top, and for the six months' preconception dose, 6.82 in the letter, 6.27 without the Bristol case and again your Lordship sees the confidence interval there.

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My Lord, the next page, page 26, provides similar tables but on this occasion not limited to leukaemia but including non-Hodgkin's lymphoma. Again, my Lord, using to demonstrate the point that is made by Prof. Gardner that the highest dose categories, your Lordship will see in the published letter for a lifetime dose in excess of 100 mSv prior to conception, there is a relative risk in respect of both leukaemia and non-Hodgkin's lymphoma put together of 6.45, which reduces to 4.73 with the exclusion of the Bristol case, but again with the confidence interval running from above unity to 21.8. The six months' preconception dose, 4.41, and without case C00106, 3.21. In that case the confidence interval running from below unity, .76 to 13.51. One could do the same exercise for the table with local controls at the bottom of that page, again identifying the change in relative risk and noting that again for the total preconception dose the confidence interval remains so that the lowest part of the confidence interval is still above unity.

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My Lord, returning then to the text, if I may. Page 19 in your Lordship's bundle:

"The salient points include the following:

(i) All eight relative risks in the highest dose categories in the published letter were statistically

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significant with the complete data sets, but five out of eight remain statistically significant with the exclusion of case C00106.

(ii) The sizes of the relative risks in the highest dose categories on excluding Case C00106 are reduced although they remain high. For the published letter the eight relative risks range from 4.41 to 8.59 compared with from 3.21 to 7.81 after the case's exclusion.

(iii) Also shown in the table are the outcomes of examining relationships between relative risks and father's occupational radiation dose using the score test for trend. This is an approach to assessing the complete data sets over all doses rather than only in the highest radiation group. The test examines whether or not there is an increase in risk as recorded exposure increases. Seven of the eight score tests for the data in the published letter were statistically significant but five out of eight remain statistically significant after the exclusion of Case C00106. For the latter analyses each of the three statistically non-significant score tests relate to dose during the six months before conception, while all four tests for total dose before conception are statistically significant.

(iv) There is, of course, some overlap of cases, controls and diagnoses in the table with consequent lack of statistical independence within the above three sections. However, the general picture is of relative risks increasing with paternal radiation exposure.

These results raise a question about the justification for the statement by Dr. MacRae (page 27) that, 'The inclusion of this case in the study is fundamental to the finding of a "statistically significant" association between paternal preconception irradiation and leukaemia relative risk in offspring.'

5. Bias and confounding (MacRae, page 1)

It is true to say that 'case-control studies are particularly susceptible to effects of bias and confounding' - in comparison, for example, to experimental studies. However, it does not follow that the 'West Cumbria study is especially so given the very small numbers upon which the results of the study are based'. Bias and confounding are fundamental properties of study design, whereas smaller sample sizes lead to larger sampling errors - which are indicated by the width of the related confidence intervals.

6. Hypothesis-generating study (MacRae, page 2)

It is not appropriate to call the West Cumbria study a 'hypothesis-generating epidemiological study.' In fact, some of the questions which the study could address were

listed by the Black Inquiry in a committee paper (copy attached) and it is noticeable that occupational radiation exposure is one of these. Thus preformulated hypotheses had been documented and the study data were collected subsequently to examine these."

My Lord, that committee paper begins at page 27, and if your Lordship just casts and eye at that.

MR. JUSTICE FRENCH: It had occurred to me already that this was not hypothesis generating but hypothesis examining.

MR. LANGSTAFF: My Lord, I am obliged. It is not necessary then to look at that in detail.

My Lord, that is the statement of Prof. Gardner which we put in as evidence.

I now call Prof. Evans.

MR. JUSTICE FRENCH: Before you do that could you please help me on one matter? The expression "statistical artifact" crops up from time to time. I fully understand that it is intended to mean a source of error?

MR. LANGSTAFF: My Lord, yes.

MR. JUSTICE FRENCH: At the moment I don't understand what kind of source of error it is. Would you rather leave that to Prof. Evans or can you help me now?

MR. LANGSTAFF: My Lord, I will try. My attempt may, of course, be inadequate, and if it is no doubt...

MR. JUSTICE FRENCH: Shall we leave it to Prof. Evans, who will undoubtedly get it right?

MR. LANGSTAFF: In my own words, and doing the best I can, my understanding is that it is a function of the design of the study which may produce error. For example, where data are grouped.

MR. JUSTICE FRENCH: I see, an artifact, a product of the study form itself?

MR. LANGSTAFF: As applied to the available data.

MR. JUSTICE FRENCH: Yes, which may produce an error. For example...

MR. LANGSTAFF: In the grouping of data for the purposes of analysis.

MR. JUSTICE FRENCH: Or selection of data?

MR. LANGSTAFF: My Lord, that may well be, yes. It is very different from the question of the bias which occurs in two areas: the question of measurement which involves in itself in the radiation context the accuracy with which you can say that certain doses are received and the timing of them and so on, and selection bias. An artifact is really a question of how one examines the data, as I understand it.

My Lord, that may be a very inadequate explanation.

MR. JUSTICE FRENCH: If one were using it in terms of a model like SEAM, which we have learned to know a bit about, an artifact would be a defect in the construction of the model rather than that which is fed into it?

MR. LANGSTAFF: My Lord, that is right. I think the resultant error is a combination of the two. It is said in this case, as your Lordship has no doubt seen, that when one considers the studies conducted round Dounreay, for example, and centres a circle on Dounreay and draws it at 12.5 km, it bisects Thurso. The point is made that if it were 10 km it would not and the leukaemias that occur in one corner of Thurso, or are reported in one quarter of Thurso, would not be within that particular geographical boundary. On the other hand, if it were 15 km there may be more. One can see that the selection of a boundary, using that one example, may, in interaction with the available data, produce a particular result or the appearance of a particular result.

MR. JUSTICE FRENCH: Any increase or decrease relatively on account of the dimensions of the circle would be an artifact of the study design?

MR. LANGSTAFF: My Lord, yes. Whether it produces an error or not is, of course, a matter of interpretation.

MR. JUSTICE FRENCH: I can see Prof. Evans is nodding. I am comforted by that!

MR. LANGSTAFF: My Lord, I am very much comforted by that. It shows that at least I may have understood something!

Prof. Evans.

STEPHEN JAMES EVANS Sworn

Examined by MR. LANGSTAFF:

Q. Is your full name Stephen John Evans?
A. No. It is Stephen James Evans.

Q. It shows I haven't got everything right! I hope some of the other answers you give me will be nearer. You are

the Professor of Medical Statistics at the London Hospital Medical College of the University of London?
A. I am.

Q. You have worked in the field of medical statistics for the last 15 years?
A. Yes.

Q. Prior to that you worked in computing and data analysis for high energy nuclear physics?
A. Yes.

Q. How many Professors of Medical Statistics are there in the country?
A. I believe there are six with that title, practising at the moment.

Q. At the time you were appointed, how many were there?
A. I was the third in the country at the time.

Q. Who were the others?
A. The first was Prof. Gardner in Southampton and the second was Prof. Pocock at the London School of Hygiene and Tropical Medicine.

Q. The Prof. Gardner at Southampton, is that the Prof. Gardner we have heard of who produced what we have called the Gardner papers?
A. Yes, he is.

Q. Prof. Evans, you have produced four reports for the purpose of this litigation, dated the 1st of June of this year, the second report dated 14th August, 1992, which I anticipate might require revision in the light of further work. A third report dated 23rd November and a fourth report dated 25th November?
A. That is correct.

Q. Do you adopt those reports subject to certain qualifications in respect of the second report, in giving your evidence?
A. I do.

Q. So far as your first report is concerned, you deal there with various other reports. I will take you through in detail in a moment. Do you stand generally by the conclusions you there express?
A. Yes, I do.

Q. In your second report, and I think I mis-dated that report, it should be the 3rd of September of this year.

MR. JUSTICE FRENCH: Not the 14th?

MR. LANGSTAFF: My Lord, no:

Q. Is that a report in which you conducted a re-analysis of the data which Prof. Gardner has used to produce his

published work, and in part re-analysed it using doses which you understood to be advanced by a Dr. Dennis?
A. Yes, I did.

Q. In your third report did you essentially report on the results of a similar exercise, in this case though in place of those doses you had been supplied with by Dr. Dennis, using doses which you understood to have been agreed between the parties for the purpose of this litigation?
A. Yes, I did.

Q. In our fourth report do you comment briefly upon some of the later epidemiological material that has come to prominence since your first report?
A. Yes.

Q. Let me then take you to page 5 of your first report. Page 5, paragraph 7, you set out the purpose to which you address your first report:

> "...to review the epidemiological work...to provide a context from which I could make an assessment as to whether radiation from the Sellafield nuclear plant was implicated as a cause for the diseases suffered by the Plaintiffs."

In doing that have you principally considered only the material arising from the United Kingdom?
A. Principally, yes.

Q. On pages 5 and 6 you deal with background statistics in relation to leukaemia and at the bottom of page 6, paragraph 11 you note:

> "With such a rare disease as leukaemia, unless it has a single cause, the problem of demonstrating that particular factors increase the risk of the disease is very great."

Although not advancing yourself as a medical expert on leukaemia, from your point of view as an epidemiologist and statistician do you understand leukaemia to have just one cause or more than one cause?
A. I would believe it would be very unlikely that it would have only one cause. May I give you an analogy? Mesothelioma is a very, very rare cancer, but we can find out the cause of it very easily because we are very certain that it occurs only in relation to asbestos and so we find it only occurring in people who have been exposed to that, whereas with leukaemia we don't see any simple pattern.

Q. You then go on to tell us, page 7, paragraph 12, that you will review the report produced under the Chairmanship of Sir Douglas Black, which is the Black Report?
A. Yes.

Q. You begin then to set out the background to that report in paragraphs 13 and 14. You deal in paragraphs 15 and 16 with various statistical matters which probably require no further explanation. At paragraph 17 you deal with material which comes from what you describe as:

> "Draper's review of the geographical epidemiology of leukaemia and NHL in the UK..."

You say this:

> "Overall the evidence accumulated so far is that the pattern of leukaemia incidence across the UK generally conforms to a Poisson distribution, and shows relatively little evidence of clustering at a national level."

A. Yes.

Q. Is clustering in leukaemia the exception rather than the rule?

A. It would appear to be so in the United Kingdom.

Q. You qualify that by saying:

> "There is some evidence for 'extra' Poisson variation and more clustering in younger age groups..."

MR. JUSTICE FRENCH: Would you pause there a moment?

Q. It would appear that in the United Kingdom clustering is the exception rather than the rule?

A. For leukaemia as a whole, yes.

Q. Clustering for leukaemia as a whole.

Q. MR. LANGSTAFF: You go on to say:

> "There is some evidence for 'extra' Poisson variation and more clustering in younger age groups (0-4 years) with lymphocytic leukaemia, but the evidence is not strong."

Does that hint at there being a pre-natal factor in the etiology of such leukaemia?

MR. ROKISON: I think that is probably a leading question, my Lord.

MR. JUSTICE FRENCH: I think it may be but when dealing with experts...

MR. ROKISON: I know, but it is...

MR. JUSTICE FRENCH: Forgive me, Mr. Rokison. The rules must be observed. I agree. However, I am only perhaps mitigating the offence.

MR. ROKISON: Indeed, and I don't want to be petty about it at all, but it is perfectly easy to ask it in a legal form as to what conclusion one draws from that, but I agree.

MR. JUSTICE FRENCH: What you are saying to Mr. Langstaff by implication is, "Be careful not to lead on matters which may importantly be contentious."

MR. ROKISON: Indeed. Your Lordship puts it better than me.

MR. HYTNER: My Lord, I think Mr. Rokison is jealous of the fact that as a leader he is more entitled to lead than Mr. Langstaff!

MR. LANGSTAFF: My Lord, the condemned man must have his say! I entirely accept it was a leading question. There are ways of re-formulating the question.

Q. Perhaps the simplest thing is simply to have the answer, Professor?
A. There is some evidence that the pattern in younger age groups is different to that in older age groups. If you are going to have a disease involving cancer in very young people, aged 0-4, they don't have very much time to have been exposed to something that might have caused it and so it is entirely possible that the exposure might possibly be pre-natal or have been caused pre-natally.

MR. JUSTICE FRENCH: I want to get this down if I may:

Q. Some difference in the pattern of what? Leukaemias?
A. The pattern of leukaemia being different in the 0-4 year olds.

Q. The pattern of leukaemias...
A. In addition can I...

Q. ...in group 0-4 is different to that in older groups?
A. That is right.

Q. You went on to say that this may be due to a difference in exposure times to infants?
A. It could be due to something that has happened before birth rather than something that has happened after birth. That is a possibility.

Q. It may be due to something before birth rather than after. Yes, thank you.

Q. MR. LANGSTAFF: Then, Professor, you deal, at page 9, with the result of the Yorkshire Television programme in producing the Black Report, and let me take you, Professor, to the Black Report.

My Lord, it is in the Common Bundle at letter B.

MR. JUSTICE FRENCH: Page or divider which?

MR. LANGSTAFF: My Lord, my divider is an earlier edition than your Lordship's.

THE WITNESS: Mine is at 13. It is the orange book.

MR. LANGSTAFF: I am very much obliged:

Q. Is this the report of the Independent Advisory Group, the Chairman Sir Douglas Black?
A. Yes.

Q. Dealing with the report, Professor, would you look at Chapter 1, the Introduction? Paragraph 1, I think, sets out the history, which we have dealt with. 1.2, the terms of reference for the Inquiry:

"To look into the recently published claims of an increased incidence of cancer in the vicinity of the Sellafield site:-

1. examine the evidence concerning the alleged cluster of cancer cases in the village of Seascale;

2. consider the need for further research;

3. and make recommendations."

Then 1.6 sets out what the Committee saw as its task:

"a. establishing the incidence of cancer in the areas adjacent to Sellafield, and comparing it with the incidence of cancer in other areas in the United Kingdom and in Cumbria;

b. considering the available data on radiation exposure in the area adjacent to Sellafield and the evidence relating radiation exposure to cancer, thus assessing the likelihood that any radiation exposure could have caused any increased incidence of cancer detected in the area;

c. assessing other possible significant factors."

Paragraph 1.10, I think, describes the Sellafield site, as the Committee saw it:

"The Sellafield site includes a reprocessing plant for spent nuclear fuel. For that reason the airborne and liquid discharges are different in composition and quantity from those from other nuclear establishments in the United Kingdom. These

discharges result in collective dose commitments to the public considerably greater than those from any other nuclear establishment in the United Kingdom. (Figure 1.1)."

If you turn over the page, I think you see a graphic illustration of that. It is perhaps what one might call a cylinder chart rather than a bar chart, and that, as we know, is based upon the doses that Black was considering.

Having set the background, do they then go on, at Chapter 2, to deal with the epidemiological evidence and recommendations, and the Background, Chapter 2, paragraph 2.1:

> "Our initial concern was to establish whether or not there was an increased incidence or cluster of cancer, particularly in young people, in the area around Sellafield. The word cluster, which has a technical meaning related to the concentration of cases in space and time, will not be used in this Chapter because we are concerned with an extended time period."

Then the next two pages, pages 13 and 14, of the report, does the Black Committee begin to set out the cases of leukaemia and other malignancies which the Black Committee considered might be relevant?

A. Yes.

Q. And Table 2.1 shows cases of leukaemia resident in Seascale since 1955 and aged under 25 years at diagnosis?

A. Yes.

Q. It is noted the diagnosis is as recorded by the certifying doctor, and one sees there seven cases?

A. Yes.

Q. Will we find, Professor Evans, that when we come to the Gardner study, that not all of those cases were cases which were considered by Prof. Gardner for the purposes of his occupational analysis?

A. You are correct.

Q. I think we know, for instance, that Prof. Gardner's study runs from 1950 until 1985 and, therefore, excluded - it is an obvious point - Case 1 shown in the Table 2.1 of the Black Report?

A. Yes.

Q. Table 2.2 deals with cases of leukaemia in the Millom Rural District since 1955, but that, I think, is a district to the south of Seascale?

A. Yes.

Q. And aged under 25 years at diagnosis, and the diagnosis is given in the right-hand column?

A. Yes.

MR. JUSTICE FRENCH: Millom RDC is to the south of and does not include Seascale - is that proposition correct - or does include Seascale?

MR. LANGSTAFF: It includes it, my Lord.

MR. JUSTICE FRENCH: So that Seascale is to the north of the RDC?

MR. LANGSTAFF: My Lord, yes, it is effectively almost on the boundary.

I stand corrected, I think. Case 1 was excluded because of the place of birth and not because of the date. Born, I think, in Barrow, outside Millom Rural District. Let me just correct that while I am at the point and I am grateful to my learned friend.

THE WITNESS: There may be more than one reason for the exclusion.

Q. MR. LANGSTAFF: But, at any rate, it was excluded and so we are not at odds on that. Table 2.3, cases of lymphoma resident in Millom Rural District under 25 years, and Table 2.4, the case of solid tumours. Just looking down the table in the case of lymphoma, one sees what is included there - lymphosarcoma, histiocytosis, a queried non-Hodgkin's lymphoma, non-Hodgkin's, and then there are three cases of Hodgkin's Disease. One notices as well in that same column a lymphocytic leukaemia, which has been classified as a lymphoma rather than as a leukaemia?

A. Yes.

Q. Table 2.4, one can cast an eye down the right-hand column and see the nature of the diagnoses there of the solid tumours. The report continues at 2.12, dealing with the nature of Seascale. Not a typical West Cumbrian village and sets out the information given to the Black Committee, that the Ministry of Supply and the United Kingdom Atomic Energy Authority built much of the accommodation to house the staff at the time that the Windscale Piles were under construction, 1952; that BNFL continues to own a significant proportion of the houses, rented mainly to young graduates, who are a mobile population, possibly more likely to be working with radioactive material than the average BNFL employee. They were also told:

> "....that the population of Seascale was more mobile than that of many adjacent villages. This could affect the estimated incidence of cancer in various ways. For instance, the annual size of the population....."

and it sets out the question of numbers and, at 2.14, the annual number of births shown in the graph opposite.

Do you have any reason to doubt the accuracy of any of that information about Seascale?

A. No, I have no reason to doubt it.

Q. Then Black begins to consider the incidence of cancer in Cumbria, page 20, and Table 2.5 on page 21 is a tabular presentation, I think, of the various reports that had at that stage been done to investigate the incidence of cancer in the general area?

A. Yes.

Q. If you turn over to page 23, we see the answer to the geographical position of Seascale and Sellafield, the map showing that Seascale is just south of the boundary between Millom and Ennerdale, and Sellafield just north?

A. Yes.

Q. The next pages then, I think, deal with the various tables of the comparisons between the expected and the observed deaths in relation to leukaemia and other malignancies around the Sellafield site and, from paragraph 2.34 onwards, the Black Report deals with the cancer incidence data for small areas in the United Kingdom?

A. Yes.

Q. At paragraph 2.36, dealing with, I think, a study earlier done by Dr. Craft of electoral wards, the Black Committee noted that in that study Seascale ranked sixth highest in incidence rates for all childhood cancers, and the ranking is given below. It then goes on to note:

> "The rate in Seascale, although based on only four cases, is statistically significantly raised above the regional incidence by an estimated factor of between 5 and 6 fold."
>
> If we go overleaf to page 32, paragraph 2.37:
>
> "For the years studied, Seascale had the third highest incidence rate of childhood 'lymphoid malignancy' among the 765 electoral wards. (Table 2.19). Again the rate in Seascale," it says, "is based on (the same) 4 cases, but is statistically significantly raised over the regional level by a factor of about 16."

Can I just ask for your comments? We see that the ward rank order, No. 3 has a little star against it, which I think indicates that is Seascale?

A. Yes.

Q. The number of cases in the child population and the rate per 1,000 children and, if one looks at the table headed "Poisson Probability", one sees there appears to be quite a difference in figures between the probability of such a result in Seascale compared to the probability of that in other wards?

A. Yes.

Q. Why would it be, can you tell us, looking at it on the data that is available to you here, that that probability is so low in comparison to the other wards which are mentioned?

A. The probability relates to, firstly, the rate itself, which is high, but, more importantly, to the number of children at risk, and so it is the 411 children, who are a larger population than any of the other wards in that table, that leads to that small probability.

Q. The Poisson probability of 0.000124, if one were to put that in English rather than in maths, it would be what?

A. If we had looked at that ward on its own, we would be very, very surprised to see such a large number of cases among a child population of that kind. Very clearly, we will sometimes find - even in a very small group of people, we will find one case. When we extend the population, we will not necessarily expect to find more than one case until we reach a larger population, and so this is a very rare finding, but I would not wish to over-interpret that.

Q. Then paragraph 2.38:

> "Comparisons with other areas were also carried out by Gardner and Winter...."

That again, I think, is Prof. Gardner?

A. Yes.

Q.

> "....who examined leukaemia mortality among young people under the age of 25 years in each of the 469 Rural Districts in England and Wales .... They found 7 with statistically significant raised leukaemia death rates in the under 25 year-old group. This is fewer than might be expected (about 12) to occur by chance if the underlying rates were the same in all areas, and the observed differences were due only to the limited number of calendar years and hence limited numbers of deaths studied. Millom Rural District, however, had the second highest rate out of 152 similar sized Rural Districts (Table 2.20)."

That sets out, I think, the distribution of mortality from leukaemia in 152 rural districts of England and Wales of a similar size to Millom Rural District.

Can I then take you through to the discussion at page 34? 2.44:

> "Seascale had the third highest incidence rate of lymphoid malignancy in under 15 year olds among 765 electoral wards in the region covered by the Northern Children's Cancer Registry between 1968-82, and Millom Rural District had the second highest death

rate from leukaemia in under 25 year-olds among 152 similar sized Rural Districts between 1968-78 throughout England and Wales. This does not necessarily mean that radioactive waste discharged from the Sellafield site into the atmosphere and sea nearby is the cause of the increase. The effect of chance or some other unidentified cause cannot be excluded, and the fact that the other electoral wards and Rural Districts with increased rates were geographically scattered outside the area around Sellafield is relevant here."

It makes a comment about:

> "In the electoral ward study the number of leukaemia cases registered in each ward was necessarily small because of the rarity of the disease, the small size of electoral wards, and the limited time period of observation. In Seascale there were four cases during 1968-82, and in Millom .... there were six deaths .... between 1968-78. Even though the above studies are based on small numbers, nevertheless they are consistent in demonstrating a higher incidence of leukaemia in young people resident in the area."

It then echoes what you were saying:

> "Most cases of childhood leukaemia are of unknown cause, and therefore caution is necessary in interpreting the results described above. An observed association between two factors does not prove a causal relationship. Some third, possibly unthought of factor might be the cause. We have already seen that Seascale is not a typical West Cumbrian village. It has been suggested to us that such factors as the consumption of unpasteurised milk and the discharge of untreated sewage into the sea may be relevant. But there is no scientific evidence that these are important in the aetiology of childhood leukaemia."

Pausing there, do you know of any scientific evidence that suggests that either of those may be a cause of leukaemia?

A. No.

Q. "Radiation is the only established environmental cause of leukaemia in children within the limits of present knowledge."

What do you say about that?

A. I would agree with that.

Q. "While there is evidence that radiation-induced leukaemia in adults usually results in myeloid leukaemia, there is not known to be such an association of myeloid histology with radiation-induced childhood leukaemia."

It then recommends further epidemiological research.

Case-control study, 2.49, and page 35, a birth cohort study. A recommendation at 2.52:

> "....a study be carried out on the records of all children born since 1950 to mothers resident in Seascale at the time of birth to examine cancer incidence and mortality."

And it notes at 2.54 that preparations for that study had commenced.

School studies at 2.55.

The rest of the Black Report, Professor - you may be asked subsequently about it - deals with the environmental aspects of the Sellafield site at Chapter 3, which I do not take you through in detail, except perhaps for this. If one looks at page 57, of the various possibilities that are examined by the Black Committee, amongst them are bacteria and viruses, and paragraph A.3.21 deals with human viruses and leukaemia and, at A.3.26 on page 58, the combined effects of various causes:

> "The joint effects of chemical, physical and biological agents are of potentially great importance, but good quality scientific data on such effects are not readily available. UNSCEAR...."

Is that the United Nations Scientific Committee on the Environmental Aspects of Radiation?

A. I think it is actually on the Effects of Atomic Radiation.

Q. I am obliged:

> "....examined the evidence for combined action of ionising radiation and carcinogens, but found available data incomplete and evidence for a promotor effect conflicting,"

and then deals with that. The conclusion, at A.3.27:

> "While it is possible to postulate agents that might act synergistically with radiation, we have found no convincing evidence for any unexpected environmental carcinogen or agent peculiar to the area around Sellafield."

Professor, in your studies of what has been written since the Black Report, what do you say about that conclusion?

A. I do not think we have found any convincing evidence for any unexpected environmental carcinogen or agent peculiar to the area around Sellafield.

Q. Chapter 4 then deals with radiation exposure of young people in Seascale, and again I do not take you through that. We come, finally, to the conclusions and recommendations of the Black Report at Chapter 6, part of which, at page 93, makes recommendations. Do we see there the first three recommendations:

> "1. A study should be carried out on the records of those cases of leukaemia and lymphoma which have been diagnosed among young people up to the age of 25, resident in West Cumbria. These cases should be compared with suitable controls in respect of factors that could be relevant to the development of leukaemia and lymphoma."

A. Yes.

Q. > "2. A study should be carried out of the records on all children born since 1950 to mothers resident in Seascale at the time of birth. Its main purpose would be to examine cancer incidence and mortality among those children, including cases which might have occurred after moving from Seascale."

The third recommendation:

> "A study should be considered of the records of school children who have attended schools in the area."

I shall not ask you about the other recommendations. It is those three recommendations, I think, that we may see to have been relevant in then what followed?

A. Yes.

Q. Page 9 of your report, Professor, returning to that, paragraph 20, you set out what, in your view, are the most significant conclusions that arise out of the Black Report?

A. Yes.

Q. First:

> "There was not a widespread public health problem of increased cancer risk resulting from radiation linked diseases around Sellafield.
>
> b. The rare disease of leukaemia did occur far more frequently than could be explained by chance variation in the immediate vicinity of Sellafield. This conclusion was reached by examining a number of different sources over different geographical areas and time periods. The excess first reported by Urquhart and Cutler was confirmed, as was a four-fold excess between 1968 and 1978 in the Millom Rural District."

A. Yes.

Q. We have seen that, but can I just ask you this? What is the importance, in your view, of the examination of the data being from a number of different sources, over different geographical areas and over different time periods?
A. If you choose one particular place, one particular time period, then it is very easy to find an excess. When you look at it over a number of different ones, then your probability of finding an excess will reduce markedly, if there is no genuine excess in that place, and so the fact that they looked at several means that it is much less likely that chance is an explanation.

Q. MR. JUSTICE FRENCH: I paraphrased this and may have got it wrong in doing so, so please tell me. "The greater the area taken, the less the possibility of the excess being observed unless it is a real one"?
A. Yes, I think it is more a matter of looking at it in a variety of different ways rather than just simply taking a larger area because, if you just increase the area, then you are not doing anything really necessarily very different. You will just perhaps dilute the effect.

Q. "The greater the area and the wider the spectrum"?
A. Yes.

Q. How else could one better express it?
A. But, for example, as you have seen from the map there, you could look at it by Millom Rural District or you could look at it by Seascale or you could look at it around Sellafield, which includes Ennerdale, and so you need to look at it in a variety of things. You could also look at it by exact geographical position of residents and not depend on Local Authority boundaries. So it is the variety of ways of dividing up your area that counts rather than just the size of it. Indeed, for all of West Cumbria, there is not an excess when we compare with England and Wales. The rest of West Cumbria seems to have a lower incidence of leukaemia. So, if we widen the area too much, then, if there is a genuine excess there, then you can eventually dilute it.

Q. So it is really the greater the number of ways of approaching the area concerned?
A. That is right.

Q. MR. LANGSTAFF: Can I perhaps approach it in this way? At the start of this morning you heard a description given of what a statistical artefact was. How accurate was that description?
A. Some parts of it were very accurate. There were a few parts that were not as accurate. Most of it was very accurate.

Q. I am obliged for that. Would a question of boundary selection and grouping of data come under the heading of "statistical artefact"?

A. It could do. It could also be an issue of bias. If you were - and this is one of the problems with TV programmes, that they are going to look for something and look for news, and so, in some senses, they are biased. If a genuine person happened to divide the data, who was not doing it in a biased way, they might, nevertheless, divide the data up in such a way that an effect appeared just by the choice of the boundaries, but we also mean by "statistical artefact" - if I can go back to answering your Lordship's question a little earlier, an example of this might be that, if we take a difference between any two numbers, having generated those numbers entirely randomly, and then plot that difference against one of them, we will find an apparent relationship, and this is strictly a statistical artefact. That is, a relationship can be induced in numbers by simply doing that sort of thing. It occurs in the medical literature all the time because of statistical ignorance of people.

So we mean by "statistical artefact" that something has been done with the data that do not show what they purport to show, and so it is a trick, if you like. A statistical artefact is a trick that could be done by somebody who was biased, but it could also just happen through ignorance.

Q. MR. JUSTICE FRENCH: Something has been done with data that produces a false reading?
A. That is right. Usually we distinguish that from bias; we in a sense make a judicial judgment as to what the intent was and an artefact usually means that there was no intent behind it.

Q. Something has been done innocently with data?
A. Yes, I think that would be right.

Q. Then bias also can be innocent or it can be, I suppose, not so innocent?
A. It can be either.

Q. MR. LANGSTAFF: Can results produced from the same data appear different if the data is grouped in different ways?
A. Yes.

Q. Is one of the advantages of having a number of studies grouping the data in different ways that one can be more sure that the apparent result reflects the message given by the data?
A. Yes, and I would look for a method that does not involve grouping at all. Where you might have had an artefact, if I can go to the Gardner data, there was a case with 97 mSv in that paper and if he had chosen to have 95 mSv as his boundary he would have an extra case in the high dose category, and then there would be an artificially raised risk in the highest dose category that would be resulting from choosing the boundary to be 95 mSv, which would be an odd choice of boundary. Because we have ten fingers

we like numbers that end in nought and so we tend to choose those boundaries but we could choose a boundary in such a way that we will demonstrate an effect to happen when some other choice, equally logical, would not show the effect. So in statistical terms we will try and find a method that avoids arbitrary choice of boundary.

Q. MR. JUSTICE FRENCH: Can I interpose a question here? Looking ahead, is this why you express a preference for the regression analysis as opposed to the grouping?
A. That is entirely so.

Q. The example about choosing 95 mSv instead of 100 mSv, of course exactly describes what you are talking of?
A. Yes, exactly. At the same time, of course, it is very helpful for an ordinary reader to see the data grouped in some way, rather than just have some magical slope produced by a statistician, so I am not trying to condemn the grouping of data but if your only analysis is based on that it can lead to artefact.

Q. MR. LANGSTAFF: I think an example might be, to see how successful a cricketer had been you would look at his average and not at the number of 50s or the number of 100s that he might have scored?
A. Yes, or if you wished to compare two cricketers you decided to look at the number of times he had scored over 90, because you wished your person who had had lots of times when he had scored in the 90s to be shown as the best, but he had failed for some psychological reason to score centuries, whereas somebody else who scored more centuries you moved your boundary in order to try and show your person up to be the best.

Q. Can I turn to a different point? In one of the answers you gave a moment ago to his Lordship you mentioned the underlying rate of leukaemia in West Cumbria as being low. Can you tell us about that? What is your understanding of the rate of leukaemia in the under 25-year-olds in West Cumbria, as compared to England and Wales nationally?
A. I cannot remember the exact data but I recall that it is lower than elsewhere and my recollection is that certainly in Black that is stated.

Q. MR. JUSTICE FRENCH: Is that West Cumbria or Cumbria generally?
A. Certainly Cumbria generally; it may be that West Cumbria is fractionally raised but to be honest I do not remember the data on that.

Q. MR. LANGSTAFF: You cannot say it of West Cumbria but certainly Cumbria?
A. Certainly Cumbria.

Q. You then deal at page 10, moving back to your report, having dealt with the strength of looking at the disposed

excess in various different ways, and confirming the excess, you turn to the third point:

> "c. The radioactive emissions from Sellafield into the environment were too low to account for the size of leukaemia excess observed in the village. This was based on the National Radiological Protection Board's assessment of the radiation doses to the children of Seascale, assuming that the data from other studies, particularly the atomic bomb data, could be used to estimate the rate of leukaemia for a given dose."

You then said this:

> "I consider that the last conclusion is very weak."

What are your reasons for saying that last conclusion is weak?

A. If we look at the logical extreme of that view it would simply say that if we had every child in Sellafield dying from leukaemia that it was very, very unlikely that it was anything to do with Sellafield at all, and the logic of the position is a failure. If you say that a lot of things are happening around there and yet it is nothing to do with the radiation that is coming from there you may be right, but it is logically a very poor position to take. Scientifically, to base all your values on theoretical models is not usually terribly sensible. People, before Galileo, based most of their things on theory.

Q. You go on in the next few paragraphs, until you get to page 11 and paragraph 25, to deal with various uncertainties in, I think, the estimates of radioactive emissions to the environment, and at paragraph 25 you conclude with this sentence:

> "In my opinion chance is now an unlikely explanation for the excess seen around Sellafield."

Is that a view which you still maintain?

A. Yes.

Q. You have mentioned Draper's review in paragraph 25 and your reference, I think, shows that is not the Draper report of 1992 which we have had for the purposes of this litigation. Have you had an opportunity to consider the Draper paper of 1992?

A. Yes.

Q. In brief, how would you explain what that shows and its consequences for the view that you expressed in the last sentence of paragraph 25?

A. There is a difficulty having found an excess in Seascale, partly as a result of the TV programme but almost any way that you look at the data will tend to continue to find

that excess if you base it on exactly the same data. If you now say, "Right, I have looked at that data up to such and such a period of time", and then look beyond it at totally independent data, you now cannot be subject to the danger of saying, "I have found this particular unusual happening", and then looked at ways to demonstrate that it is unusual, and I then look at the same geographical area in a subsequent calendar period, not using any of the previous data, and go on finding the excess, that tends to make one believe that the excess was there occasionally. Once is coincidence, twice is --- sorry, I should not quote James Bond! Basically, the fact that you have two independent observations means that it is less likely that either of them originally was a chance finding.

Q. I shall ask you about the second Draper report in a little more detail in due course, but effectively your answer is that your opinion is the stronger because of the 1992 report?
A. Yes.

Q. MR. JUSTICE FRENCH: Is it the progression of a trend or is that no part of it?
A. It is partly that, but it is particularly that having looked at one set of data that you might say this was possibly hypothesis generating. You might say that, and having looked at that, and then we look at the same area a little bit later, that earlier data cannot affect this one in the same way. We have looked at an independent set of things and in the 1992 Draper paper then you find that there is some evidence still of an increase. That makes it less likely that the previous one was also a chance finding, whereas you might expect to find no difference in a succeeding year if the first one was only chance.

Q. MR. LANGSTAFF: Professor, before you looked at the 1992 Draper study here you were in your report saying that you viewed chance as an unlikely explanation for the excess seen round Sellafield. What were the principal matters that convinced you that chance was unlikely?
A. At the time of Black it seemed as though chance was just possible as an explanation.

Q. MR. JUSTICE FRENCH: Is that before or after Black?
A. That was after Black, even after Black. Black said that chance is a possible explanation, you do have unusual things happening and this could be one of those very rare events. It was not very likely but it was still conceivably possible. When we come to Draper's review, they looked at the data in a great variety of different ways, and this is where we come back to the looking at it in lots of different ways rather than just over a large area. The Draper review had a number of different methodologies and it did not find in that a confirmation that there was a cluster of cases around Dounreay as a

result of using all the methods, but all the methods found a cluster around Seascale. So I found that Draper review, essentially the book published by OPCS, to be very strong evidence indeed against the possibility that Sellafield was a chance occurrence.

Q. MR. LANGSTAFF: I think we have to be careful here, haven't we, Prof. Evans, to distinguish between what you have called Draper's review, the OPCS study, and what we have called the Draper 1992 report?
A. Yes. The first one was a 1991 publication.

Q. MR. JUSTICE FRENCH: So Draper 1992 had looked at all the data in a variety of ways?
A. No, Draper 1991 looked in a variety of ways; Draper 1992 looked in just one way but in a later time period.

Q. MR. LANGSTAFF: You go on, Professor, at paragraph 26, pages 11 and 12, to introduce the studies from elsewhere around the United Kingdom and what they might be able to tell us. At paragraph 28 you deal with the 1987 study, of which the principal author was Dr. Cook-Mozaffari, and that you say is:

> "... a geographical cross-section analysis of cancer rates in the age groups 0-25 years and over 25-75 years in Local Authority areas around nuclear plants, and from the coast throughout the whole of England and Wales between 1959 and 1980."

I think, without fear of being accused of leading, that was a very large study which occupies virtually the whole of one ringbinder in our documentation, and was that the reason, I think, for a short summary to be published later in the scientific journal Nature?
A. Yes.

Q. In paragraph 30 you mention problems in the design of the study. Briefly can you tell us what those problems were?
A. Part of the problems are that they are a geographical study, and my paragraph 27 talks about them being a fairly crude form of analysis. They are also based on local authority areas where the boundaries are drawn without regard to possible scientific interest in future, and so the boundaries that are drawn in that way and the classification, therefore, of local authority areas can be subject to considerable error. So I think that it was not necessarily a study that was biased but was a study that may be insensitive at the very least.

Q. But you note that it shows a statistically significant excess of lymphoid leukaemia cases in young people in the vicinity of nuclear plants, and that was excluding Sellafield from the analysis?
A. Yes.

Q. Greatest for the installations built before 1955?
A. Yes.

Q. In paragraph 31 you deal with a later paper, and this I think is the 1989 study by Dr. Cook-Mozaffari and colleagues?
A. Yes.

Q. Re-analysing:

> "... the data for leukaemia and other cancers using a more conventional form of analysis using the rates in England and Wales as a whole as a comparison population."

What was the comparison population of the first study?
A. My recollection is that it was other local authority areas that were regarded as a similar local authority area to one that was adjacent, so it did not use every part of the country.

Q. So here you had a 1989 study examining the same installations but from a different statistical viewpoint?
A. Yes.

Q. The results, you say, confirmed those in the earlier study that there was an excess in leukaemia cases in the 0-25-year-old population living within 10 km of nuclear plants, when compared to the rest of the United Kingdom?
A. Yes.

Q. You are aware, I think, that in the Defendants' reports focus has been drawn to the fact that of the bands, the grouping of distance and population, that the greatest excess, the significant excess, was confined to those areas with less than two-thirds of the population living within 10 km, and by contrast the area with the greater population living nearer the plants showed less of an association. What do you say about that?
A. First of all I do not think that there were any direct comparisons between the areas that were close and those that were a little further away. The second thing is that in terms of environmental radiation it may actually depend more on the exact geographical spread, and it is entirely possible that there is more contamination a little further away from the plant than immediately near it, particularly if the emissions were through chimneys, which are designed to throw contamination into the higher atmosphere if they can. The second thing is that it is an issue, if it involves anything occupational, where people live is not necessarily exactly close to the plant, particularly if they are research workers, perhaps, who might work a little further away, but I think that paper as a whole did not show any strong associations, it showed something of an association.

Q. You say in paragraph 32 that:

> "Despite the relative insensitivity of these analyses the fact that statistically significant

excesses were seen lends support to the supposition that the excess around Sellafield is not just an isolated occurrence, and that there may well be a more generalised phenomenon around nuclear plants."

A. That is possible.

Q. Would you take, please, the Defendants' report from Prof. MacMahon, the first report, page 68, paragraph 5.f? Prof. MacMahon's conclusion relating to residents near a nuclear installation says this:

> "None of the reported individual clusters of childhood leukaemia and/or lymphoma around nuclear facilities holds up convincingly as a biologically meaningful cluster; with the possible exception of the cluster in Seascale, all appear to result from artificial boundary manipulation and/or chance."

What do you say about that?

A. I think that the artificial boundary manipulation implies a non innocent manipulation, and I do not think that any of the studies that I have referred to there can be accused of that. I think that this is over-stating the case and certainly in regard to Draper 1991 there is a suggestion that there are other clusters that have been confirmed.

Q. I will return by way of general questions to what is said in most of the rest of the paragraph of that page until we get to the bottom, where Prof. MacMahon comments upon the studies you have just been giving evidence about:

> "Although a small excess of childhood leukaemia was found in a systematic study of all County Districts in England and Wales with some of their populations living within 10 miles of a nuclear facility, the fact that the rate was not significantly related to the proportion of the population living within that radius, and the fact that a similar slight excess was found in districts selected as nuclear power sites but in which the facilities had not yet been built, raises questions about the meaningfulness of this finding."

What do you say about that?

A. I think it does raise questions but it does not dismiss the finding.

Q. "Systematic studies of populations living close to nuclear sites in the United States, France and the former West Germany have found no such relationship."

What comment would you wish to make about that?

A. I think my paragraph 42 of my evidence gives my opinion on that, that the difficulty is that you need to find a site which has got similar releases perhaps to the

environment, similar doses to the people who work there in order to find it, you also need to have a country which has extraordinarily good collection of data on cancer, registration and deaths and on population data.

Q. Can I just stop you there? You have mentioned three things, the areas of similarity that you would look for. Could you just go through them again, one by one?
A. If we assume something that we do not yet know, that radiation is causing leukaemias in children, and that Sellafield has contributed to that, then we would expect to find that similar places would also have an excess of leukaemia around them. They would then have to have a similar, in principle, release to the environment of radiation ....

Q. Just stop there, so similar releases of radiation to the environment.
A. They would also have to have similar exposure of their employees to the radiation.

Q. Stop there - similar exposures to the radiation.
A. Occupational exposures. Thirdly, they need to have a quality of data that is as good as we have in the United Kingdom. I would expect to find around Chernobyl some excesses of leukaemia because that would meet almost undoubtedly, to some degree at least, similarities in terms of discharge and occupational exposure, and in fact obviously much more extreme than has happened around Sellafield, but the third requirement of having good data is not yet met and unlikely to be met in that area.

Q. Are you in a position to comment upon the quality of data in the United States?
A. There are considerable difficulties with obtaining nationally based data in the United States. Their federal system tends to lead to having individual state data and so local studies can be done but national studies are a little more difficult to do, which we can do in this country.

Q. What about France?
A. In France their laws on death registration mean that the data available and the ability to link deaths to births and things of that kind is very much more limited. They have restrictive laws that do not permit - the death certificate, as far as I recall, is not allowed to be in the public domain in the way that it is in this country.

Q. You can put away the report from Prof. MacMahon for the moment, Prof. Evans. Returning now to your report, page 13, f2, you review the Dounreay study, the incidence of leukaemia around Dounreay, and you note in paragraph 36:

> "This report, in general, failed to confirm the excess of cases around Dounreay ...."

I am sorry, that the OPCS report which you discussed earlier had failed to confirm the excess around Dounreay, although it had confirmed that around Sellafield.

At f3 you deal with Aldermaston, Burghfield and Harwell. On page 15, in which I think is a second f3, you deal with the survey around Hinkley Point, and then draw conclusions at f4 about the geographical studies as a whole. In paragraph 42 you make the point:

> "... it is not surprising that many of the studies show no evidence of cancer excesses around nuclear installations. Whether or not radiation-induced excesses exist, these studies are unlikely to be able to distinguish a small effect from no effect particularly where the geographical area or population examined are large and a genuine increase in rare disease may be concealed."

Could I just ask you about that? Why is it that in your view some of the geographical/ecological studies that can be carried out may not detect radiation induced disease if it exists?

A. The problem is, in terms of trying to understand the epidemiology, that leukaemia is a very, very rare disease. Of course, that is no problem at all, one has to be only grateful that it is a rare disease, and from a public health point of view we do not have an awful epidemic of leukaemia rushing through the country, indeed, in this country or as far as we know anywhere else, and so the problem is going to be that there are going to be very small numbers of leukaemias so even if the risk is considerably increased there will still be only small numbers. If I perhaps quadruple the risk of leukaemia I still will not get very many leukaemias.

Q. Why is it that a study of the geographical area, a cross-sectional type of study, may not be able to detect such an increase?

A. The difficulty is, of course, that the geographical study does not directly measure radiation exposure if radiation is the cause.

Q. Does it depend on the size of the population you are considering in your geographical study?

A. I am sorry, does what depend?

Q. Does the likely appearance of any result depend on the overall size of the study population?

A. Yes, in the sense that in order to achieve a statistically significant result you are going to need a very large number of people who are at risk, and at increased risk, of having leukaemia, so you certainly do need large studies, but not just large studies in terms of studying the whole country but large numbers of people who are exposed to whatever it is, and if we assume that radiation is the cause, large numbers of people who are exposed to radiation.

Q. If you have not got large numbers of people exposed to radiation, the consequence would be that you wouldn't have a study likely to show the result, however true that result might be?
A. That's right.

Q. You then turn, having considered those geographical studies, to look at the births and the school cohort studies conducted round Sellafield. We have seen, having looked at Black, that the Black Committee suggested that those reports should be prepared and, indeed, were under way. You deal at paragraph 44 with the nature of cohort studies, and 45, that was the recommendation of the Black Committee and at 46 you turn to the results. Let me ask you, Prof. Evans, to have before you those reports. You find them in the common bundle G.
A. They are at 87 and 88 in my copy, but right at the beginning.

Q. If you would go to the one which I think was published first. That was one of the schools cohort which I think is at 88.
A. It was published first - they were in the same issue of the Journal, but on successive pages.

Q. I think one followed the other, didn't it?
A. Yes.

Q. Here we have a study conducted by Prof. Gardner, looking at the schools cohort study, the abstract:

> "Records on 1546 children who were identified as having attended schools in Seascale up to November 1984 and were born since 1950 but not in the civil parish were studied. These children lived in or near Seascale for a period of time while they were attending one or more of three local schools and are an additional group to the 1068 children who were identified as born to mothers resident in Seascale in an accompanying study."

That is the birth study which we will return to:

> "Even though some of the schoolchildren apparently remained in the village for a short period only all but 7% were followed up through the National Health Service Central Register."

Is that a high or low percentage of follow-up?
A. Using the National Health Service Central Register, that is about what you would expect. For other studies it is a very, very high rate of follow-up. That is part of the good quality of data we have in the UK.

Q. Would you every expect 100% follow-up?
A. No.

Q. It says:

> "Mortality among these children to 30th June, 1986 is comparable to that expected at national rates. From all causes there were 10 observed deaths compared with 12.89 expected - a ratio of 0.79 and from cancer 1 observed death compared with 2.04 expected."

In that group of 1546, looked at almost 37 years, one death from cancer and no deaths from leukaemia or lymphoma, we see, although on national rates 0.83 of a death was expected:

> "Since 1971 three non-fatal cases of cancer were reported, including two lymphomas, compared with 2.04 expected and two cases of carcinoma in situ of the cervix compared with 1.79 expected. In addition, there was a case of leukaemia among the schoolchildren which was known previously and had been diagnosed in 1968."

Then it says this:

> "There is an interesting difference between the results of this study and the results of the study of children born to mothers who were resident in Seascale. In the latter study there was an excess of leukaemia and of other cancers, but a similar finding is not apparent among children who spent some time at schools in Seascale but were born elsewhere. This raises the question of whether one or more etiological factors in childhood cancer were acting on a locality specific basis before birth or early in life. This cannot be answered from these cohort studies, but it is hoped that the case-control study that is under way in West Cumbria will provide relevant information."

I don't propose to take you to the tables, the abstract saying effectively what the report says, but if you go to page 821 under "Discussion", the second paragraph:

> "Given the ages at which the excess of leukaemia mainly occurred in the Seascale birth cohort, most children entered the schools cohort after the maximal age of risk had passed among the births since two of the deaths occurred at age 2 years and a third at age 3. These are also the most common ages for the diagnosis of childhood leukaemia in Britain."

Is that what you were referring to earlier on when you spoke about the particular form of leukaemia having an extra Poisson distribution and there perhaps being a possibility of a factor round about the time of birth or before being involved in that sort of leukaemia?

A. It was some degree something of that type. The important point being that it is a different pattern to that which you see in leukaemia in older people.

Q. It goes on:

> "Although in the schools cohort overall the expected number of deaths from leukaemia (0.54) was similar to that in the birth cohort (0.53), no deaths from leukaemia were reported compared with five among the birth cohort. The combined figure is five deaths observed compared with 1.07 expected - a ratio of 4.67. The apparent limitation of the high leukaemia death rate to children born in Seascale is notable, although the lower 95% confidence limit for the ratio of the rates in the birth cohort to the schools cohort is 0.93. In terms of cases of cancer one case of leukaemia is known among the schoolchildren and diagnosed before 1971 which was the year when the National Cancer Registry first passed on details to the NHS Central Register. Since then three other cases of cancer have been reported in the follow-up of these schoolchildren, which is about one more than the expected number of non-fatal cases, plus two cases of carcinoma in situ of the cervix..."

With that in mind would you turn to the subsequent report which is at divider 87? This is what we know as the birth cohort study compared with the schools cohort?

A. Yes.

Q. You see from the abstract:

> "Records on 1068 children who were born to mothers resident in Seascale Civil Parish during 1950-83 were studied. There was a large degree of mobility among the families, and nearly half of the children did not subsequently attend the main local school. Use of the National Health Service Central Register, however, enabled us to follow up the children's records regardless of place of residence. the excess of leukaemia among Seascale children first supported from the analysis of geographical areas is confirmed. There were five deaths from leukaemia identified to 30 June 1986 compared with 0.53 expected at national rates - a ratio of 9.36."

And it gives the 95% confidence interval. Is that a ratio of some - using the word in a lawyers's sense, or a non-statistical sense - of some significance to you, Professor?

A. Well, it is fairly obviously very raised.

Q. We see the confidence interval goes from 3.04 to 21.84. What would you say about the lowest end of that confidence interval, 3.04? Would that be a very raised, or a just raised, or quite a lot raised?

A. That certainly is quite a lot raised.

Q. It goes on:

> "One of these deaths occurred after the child had left Seascale. There were four deaths from other cancers compared with 1.06 expected - a ratio of 3.76."

Does the same apply to that 3.76, that that is quite a lot raised, as would to the 3.04?

A. Yes, that is quite a lot raised.

Q. It notes further cases of cancer were reported. Finally:

> "In view of the importance of this cohort at births continued follow up is planned, with the possibility of extending it to include births since 1983, and the methods available for this type of study will be examined further."

Would you turn to page 825 and look at table 5 at the bottom left hand corner of the page?

A. Yes.

Q. Does that set out the number of deaths observed as against those expected and calculate the observed as against the expected, the ratio of the one to the other?

A. Yes.

Q. We see there the tabular basis, do we, for the conclusion that has already been echoed in the abstract - 5 leukaemias observed as against 0.53 expected; 3 other cancers as against 0.88 expected?

A. Yes.

Q. Treating non-Hodgkin's lymphoma separately, can I ask you about that? One observed, 0.12 expected, a ratio of 8.45. What would you say about that?

A. I would also pay attention to the 95% confidence interval which makes it clear that their data are compatible with a considerable rise in rate in non-Hodgkin's lymphoma, but that could be a chance finding and clearly just one is not enough to build a theory on.

Q. What one does not see there is the two combined, exceptt under the heading of "Malignant neoplasms", but under that heading we see 9 malignant neoplasms observed as against 1.6 expected. What do you say about the confidence interval for that?

A. That clearly excludes one and makes a much stronger suggestion that malignant neoplasms - at least some of them - are raised in this cohort.

Q. Can I invite your attention next to page 826, to the "Discussion":

"One of the important purposes of this study was to investigate further the findings of the earlier geographical analyses of the incidence of cancer among young people in Seascale where the main observation had been an excess of leukaemia. We have corroborated that result in reporting five deaths from leukaemia among children born during 1950-83 to mothers who were resident in Seascale compared with 0.51 expected from death rates in England and Wales. Thus by approaching the estimation of the local rates by another method we found a similar estimated level to that originally suggested - that is, about 10-fold higher than expected on national rates. The previous figure of 10-fold referred to children under the age of 10 years, whereas this study reported on births followed up to the ages reached by 30 June 1986. Examination of leukaemia done up to the age of 10 years only in this study, however, produces a similar outcome of four observed compared with 0.32 expected."

It then compares that with the leukaemia, or notes the leukaemia death rate in relation to Cumberland and notes that the county of Cumberland as a whole is 12% lower than England and Wales. Using county figures rather than the national figures for comparison the observed against the expected ratios would rise?

A. Yes.

Q. MR. JUSTICE FRENCH: That is the passage you were searching for?

A. That is one of the places we mentioned, but I...

Q. MR. LANGSTAFF: Tell me this, Professor, if you were seeking to draw conclusions, certainly the conclusions that might be appropriate from a statistical investigation such as this, would you regard the comparison as being more appropriately done with Cumberland or more appropriately done with England and Wales?

A. If you are trying to argue a case, as you might say as a scientist, you look for the weakest bit of your evidence, and hence as a scientist I think that Martin Gardner in this used England and Wales, which does not tend to exaggerate the finding. However, in reality, if you wish to say without knowing anything about it at all what is the most appropriate control group, then the local area may be more appropriate than England and Wales as a whole.

Q. MR. JUSTICE FRENCH: Would it be fair to say that by taking England and Wales, which is 12% higher than Cumbria, he is introducing a bias unfavourable to the hypothesis?

A. That is exactly so, and that would be the mark of a good scientist.

Q. MR. LANGSTAFF: Professor, you can fold up the grey bundle and put it to one side for the moment. We will come back to it shortly when we look at the Gardner study itself. Now, Professor, page 17 of your report, paragraph 47. You deal with the importance, as you see it, of those two studies combined. You say:

> "They suggested that the cause of the excess of childhood leukaemia at Seascale is not likely entirely to be due to environmental exposure as a child."

Why do you say that?

A. What I mean there is that had the cause been an environmental exposure that was acting equally over all ages from 0-15, then you would expect to find that the excess of leukaemia, whether it is chance or has some other genuine cause, distributed evenly between the birth cohort and the schools cohort. If the environmental factor is acting, or some factor is acting after birth and perhaps after the first few years of life, then those children who come into school in Seascale are then at risk of being exposed to that factor, whatever it is. Then you would expect that they would get leukaemia or cancer. Whereas if the factor is acting before the age of 2 and if it were acting pre-natally, then we would not expect to find any effect in the schools cohort, and we would expect to find it in the birth cohort.

Q. I think you make that point at (b). You consider the paper important for a third reason:

> "They indicated that the excesses of cancers in Seascale are not confined to leukaemia and that there may well be an excess of other childhood cancers."

In brief, and anticipating what we will come to in your evidence subsequently as to the reasons you ascribe for the development of the diseases in these two cases in court, what do you regard as the importance of that third finding?

A. I am sorry, that third...?

Q. The third matter that you regard as of importance, that there is an excess of cancers not confined to leukaemia and "there may well be an excess of other childhood cancers"?

A. I think that that is a possibility. I think there exists data, and if we look at Draper 1992, as we have said, we find there is some evidence from that. I don't think it is a strong case, but I think there is some evidence along those lines.

Q. Having looked at the evidence for there being a cluster or an excess around Seascale and Sellafield, having looked at the geographical studies in England and Wales

showing there might be similar excesses around other power stations and having looked at the schools and birth cohort studies, you then turn at page 18 of your report to deal with the Gardner 1990 study. By way of background you set out the difference between case control studies and others as to what they may be able to tell you in a situation such as this. Can I just simply ask you: what would you regard as the most appropriate form of design of study given the studies showing a cluster and the birth and schools cohort study, to try to isolate the causative factor?

A. It depends really on what your resources are and what information is available to you. If you were able to obtain all the information regarding every child in, say, the birth cohort and the schools cohort, and you were able to obtain detailed information on each of them on all 2,000 or so in each of those cohorts, then a cohort study would be the best type of study. That study will take you a lot longer to do, will be very, very expensive to do, and will not necessarily have any great power for showing you the answer. Nevertheless, it is less likely to be subject to bias if you obtain the data at the time the person entered the cohort. Now in practice, if we were wanting to ideally do a study of this kind on a true cohort, we would need to examine those children. We would need a time machine to go back to 1950 and examine the children and see whether they did play on the beach, whether they ate vegetables, whether they ate fish, and whether their fathers worked - following them up having begun the study in 1950.

Of course, to say what is the ideal, we clearly don't have a time machine and we don't have infinite resources. We cannot press back time, so in those circumstances the study that is likely to show you causative factors most clearly will be a case control study.

Q. MR. JUSTICE FRENCH: A cohort study, on the other hand, is best, given impossibly ideal conditions?

A. Yes. I think in the circumstances of Sellafield it is absolutely impossible. The other thing you could do, of course, would be to practise some Nazi medicine and carry out an experiment of randomly allocating people to receive radiation or not and then follow them up, but on the whole we don't go in for that sort of thing I am glad to say!

MR. LANGSTAFF: My Lord, would that be a convenient moment?

MR. JUSTICE FRENCH: Certainly.

(Luncheon adjournment)

Q. MR. LANGSTAFF: Prof. Evans, would you get out, please, from, I think it is in the bundle for the Court, page 1, Prof. Gardner's study of leukaemia and lymphoma near Sellafield.

MR. JUSTICE FRENCH: Is that Gardner Re-analysis, Bundle 1?

MR. LANGSTAFF: My Lord, it is.

MR. JUSTICE FRENCH: Is there any shorter way of referring to it?

MR. LANGSTAFF: Perhaps if we call it the blue bundle, my Lord, for present purposes, it would suffice.

MR. JUSTICE FRENCH: What about P2?

MR. LANGSTAFF: My Lord, yes, that is better. I am told by Mr. Rokison that I would have caused him some confusion if I called it the blue bundle. P3, my Lord, I think it is.

MR. JUSTICE FRENCH: That may have been nobbled for some other purpose. P4.

MR. LANGSTAFF: P4, I am obliged:

Q. Before we look at P4, Prof. Evans, can you just tell me this? What sort of regard generally is Prof. Gardner held in?

A. I think it is probably true to say he is held in really very high regard indeed. He was the statistician who was asked to join the Black Committee and subsequently was on COMARE and, in the field of geographical epidemiology and the statistical analysis of such work, I would have thought that he was very much a worldwide leading figure.

Q. At the time that he produced the 1990 report, how many Professors of Statistics and Epidemiology were there?

A. I think we have already said there were two, I reckon, in February 1990.

Q. Shall we look then at his report? Page 1 sets out the objective:

> "To examine whether the observed excess for childhood leukaemia and lymphoma near the Sellafield nuclear plant is associated with established risk factors or with factors related to the plant."

Would you, for your part, describe that as hypothesis generating or hypothesis examining?

A. I would say that that was hypothesis examining.

Q. It sets out the design, a case-control study - we dealt with that shortly before the short adjournment - in the West Cumbria health district. The subjects:

"52 cases of leukaemia, 22 of non-Hodgkin's lymphoma, and 23 of Hodgkin's disease...."

A

So that is 74 leukaemia and non-Hodgkin's and 97 cases altogether:

"....occurring in people born in the area and diagnosed there in 1950-85...."

So it is a period of 36 years:

B

"....under the age of 25 and 1,001 controls matched for sex and date of birth taken from the same birth registers as the cases."

The main outcome measures are set out and then the results summarised:

C

"Expected associations with prenatal exposure to X-rays were found, but little information was available on viral illnesses. Relative risks for leukaemia and non-Hodgkin's lymphoma were higher in children born near Sellafield and in children of fathers employed at the plant, particularly those with high radiation dose recordings before their child's conception. For example, the relative risks

D

compared with area controls were 0.17 (95% confidence interval 0.05 to 0.53) for being born further than 5 km from Sellafield, 2.44 for children of fathers employed at Sellafield at their conception, and 6.42 for children of fathers receiving a total preconceptual ionising radiation dose of 100 mSv or more. Others factors, including exposure to X-rays, maternal age, employment

E

elsewhere, eating seafood, and playing on the beach did not explain these relationships. Focusing on Seascale, where the excess incidence has predominantly been reported, showed for the four out of five cases of leukaemia and one case of non-Hodgkin's lymphoma whose fathers were employed at Sellafield and for whom dose information was

F

obtained that the fathers of each case had higher radiation doses before their child's conception than all their matched control fathers; the father of the other Seascale case (non-Hodgkin's lymphoma) was not employed at the plant. These results seem to explain statistically the geographical association. For Hodgkin's disease neither geographical nor employment associations with Sellafield were found."

G

Would you turn to page 427 and look, at the bottom left-hand of the page - this is page 5 in P4, my Lord - would you look at the diagram there, and does that chart demonstrate the relative doses of the five cases to which reference is made in the Abstract compared to their controls?

H

A. Yes.

Q. MR. JUSTICE FRENCH: There we see your 95, do we not, just below the 100 mark?
A. That is correct, yes.

MR. LANGSTAFF: 97, I think it was, my Lord.

Q. MR. JUSTICE FRENCH: Was it 97, I am sorry?
A. 97. 95 might be the cut-off point.

Q. MR. LANGSTAFF: Returning to the Abstract:

> "Conclusions - 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. This result suggests an effect of ionising radiation on fathers that may be leukaemogenic in their offspring, though other, less likely, explanations are possible. There are important potential implications for radiobiology and for protection of radiation workers and their children."

I am going to take you through in a little detail, Professor, the methods and results of the Gardner study, particularly in view of some of the criticisms, of which you are no doubt aware, in the Defendants' reports.

Dealing, first of all, with the Methods, it is pointed out that:

> "The design of the study, methods of data collection, and basic information are described in an accompanying paper...."

and for that we have to go to page 7 of P4.

Professor, at page 18 of your report - and it is necessary, I think, just to read it out. It is not necessary, I think, for you to look at it, but I will read out to you what you wrote and then ask you about it - you say, at paragraph 51, the very last line on page 18:

> "The selection method for controls used by Gardner and colleagues is reasonable, and does not exclude or include children as controls unless they would have also been excluded as cases. In his paper Gardner has two different series of controls ('area' and 'local') which should help to reduce the chance of bias, although these control series are not very different, and are clearly not independent of one another."

Then you say this:

> "The description of the methods of the study is one of the most extensive I have read in the scientific literature, and has not to date been the subject of any major criticisms in the scientific press."

How usual is it for there to be as extensive a description of the methods of the study as here?

A. I would say it was very unusual.

Q. What is the purpose, in general terms - perhaps it is obvious, but you can tell us - of setting out the methods in some detail?

A. When this sort of description does appear, it is usually when a study has very important implications and so that I can think of a few other epidemiological studies and a few clinical trials in which the methodology has been published separately. So it is a reflection of the importance of a study and I think, in the context of this one, the fact that the findings were not exactly as people had anticipated.

Q. On page 8, the second page of the Methods paper, it says, towards the top of the left-hand column:

> "This study, carried out in response to this recommendation, addressed the following hypotheses...."

and then it sets out the hypotheses we have already dealt with, and adds this:

> "More specifically, the identified cases and controls served the following four predetermined study aims."

It sets them out:

> "(1) To examine maternal exposure to medical x-rays and the occurrence of infectious diseases during pregnancy, since the former is an accepted cause of leukaemia in children and the latter is suspected.
>
> (2) To examine the geographical distribution at birth, in particular to obtain information on proximity to Sellafield."

Sorry, Professor, are you with me? Page 8?

A. Yes, I am.

Q. > "(3) To examine habits that might have enhanced exposure to radionuclides released from Sellafield - for example, consumption of fresh seafood and playing on the beach.
>
> "(4) To examine the occupations of the parent population, in particular to obtain information on

employment at Sellafield and occupational radiation dose."

What is the importance of setting out predetermined aims for a case control study?

A. I think it is basically to demonstrate that one is not going in for a fishing expedition. If you cast your net very wide over a very large number of possibilities, in a study in which you have no idea what you hope to find, then the findings are going to be reduced in importance because of the very large number of possible things that you could have looked at. Setting out these predetermined study aims says that you are not looking for an indefinitely large number of possibilities. You are looking at certain specified ones that you have said are of interest to you beforehand.

Q. It then deals with West Cumbria and, at the top of the right-hand column:

> "Non-Hodgkin's lymphomas," says Prof. Gardner in his report, "were included because there is evidence of some relation with radiation and also because non-Hodgkin's lymphoma could have been confused with leukaemia during the early years of this study. Hodgkin's disease was included, although it is not thought to be related to radiation. Thus we decided in advance to examine leukaemia and non-Hodgkin's lymphoma separately from Hodgkin's disease in the main analysis and also to look at Seascale particularly."

What would be the purpose of including data in relation to a disease that was not thought to be linked to radiation?

A. If someone has a child with a particularly nasty disease and they are asked questions about what they might have been exposed to, the intensity of their memory is likely to be enhanced by the fact that they have had an untoward event and they seek in their past history to find some explanation for it. In this particular case, it could potentially be an extreme example of this situation, which is what we call "recall bias". That is, that your recall of events in the past is biased according to your current state.

Q. Assuming that the hypothesis is right, that there is no relation between Hodgkin's disease and radiation, if the study is unbiased, what would one expect it to show?

A. One would expect to find that there was no evidence of things that a mother, for example, might be questioned about being associated with that disease.

Q. If at the same time as this one a study looked at diseases which might well be associated with radiation, such as leukaemia and non-Hodgkin's lymphoma and came up with a statistical association between the two, what would the importance be of a nil association in respect of the Hodgkin's?

A. If, for example, one had found in the case control study that, let us say, playing on the beach was regarded as very important, if this was a result of recall bias, you would expect to find that playing on the beach was associated with disease for both leukaemia and non-Hodgkin's lymphoma. Let us assume for the moment that playing on the beach itself gave rise to increased exposure to radiation, and you would then expect, because of the recall bias, that the Hodgkin's lymphoma would also show that there was an association with playing on the beach. So, in other words, the association of playing on the beach was caused by recall bias in both groups.

If the study had shown playing on the beach just in the leukaemias and NHLs, but not in the others, this would tend to give rise to the thought that it was an unbiased study and that there may be something genuine.

Q. MR. JUSTICE FRENCH: Sorry, can I pose a question in terms perhaps I can follow? Is it saying this: the fact that you find an absence of bias in relation to one group reflects on the other two groups and suggests that there may be an absence of bias there as well?
A. Exactly so.

Q. I suppose too, but tell me if this is right or wrong, the bias may exist in the mind of the questioner?
A. Oh, exactly so.

Q. So that it suggests that the questioner may be putting questions in an unbiased form?
A. It may suggest that, yes.

Q. May suggest that. Can I sum it up in this way? It may also reflect on the quality of the questioner?
A. It may, indeed.

Q. MR. LANGSTAFF: Then, in the right-hand column, underneath "Methods, Identification of study subjects," Prof. Gardner sets out the way in which the list of cases was compiled and I think I summarise it - tell me if you think fairly - by saying that a number of different sources were culled and cross-checked to see that all cases had been identified?
A. Yes.

Q. Page 9 of P4, the result of that culling is shown in the number of cases and the number of controls linked to each of those cases. This page, on the left-hand side and partly in the right, deals with the question of controls. If one looks at the table, one can see that the controls are a maximum of 8 from the area and a maximum of 8 known as local controls. Can I ask you this? Why would a case control study use more than one control per case?
A. The main issue is that a lot of the studies that one is likely to do, particularly of a case control nature,

cases are very difficult to find and controls are relatively easy to find and, when the cases are very difficult to find and you are dealing with a rare disease, then you are going to find a better answer to your questions by having a larger sample, if possible, and when the number of cases is limited, the only way of increasing the overall sample size is by increasing the number of controls.

Q. MR. JUSTICE FRENCH: I am afraid that passes right over my head. I do not see why you increase your sample size simply by increasing the number of controls. I would suspect you ought to increase the number of cases as well?

A. The point is that you do not have any option to increase the number of cases. You have found all that there are and so you cannot increase the number of cases. You are quite right. The right thing to do is to increase the number of cases if you can, but usually - and again it is where epidemiologically it is unfortunate that leukaemia is rare. If it were a more common disease, then we could more easily increase the number of cases, but we are pleased to say that it is a rare disease and we have a limited number of cases.

Q. That I follow very well, but I do not at the moment see how you improve matters by increasing the number of controls?

A. If you think about decreasing the number of controls so that you do not have very many controls at all, you see that you do not have very good information; that if you only had cases and no controls, you would not have much information. If you have one control for each case, that is splendid, but the uncertainty in any measurement you make on the controls is going to mean that your study is not as sensitive as it might be and, by increasing the number of controls, you win a little bit. You do not win a lot, and you are quite right intuitively in saying that you do not win a lot by having eight controls, but you win a little bit and, when you end up with your table of numbers, you are going to have a certain number of cases and a larger number of controls and the overall information in there is partly dependent on your total sample size.

Q. So that you are improving your information about factors which may prove relevant or may prove irrelevant?

A. Absolutely.

Q. So a large number of controls contributes something, in that it improves background information?

A. Yes.

Q. As to factors which may or may not prove relevant?

A. Yes.

Q. MR. LANGSTAFF: In the second paragraph in the left-hand column, the difference between area controls

and local controls is set out. Let us just, first of all, identify that difference and then I will ask you about it. It notes that the area controls were obtained by making searches backwards and forwards from the case's entry in the birth register until the nearest four appropriate controls in each direction were found. That would be a process, presumably, of going to the birth register, seeing when a case was registered and looking through the information to find the nearest four births. It notes that:

> "Only births to mothers with a West Cumbria address were included."

So you are limiting the area to West Cumbria:

> "For the second group (local controls) the residence of their mothers was matched for residence (civil parish) of the mothers of the case at the date of birth...."

Does that mean that, in looking through the birth register, efforts were made to ensure that the controls came from not just West Cumbria, but from the same parish as the case you were looking at?

A. That is exactly so.

Q. And it goes on:

> "....although otherwise the procedure was as for the first group. Date of birth matching was within six months for 99% of area controls and 92% of local controls. The area controls were particularly relevant to the geographical analysis mentioned in study aim 2, although their selection was stratified by birth registration district."

In this case, why have two separate sets of controls? What would be the purpose, from a statistical point of view?

A. Generally, in case control studies with more than one control group, you look for different sources of bias. There may be a biased way in which you have selected your controls and, if you have two slightly different methods or perhaps, in some instances, very different methods of selecting your controls and you then, at the end of the day, find disparate results in the two, then you may believe that your results are simply due to bias. If you have two different methods of....

Q. Pause there for a moment.

Q. MR. JUSTICE FRENCH: I have again somewhat paraphrased it, but you tell me whether it is right or wrong. Two sets of controls were used because one looks for sources of bias and two methods of selection of controls producing disparate results may lead to doubt as to the validity of one or other conclusion?

A. Absolutely correct.

Q. And therefore of both?
A. Absolutely.

Q. MR. LANGSTAFF: You were going to go on?
A. I was going to go on and say that the corollary is that if they both show an effect you believe it is more genuine, or more likely to be genuine.

Q. Anticipating forward for a moment in the evidence, you know that the relative risks produced by looking at area controls, are in the main higher than those produced by examining the relative risks compared with local controls in this particular case. Without looking at the precise figures at the moment, would you comment: is the difference such as to lead to a suspicion of bias, or such as to be broadly confirmatory that there is no bias?
A. No, I think that it is broadly confirmatory that there is no bias. The results are sufficiently similar.

Q. Would there be any particular usefulness in having a distinction between area and local controls in a case such as this where a cluster of disease had been identified in a locality?
A. Yes. I think it is particularly a good idea to have both area and local controls in these circumstances.

Q. Is that just to exclude bias or is there some other reason?
A. I think a difference is likely to give you some sort of insight into the possible mechanism for the causes for the disease you are interested in.

Q. The paper continues, having set out the nature of the controls, how they were matched and the checks that were made, and then the top right hand paragraph deals with the question of the status of the parents of cases and controls and shows that they were identified, and then deals with data collection on cases and controls. We see the data was collected from hospital records, and at the beginning of the second paragraph:

> "Hospital records were available for all but two of the cases."

Is it a matter of importance or of indifference that one has hospital records and, if possible, pathological confirmation of disease?
A. Yes, it is important wherever possible.

Q. Then the following page, page 10, it sets out a questionnaire procedure:

> "...with information being sought directly from parents of cases and controls. This was carried out through parents' general practitioners."

The result of that is summarised at the top of the right hand column, showing the fact that not everyone responded

to a questionnaire. Would you expect everyone to respond to a questionnaire in a case control study?

A. I would not expect everyone to respond to a questionnaire in any study.

Q. It deals with "Geographical data":

> "One aspect of the study was to compare the geographical distributions of the cases and controls in relation to Sellafield. For this purpose residential addresses at birth for cases and controls were identified on Ordnance Survey maps, and national grid references accurate to 100 metre squares were obtained for most (87%) addresses. For the remainder the accuracy was less, and in some instances addresses were untraceable, mainly those from the earlier years covered by the study. This method allowed a modified approach to the geography of cases rather than simply examining routine mortality and cancer registration statistics."

Is there an advantage in mapping the distribution geographically of disease by using Ordnance Survey squares, over a method which would concentrate on such as Electoral Wards or administrative boundaries?

A. If some putative factor is genuinely geographically distributed, then clearly it is much better to have exact geographical references, rather than depend on the vagaries of several parish boundaries and so on.

Q. Then "Occupational data". Three different sources, it says parental occupation from the birth certificates; occupational histories by questionnaire and a cross matching of a computer file of study subjects with that of the past and present Sellafield workforce to identify people who appeared on both files. It goes on to say:

> "For those subjects identified as having worked at Sellafield, British Nuclear Fuels subsequently supplied us with dates of employment at the site and external whole body ionising radiation dosimetry on an annual basis. The radiation dose in each year had been estimated from monitoring with dose meters worn on the trunk, and our figures came from the data on which satisfactory quality checks have been reported. No details of exposure to internally incorporated radionuclides are yet available, though they will become so. This information was used to examine the relative frequency of employment and radiation exposure at Sellafield among parents of cases and controls and also to examine relations with other occupations and industries."

It says:

> "Table VI shows the extent to which job data were available."

Dealing with the concordance of data:

> "Employment at Sellafield - Table VIII shows findings on fathers' employment at Sellafield at the birth of their children from the three varying sources. There was good general agreement among the different datasets. For example, for the 10 cases identified as employed at Sellafield by computer linkage this was agreed when suitable data were available from the other two sources. One case of Hodgkin's disease was not linked to Sellafield, although employment there was recorded on the birth certificate. Concordance on Sellafield employment status was also high among controls. Agreement for non-Sellafield occupation and industry data between birth certificates and questionnaires was also high, although results are not shown here."

In terms of raw data, how reliable, or in comparison with other epidemiological studies, is data of this sort, this sort of occupational data?

A. Those for whom there was data available, the concordance is very high indeed - very, very high.

Q. In terms of assessing exposure to radiation, did the data appear to be of high or low or of medium quality?

A. First of all, the data on, you said, employment and radiation?

Q. Of occupational exposure to radiation.

A. That is particularly high because it does not involve questioning people, but rather using data that was collected beforehand, not subject to recall bias.

Q. One might say objectively rather than subjectively determined?

A. Yes.

Q. Asking you to keep the Gardner report there for the moment, can I ask you to go to your third report at the very end, where you deal with criticisms that have been made of the methodology? It is your third report, page 19. You deal firstly with the criticism that Dr. MacRae makes to the "Exclusions of cases and matched controls born outside West Cumbria". Do you regard that criticism as a valid criticism of the methodology that Prof. Gardner adopted?

A. Criticism in the sense of saying, "It is a pity it was not done. Had it been done it would have larger numbers and we are looking for larger numbers." However, criticisms in the sense of, "It is biasing", no.

Q. "Case 106". The criticism there made, as we know, that this was a case included in the study when it should not have been. At what stage in a case control study do the researchers, the statisticians, have to determine whether or not a case will or will not be included?

A. It depends on the quality of the investigators. Some of them will carry out their exclusion and inclusion criteria at the end of the day much as they might move the boundaries of their categories to display their data. Reputable investigators will do it at the beginning of the study before they have made the measurements of risk factors.

Q. Do what extent do you think this criticism made by Dr. MacRae of Prof. Gardner's approach is justified?
A. I don't think it is justified in this circumstance.

Q. You deal at paragraph 50, with a point made by Dr. MacRae, even after the statement was taken from Prof. Gardner and he makes a point that leukaemias are of different sub-types. Do you regard it as an objection to the validity of the Gardner study, or its results, that first of all it looked at leukaemia and non-Hodgkin's lymphoma together?
A. It is a point to be made. If let us say for the purposes of argument, leukaemia was caused by radiation and non-Hodgkin's lymphoma was not, then including it would dilute any effect that one found. If they are both caused by radiation then it is entirely sensible to include the two together. If neither is caused, then increasing the group in which the cause isn't there would merely help to demonstrate that radiation is a cause for neither.

Q. MR. JUSTICE FRENCH: That argument applies equally to leukaemias which are myeloid and lymphoblastic?
A. Yes. I am not an expert at all in the different diagnoses, but the same thing would apply there.

Q. MR. LANGSTAFF: Finally, we are told by Prof. Gardner that there are some additional cases which were not apparent to him from the information initially supplied by British Nuclear Fuels, and you have added in your later analyses what have come to be known as the 39 additional cases - cases and controls?
A. Yes, that is a misuse of the word, really. You said there are extra cases. It is slightly confusing here. "Case" in the words used in regard to the Gardner Report means an individual with leukaemia, whereas when we talk about the 39 extra, they are 39 extra individual fathers who worked at Sellafield, and they are not all cases by any means. It is a pity that that word has crept into a lot of the correspondence and even perhaps into some of my reports. If we refer to the 39 workers, they are not by any means all cases.

Q. MR. JUSTICE FRENCH: Perhaps we could put the matter beyond doubt by labelling them the 39 extra workers?
A. Exactly.

Q. Now I should be very happy to learn, because I am puzzled, as to how many of those extra workers were concerned as being cases and how many as being controls?

A. I think that in my third report I have made that fairly clear.

A Q. Well, I am sure you have, but I...
A. Would you like me to do that now?

Q. Yes, I haven't got it clear in my own head.
A. My recollection is that it is in paragraph 27 where I begin in this third report, entitled, "Agreed Dose Data Using all Cases and Controls Including all Data from the Extra 39". A couple of pages later...

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MR. SPENCER: Paragraph 31, page 12.

THE WITNESS: Yes, at paragraph 31 I say:

"...39 extra workers have been included...only 10 of them have gamma doses...and of those only 7 have neutron and internal doses."

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Therefore, 10 out of the 39 have doses. My recollection is that it is 3 of those 39 who were actually cases in having disease; 1 of those 3 being a Hodgkin's lymphoma and the other two being leukaemia and non-Hodgkin's lymphoma.

D Q. MR. JUSTICE FRENCH: Ten had doses and of the ten, three or...
A. Well, out of the total 39 that we have, refer to three cases only, but I cannot now be exactly certain how many of those... I think all three had doses, but I am not absolutely sure. I think I need to go and look at my papers on that.

E Q. MR. LANGSTAFF: I think you deal with this at paragraph 15, Prof. Evans.
A. Yes, I was sure I did deal with it.

MR. JUSTICE FRENCH: Paragraph 15 of number 3?

MR. LANGSTAFF: Paragraph 15, page 6, my Lord.

F THE WITNESS: Yes, the last part there:

"The data on the extra 39 workers revealed that ten, one leukaemia case and nine controls...Of the twenty-nine there were two leukaemia cases, one of HL and twenty-six controls."

G If you like, in terms of leukaemia and non-Hodgkin's lymphomas there were three extra people with cases who are on there, but two of them didn't have a dose anyway.

Q. MR. LANGSTAFF: So three leukaemias, one Hodgkin's, and the rest non-disease?
A. Yes.

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Q. MR. JUSTICE FRENCH: So of the 39 extra workers, 10 had doses?
A. Yes.

Q. Three of the 39 were cases, is that right?
A. Yes, but only one had a dose.

Q. Only one, and that leukaemia or lymphoma?
A. That was a leukaemia.

MR. LANGSTAFF: My Lord, I am told by Mr. Rokison, and of course I make it clear that the information was not supplied because the date of birth was not given to British Nuclear Fuels and so the information could not be extracted from their computers.

MR. JUSTICE FRENCH: Well, I will not impute any...

MR. ROKISON: My Lord, I merely wanted it to be made clear that as I understand it there is no criticism of British Nuclear Fuels in relation to these...

MR. JUSTICE FRENCH: I did not understand there to be any.

MR. ROKISON: Then I am content.

MR. LANGSTAFF: I certainly hope I had not given any impression of being at all critical in that respect. It was one of those things, I think:

Q. Professor, I have taken you a little out of your way. I was going to come to paragraph 51, the last point which Dr. MacRae made, which you deal with here. His complaint and criticism was of incomplete tracing. With the best will in the world to what extent is it possible in a case control study to have a completeness of tracing?
A. I haven't come across any substantial study with perfect tracing.

Q. Having read, and in the last few minutes in this court reviewed, the lengths to which Prof. Gardner went to trace cases and controls, would you make any criticism of the efforts to trace individuals for his study?
A. No.

Q. Do you regard the failure to trace completely as a criticism properly to be made of his study?
A. No.

Q. Can I then take you back to the Gardner study?

MR. LANGSTAFF: My Lord, it is P.4, page 1:

Q. At page 1 the "Methods" are amplified because the "Methods" refer to the Methods paper which we have looked at, and then towards the bottom of the right hand page, page 423 in the British Medical Journal:

"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. The results were calculated using conditional logistic regression analysis..."

Could I just ask you to confirm; "logistic", the word "log" relates to what we might know as logarithms?
A. Yes.

Q. It is not logistic in any conventional sense of the word which might be used by an English student?
A. No.

Q. I will ask you in due course when we come to your study to tell us in straightforward way what a regression analysis is. If asked you can explain some of the subtleties of the science?
A. I will endeavour to do so.

MR. JUSTICE FRENCH: Most of us will be panting behind you!

Q. MR. LANGSTAFF: It goes on:

"...which produces estimates of odds ratios that approximate closely to relative risks, with the computer program EGRET."
A. Yes.

Q. I doubt there will be any dispute about this. A study like this produces odds ratios and odds ratios are equivalent, for all intents and purposes, to relative risks in this context?
A. They are in case control studies.

Q. It mentions the computer program EGRET. Tell me about that computer program. Is that one specifically produced for studies such as this?
A. It is produced specifically for studies such as this and a range of other types of study.

Q. Where does it emanate from?
A. It emanates from Seattle. Its original provenance is probably from the National Institute of Health in Washington some time before.

Q. Are you acquainted with the authors of the package?
A. I am only acquainted with them by correspondence and not face to face.

Q. You deal then with the "Results and comment" produced by EGRET:

"Findings are shown for leukaemia alone and for leukaemia and non-Hodgkin's lymphoma combined for area and local controls separately."

If I can take you straight to table VI on page 4, a table setting out the "Numbers of cases and controls with relative risks for leukaemia and non-Hodgkin's lymphoma in children by timing of paternal employment and external ionising radiation dosimetry at Sellafield." Do we see there the different employment and radiation groups to which the father belonged, the type of controls for which each risk is assessed and the results, reading across from left to right?

A. Yes.

Q. So far as employment before conception is concerned, it appears there was a relative risk of 1.97, compared to area controls; 1.39 compared to local controls. So far as total dose before conception, the fourth of the tables within this whole table, there are three categories chosen: 1-49 mSv, 50-99 mSv and greater than 100 mSv. So far as 1-49 is concerned, we see there are three cases of leukaemia and a relative risk of 1.12; 50-99, a relative risk of 0.69 and in excess of 100 mSv a risk of 6.24. For the local controls, 8.38?

A. Yes.

Q. Of what importance would you regard the relative risks shown there to be?

A. In terms of seeing whether dose before conception is of importance there are two things that one would look for. The first is evidence of some substantial risk, and by substantial I would be looking for relative risks of two or more being substantial, in this sort of context, and I would also look to see that the relative risk tended to go up as the dose went up.

Q. MR. JUSTICE FRENCH: I have managed to get the second of those, the dose relation. What was the first?

A. The first one is that if they had gone, let us say, 1.2, 0.9, 2.3, that would not be substantial. The fact that there is a large number there is my first point. The 6 and the 8 that appear there say this is of interest.

Q. That is relative risk?

A. Relative risk of 6 is a substantial one.

Q. It is important in regard to (1) the high numbers 6 and 8 of relative risk.

Q. MR. LANGSTAFF: I think you said a moment ago, Professor, that anything over 2 you would regard as being of potential importance?

A. In a study of this kind it depends on the context really. If you are looking at the relative risk in a large geographic area, then a relative risk of 1.2 might be of importance, a 20% rise may be quite important, whereas in a study of this kind a 20% rise in risk could be of much less importance.

Q. I think you used the words "very substantial" for a risk of over 2 in a case such as this?
A. Yes, that is where I begin from.

Q. MR. JUSTICE FRENCH: So the high numbers 6 and 8 of relative risk, over 2 is very substantial in a study of this kind?
A. It is starting to be substantial in a study of this kind.

Q. It is starting to be substantial, and (2) as regards dose risk relation?
A. That is right. Can I now add a third? The third aspect that I will be interested in is the confidence intervals, as to showing me how much uncertainty there is in that, so that if I have a risk of 30, which is very, very uncertain, that may not be of as great interest as a risk of 6, which is relatively certain.

Q. So an RR of 30 with a low confidence interval?
A. A very wide confidence interval.

Q. A wide confidence interval.
A. So that would happen, for example, going back slightly to the geographical study where you had one death and you had only expected 0.03 of a death at that point, and so although you have got something that is 30 times as big as it, nevertheless it is still only 1 so you do not have a lot of confidence in the risk. Those three features are what I will look at in that sort of table, as I begin to try and assess its scientific merit.

Q. I have not quite finished (3) - the confidence interval is important, thus an RR of 30 with a wide confidence interval, is less significant than a much lower RR with a narrow confidence?
A. With a narrower confidence.

Q. MR. LANGSTAFF: We looked at leukaemia and the total dose before conception. Shall we look at the results that Prof. Gardner produced for the dose during the six months before conception? There we see the relative risk for 1-4 mSv, 1.3 compared to area controls, 1.1 as against local; area controls 3.54 and local 3.04 when it is 5-9 mSv, and 7.17 and 8.21 when it is greater than 10 mSv. Despite the fact that the doses are obviously banded or grouped does there appear to be some suggestion of a dose response in that table?
A. Yes.

Q. How important a result is a finding that there is a relationship between dose and response?
A. If, for example, it had been the other way round, that it had been 8 in the 1-4, 3 still in the 5-9 and only 1 in the greater than 10 you would think, well, this is not the sort of effect that we are looking for, the lower the amount of radiation the higher risk. That would be evidence against radiation being a true cause of leukaemia.

Q. Is the converse true?
A. The converse is true, that sort of trend is evidence in favour.

A

Q. If one then looks at the leukaemia and non-Hodgkin's lymphoma combined we see here that there was a total of 66 cases of both leukaemia and non-Hodgkin's considered, as against area and local controls; the total dose before conception as against the area in the three bands is 1.06, 1.16 and 6.42 by way of relative risks, and the cases compared to the local controls, 0.53, 0.95 and 8.3. One can see what the results for the same categories show for the six months preconception. Is there some evidence there of a relationship between dose and response?

B

A. There is some evidence.

Q. How ideal is it to look at the relationship between dose and response from your point of view by grouping doses in the way that Prof. Gardner did in his three bands, 1-49, 50-99 and in excess of 100 mSv preconception dose?

C

A. I think it is very useful to do it when trying to communicate the results to people but I do not think that it is the best method of analysis of the data.

Q. Prof. Gardner himself in the statement that was read to the Court this morning said this, if you take the bundle P4 it is at page 13 where it starts, and at page 19 (iii), Prof. Gardner refers there to something which is called a score test for trend?

D

A. Yes.

Q. First of all, do we see a score test for trend in the published paper in the British Medical Journal?
A. No.

E

Q. What, in very brief outline, is a score test for trend?
A. It is a way of looking at the trend across the three categories that the data have been presented in.

Q. So avoiding the problems of boundaries?
A. It does not entirely avoid the problems of boundaries.

F

Q. How reliable a test is it by comparison with examining data on a group basis for showing a dose response relationship?
A. It is a test that is specific for a dose response relationship but is not getting round the problem of the category boundaries.

G

Q. And we see what Prof. Gardner says there about his analysis, leaving out case C00106, that five out of the eight score tests for trend show statistical significance?
A. Yes.

Q. Does that mean that there was evidence beyond a 95% level on that particular test but there was a relationship between dose and response?

H

A. Yes.

Q. If we return then to the Gardner Study, if we may, and look at the discussion which begins on page 5, Prof. Gardner says:

> "The main finding of this study is that the recorded external dose of whole body ionising radiation to fathers during their employment at Sellafield is associated with the development of leukaemia among their children. Since radiation badge recording will reflect gonadal dose we interpret this finding to suggest an effect of the radiation exposure on germ cells producing a mutation in sperm that may be leukaemogenic in subsequent offspring. Other explanations may be possible, such as exposure to internally incorporated radionuclides or other concomitant exposures in the workplace: it has not been possible to examine the first of these so far, and the second seems unlikely (see below). Additionally, contamination of the home with radioactive or other material through occupational exposure may be relevant, although there is no evidence to support this."

Again, perhaps anticipating what you later say, have you had an opportunity to consider exposure to internally incorporated radionuclides?

A. Yes.

Q. Again in outline, because I will take you through this in detail, what do your results show in respect of those alone if considered on their own?

A. There is some evidence for a trend of increasing risk with increasing dose, some slight evidence.

Q. If those internally incorporated radionuclides, the exposure from those is added to the exposure from external gamma and neutron, what were your findings as to the difference, if any, they made to the Gardner results?

A. I found that the trend very clearly, if there is a trend in both of them, then adding them together will also produce a trend.

Q. MR. JUSTICE FRENCH: I just want to make sure I am not following a false trail in my own head. When you speak about internal radionuclides, are you referring to the fathers or are you referring to the offspring?

A. It is referring to the fathers entirely.

Q. I just wanted to be sure. So what you are saying, tell me if this is right, is that the trend is similar whether one has regard to external or internal radiation?

A. Yes.

Q. Paternal radiation.

Q. MR. LANGSTAFF: He said he would deal with chemicals below, or rather other concomitant exposures, I should say, and we see that, I think, half-way down the right-hand column, page 427, in a paragraph beginning:

"Of the four cases of leukaemia in the highest radiation dose group three were acute lymphatic leukaemia. The father of the non-Seascale case in this group had a total preconceptual dose of 370 mSv (over about 10 years). On their children's birth certificates two of the fathers were described as process workers, one as an analytical chemist, and the other as a fitter's mate. Although we have not yet examined jobs in detail, these various occupations do not suggest common non-radiation exposures that might be relevant to these findings."

Would you agree or disagree with that as an acceptable conclusion?

A. I think that is an acceptable conclusion.

Q. It goes on in the next paragraph:

"The results for non-Hodgkin's lymphoma, for which the number of cases was much smaller, were less suggestive than for leukaemia. However, one of the two Seascale cases in this study had a father with a total preconceptual radiation dose of 97 mSv (during about 15 years' employment), higher than all 11 related control fathers, of whom six had a radiation record before their child's conception. The father of the other case was not employed at Sellafield. There were no cases of Hodgkin's disease with paternal ionising radiation dose records at Sellafield before their conception nor among Seascale children; this lack of association with radiation exposure is as could be expected (see accompanying paper) and strengthens the findings in this paper."

Do I take it from your earlier answers about the importance of Hodgkin's as a test that you would agree with that?

A. Yes.

Q. It deals then with the possible weaknesses:

"One of the weaknesses of this study might be considered to be the relatively low quality information on potential confounding factors such as antenatal exposure to x-rays and infectious illnesses in the mother during pregnancy. Nevertheless, the strength of the observed finding ...."

- is the way that he describes it. What is he referring to by "the strength of the observed finding", in your understanding?

A. I think that he is referring there to the strength of the observed finding in regard to paternal radiation. That is what I take it he is referring to.

Q. The implication might be that the findings were strong, what would you say about that?
A. It means that confounding factors are less likely to be causing the problem if they are measured imprecisely.

Q. It deals with the other findings and the next paragraph begins:

> "These findings 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 ...."

and then he examines that. Professor, if I can ask you now to close P4 and put it to one side, and return you to your report where you deal with this ....
A. Do you mean my first or my third?

Q. Your first report, page 22 - I am rightly reminded, I have gone to page 22 which is where I intend to take you Prof. Evans, but we were at page 19. You deal, I think, in those pages with the Gardner Study and would not wish to add anything at this stage to what you have said there?
A. No.

Q. At page 22 you deal with your conclusions on the Gardner paper. You begin - and of course this was written at a time when you had not had an opportunity to see and evaluate the criticisms that might be made by the Defendants' statisticians such as Dr. MacRae -

> "I consider that Professor Gardner has done as good a job as possible with the available material and I do not believe there are any serious subjective biases in the occupational data derived from British Nuclear Fuels."

Do you think that needs to be modified in any way, having considered the criticisms that have been levelled at the methodology of the Gardner Study by Dr. MacRae?
A. No.

Q.

> "The radiation dosimetry findings are most dramatic and highly statistically significant, even though the results are heavily dependent on a small number of cases and must be treated with caution. Further correspondence in the scientific press following the publication of the Gardner paper has not undermined it."

You then say this:

> "The study goes a long way to explain the Black findings and his [Prof. Gardner's] earlier cohort

> studies. It numerically explains the excess of childhood leukaemia cases confirmed by the Black report and is also consistent with the findings of cohort studies ...."

Then you say that the remainder of the findings are rather weaker. At paragraph 62 you say this:

> "In his discussion Gardner puts forward the hypothesis that paternal occupational radiation exposure damages the sperm of the father in such a way that an enhanced risk of leukaemia is passed on to his offspring. The overall hypothesis given is plausible but the mechanisms involved are outside the competence of both Martin Gardner and myself to assess. Another competing hypothesis might be that the high risk associated with paternal radiation exposure prior to a child's conception could be a surrogate for an alternative mechanism such as exposure of the child, developing in utero, from radionuclides attached to the father's clothing when he comes home from work.
>
> 63. The fact that we are not certain of the biological mechanism involved does not mean that the overall statistical inference that there is an association between paternal preconception exposure and the risk of leukaemia or NHL in subsequent children is wrong. Further work may be able to demonstrate a new biological mechanism ...."

I think you may have read the report of Prof. Howe for the Defendants where he comments upon the question of the biological mechanism and whether one knows of it at page 31. I wonder if we could just take a look at that now and see if you would wish to comment?

A. This is his paragraph (d) "Biological Implausibility"?

Q. That is right.

A. He says that it is one of the weaker criteria of causality. There are a series of criteria of causality, three of which we have addressed earlier, that was number (1), strength, which we were looking at in Table 6 of Gardner, (2), a dose response relationship, and (3) that it should be statistically significant. A fourth criterion is biological implausibility and that will obviously lend strength to things. However, first of all it is well known that any medical man can invent a theory for any finding that he has, in whatever direction that you happen to show him. They are very, very quick, especially if they are from North America, at finding an explanation for any particular findings. The other thing is that we are really so ignorant about so many things in science that if we ignore actual data and refuse to believe in the data, because our theories do not fit it, then this is the way that science stumbles and indeed falls, and so I think that the other side of the coin

here, the fact that you do not have a biological mechanism, is not necessarily quite as strong an argument as it is sometimes made out to be.

Q. Thank you. You can put Prof. Howe on one side. You then in your report go on to deal with various other epidemiological studies undertaken in the United Kingdom, and published subsequent to the Gardner Study. At page 24 you deal first of all with a report from the Childhood Cancer Research Group in Oxford, paragraph 66 of your first report, and I think this is another report from the ubiquitous Dr. Draper. All I want to ask you about what you have said there, because it will be relevant to that which I have to ask you about later, is this, you say:

> "... the paper is not supportive of the Gardner hypothesis it does not directly contradict it."

Is there a reason why you say it does not directly contradict though it does not support?

A. I do not have the paper to hand now and my recollection is that it is not a dramatically powerful study.

Q. That is what I was going to ask you about, the power of a study. Can you tell me what a statistician means by the power of a study, briefly?

A. If you do a study in which you are looking for a risk factor, it is slightly analogous again to a legal situation. Let's assume that we regard the risk factor as being in the dock, then finding them guilty is a positive finding, so we find that the risk factor is associated. If we fail to find that the risk factor is associated we are effectively finding them to be innocent and just as in the courts of law occasionally people are convicted wrongly, so they are found to be innocent wrongly. So a study that has a lot of power is one that is going to be very good at finding the truth, and in particular at finding sufficient evidence, if someone is really guilty, to prove them so. So it is having a substantial enough study to be able to demonstrate that a risk factor is truly associated with that disease.

Q. What factors about a study lead to power?

A. Almost entirely the size of the study, how many people are involved in it, almost entirely, not quite.

Q. Again, perhaps it is obvious, but is the power of a study in any way the same thing as the key value attributed to results in that study?

A. No.

Q. MR. JUSTICE FRENCH: Can I see whether I am beginning to get the concept right? Power is dependent on the RR, as demonstrated by adequate data?

A. Mm-yes.

Q. That sounds like a mm-no? (Laughter)

A. No, my Lord, I think it is mm-yes. Let me try and find another way of expressing the power. If we think about this, be very specific in regard to paragraph 66, what we are going to need to have a powerful study to show that radiation to someone when they were a child causes them, when they are then adults, to have children with leukaemia - right - we are going to need to have a very, very large number of people who were exposed to that radiation because the leukaemia in their children will be very rare. We will expect very few of them, so we need a very, very large study to be able to show that, because we cannot go and find the children, the grandchildren almost - well, no, the children - of those who were patients as children themselves. We cannot go and find very many leukaemias, so we need a very large study to demonstrate any real increase in risk.

Q. Is this, putting it in concrete terms, expressing the concept, that you need a very large number of irradiated persons in order to demonstrate the probability or otherwise of a significant number of them producing leukaemia in F1?
A. That is right.

Q. MR. LANGSTAFF: May I ask you this, Professor, by way of perhaps further elucidation? If the reality were that a particular exposure created a slightly increased relative risk - let us say a relative risk of 1.5 - in those who are exposed, would you need a larger or a smaller study to detect such a risk compared with an exposure which produced, let us say, a relative risk of 10?
A. You would need a dramatically larger study.

Q. MR. JUSTICE FRENCH: So the smaller the relative risk, the larger the study needed to show a statistically significant relationship?
A. Exactly so.

Q. MR. LANGSTAFF: You are talking here, are you not, Professor, in relation to a study of the exposed as opposed to a study of those in whom the disease has become apparent?
A. Exactly.

Q. So when, in some of the papers, we see reference to a study having 80 per cent power to determine a relative risk of - and I use it for the sake of example - 7 or more, that would indicate a study with sufficient numbers to show four times out of five if such a high relative risk existed, but it would be of limited utility in considering any relative risks of less than the 7?
A. It would become progressively more limited the lower the relative risk became, yes.

Q. But, equally, a study with 80 per cent power to determine a relative risk of 1.5 would be expected to be highly reliable if you were considering a true relative risk of 7?

A. Absolutely.

MR. LANGSTAFF: My Lord, I hope that is helpful.

MR. JUSTICE FRENCH: Yes, thank you.

Q. MR. LANGSTAFF: You deal at page 24 then with the second of the reports since the Gardner Report, an analysis of parental occupational risks and leukaemia in Cumbria, North Humberside and Gateshead, and note that that finds "a statistically significant relationship between the pre-conceptional exposure of fathers to ionising radiation and leukaemia incidence in their offspring." Is that a report produced by McKinney?
A. It is.

Q. Would you take that report? That is Common Bundle M, at 172. This is a report by McKinney, Alexander, Cartwright and Parker in relation to "Parental occupations of children with leukaemia in West Cumbria, North Humberside and Gateshead"?
A. Yes.

Q. The Objective:

"To determine whether parental occupations and chemical and other specific exposures are risk factors for childhood leukaemia."

The Design:

"Case-control study."

That is the same type of design as the Gardner 1990 study we just looked at?
A. Yes.

Q. And the Setting: Three areas. That is Copeland and South Lakeland (west Cumbria), Kingston upon Hull, Beverley, East Yorkshire, and Holderness (north Humberside), and Gateshead.

It looks at 109 children 0-14 and again it puts together leukaemia and non-Hodgkin's lymphoma during the 15 years 1974-88. Two controls in that case for each child.

The results:

"Few risk factors were identified for mothers, although preconceptional association with the food industry was significantly increased in case mothers. 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," and the confidence intervals are set out, "(0.92 to 6.22). Raised odds ratios were found

for paternal exposure during gestation, but no independent postnatal effect was evident."

The 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."

Will you turn to the third page, page 683 in the BMJ, Table III, Occupation and exposure of the fathers as risk factor for childhood leukaemia and non-Hodgkin's lymphoma according to the time of exposure. Second from the bottom, do you see the line that sets out the number of cases, the number of controls and the odds ratio for preconceptional exposure to radiation? That, I think, is on the left-hand side of the table. The odds ratio given there to radiation is 3.23; confidence interval 1.36 to 7.72.

In the context of a study such as this, what do you say about a relative risk of 3.23?

A. I say that it is of interest, but it is not as strong as the same relative risk in Gardner's study.

Q. There is a discussion at the bottom of page 685 dealing with the validity of the findings:

"Our results are based only on data obtained by home interview, and reported exposures in the workplace or home were not validated, except for positive reports of exposure to radiation,"

appearing to suggest that negative reports were not further investigated?

A. Yes.

Q. Is that a weakness?

A. Not a very strong weakness.

Q. "In addition exposure was not quantified, which precludes the calculation of dose response."

Is that a weakness?

A. Yes.

Q. "For all these reasons our findings must be interpreted as epidemiological associations, which may or may not agree with other independent observations, but cannot be considered to show a direct causal link."

Having said that, overleaf to 686, it deals with the results that we have looked at in relation to radiation

and, about half-way down the page, do you see, just underneath the first punch hole in the left-hand column, a sentence beginning, "Our results offer support...."

A. Yes.

Q. "....for the hypothesis that parental exposure to radiation has an effect prenatally. The increased odds ratio for fathers across the three periods analysed were highly correlated; there was no evidence of independent risk from postnatal exposure. Exposure of parents before their child's birth makes a significant contribution to the risk, and although the data are sparse and ambiguous, this risk seems greatest in the 40 weeks before birth, which includes the time of conception. Further examination by using additional data on individual exposure histories is consistent with this. This risk is not confined to Cumbria and exposed case fathers did not work exclusively in the nuclear industry."

Do you happen to know where some of them did work?

A. I believe that some of them worked in Gateshead.

Q. Was there a source of radiation there, of which you are aware?

A. I believe that, first of all, Gateshead was identified at one stage as having a cluster; secondly, I believe that in the documents under discovery, we found that most of the public were not aware that there were sources of radiation, I believe, in an engineering company, quite extensively, in Gateshead.

Q. It goes on, in the next paragraph:

"Our findings are not independent of those of Gardner because of the geographical overlap and similarity of methods of selecting controls."

And it deals with the matches with Gardner and says this:

"The raised odds ratio for confirmed parental exposure to radiation in the periconceptional and gestational period is entirely dependent on cases included in the study by Gardner et al."

Have you since become aware of a further study or a further report in relation to this study, which takes those comments further?

A. Yes, there has been a letter in the BMJ recently with McKinney as one of the authors and Alexander, I believe, as the first author, doing an analysis that had excluded the Gardner cases entirely.

Q. Shall we just have a look at that? That is in P4, the very back, page 276.

Q. MR. JUSTICE FRENCH: A letter to the BMJ, is it?
A. That is right.

A Q. MR. LANGSTAFF: Sorry, page 275, I beg your pardon, P4?
A. It begins at the very bottom of page 715, bottom right-hand corner under the table.

Q. "We reported last year an analysis of a case-control study we had conducted in three areas of northern England. Significant associations were
B found for childhood leukaemia and certain exposures of fathers before the affected children were born; these included...."

MR. JUSTICE FRENCH: I am sorry, I am getting left behind.

MR. LANGSTAFF: I am sorry, my Lord. My Lord, the
C bottom right-hand corner of page 275. It begins:

"Editor,

We reported last year....."

MR. JUSTICE FRENCH: Yes.

D Q. MR. LANGSTAFF: And, after that introduction, at the top of 276, Professor, does it say in the first paragraph this:

"Gardner et al's results were not published until after our interviews were completed. Thus they cannot have led to any recall bias related
E specifically to the prenatal period."

What is the point being made there?
A. What they are suggesting there is that, had the interviews been done after Gardner's results were published and became in the public domain and on the news and so on, that those mothers or fathers who had had children with leukaemia might think very carefully about
F their possible exposure to radiation and remember it in a way that those who had not had children with leukaemia would not be as good at remembering.

Q. It goes on to say:

"We have now been able" - this is the third sentence in that paragraph - "to cross check our entire study
G population against their" - that is Prof. Gardner's - "data base (which includes more recent cases and controls added since the original report). We excluded all subjects who were present on their data base and analysed all remaining case-control sets that were discordant for paternal radiation exposure (in one of the three time periods) using exact
H methods of analysis with the statistical package EGRET."

That is, I think, the same package that we have identified that Prof. Gardner himself used?

A. Yes.

Q. "The table provides exposure classifications for the subjects in this analysis. The overall numbers are reduced, as was anticipated; in particular, the numbers classified as certainly exposed to ionising radiation have become almost negligible (one case "exposed" before conception and one control exposed postnatally, both with extremely small lifetime doses).

Several points," it goes on, "noted in the first report persist. First our data provide no evidence of independent risk associated with paternal postnatal exposure. Secondly, they do show significant associations of leukaemia risk for paternal exposure before conception (11 cases, four controls);" - it sets out the odds ratio - "a stronger effect but based on smaller numbers remains evidence for periconceptional exposure (six cases,

no controls). These results include four cases and no controls exposed to non-ionising radiation and two cases unlikely to have been exposed. If all these are excluded the strengths of the associations are reduced and they are no longer significant ..... The evidence for increased risk is not confined to West Cumbria. All the case children included in this analysis of prenatal parental exposure had diagnoses of acute lymphoblastic leukaemia."

And it says this at the end:

"These results yield a modest independent contribution to the scientific debate concerning possible effects of paternal radiation exposure before the birth of children. We recommend extreme caution in their interpretation."

Would you agree with the need for caution?

A. Yes, I would agree with the need for caution if you take this report on its own.

Q. Does that report, taken with the Gardner report, add, in your view, or subtract, in your view, from the findings of the Gardner Report?

A. I think it adds to the findings of the Gardner Report.

Q. Putting that to one side then, Professor, and returning to your first report, you deal at page 25....

MR. JUSTICE FRENCH: So we are back to Evans 1, page 25.

Q. MR. LANGSTAFF: You deal here, at paragraphs 69 and 70 with the case-control study done around the Dounreay nuclear plant, I think done by the Scottish Urquhart.

You say this at the start of paragraph 70:

> "The study was unlikely to demonstrate a similar effect to Gardner; the overall levels of radiation to which workers at Dounreay were exposed are less than the levels to which workers have been exposed at Sellafield. Only one of the six cases of leukaemia in the study had a father who worked at the Dounreay plant...."

So there were six cases of leukaemia in the study compared to the 52 in Gardner. Why do you say that the study was unlikely to demonstrate a similar effect to Gardner?

A. I think the number of cases may have been a little larger than that, but I cannot recall. Basically, the power of the study will be dependent on the number of workers exposed to sufficiently high doses and also on the number of cases overall, and both of these were rather smaller.

Q. You make that point, I think, in the last sentence there and we have already dealt with what was meant by "power".

Page 26, you deal with the birth and school cohort study around Dounreay and, I think, point out that the findings there were not the same as the findings of the birth and school cohorts around Sellafield?

A. Yes.

Q. Taking the reports of Urquhart and the birth and school cohorts around Dounreay, is there a contradiction between the Dounreay results and the Sellafield results?

A. No, I do not think there is a contradiction between them.

Q. Why does the negative result, the failure to find an association in Dounreay, not contradict the finding of an association in Sellafield, in your view?

A. Basically because the confidence interval on the risk that they found would include, nevertheless, substantially raised risks that were also compatible with Gardner.

Q. Since those studies were reviewed by you in your first report, I think you have become aware of three further studies, with which you deal in your fourth report, and it is probably convenient to take you to those now before I take you to your overall conclusions on the reports for you to deal with.

Q. MR. JUSTICE FRENCH: Just before we do that, what I have noted on your last answer is, "The Dounreay cohort study does not contradict Gardner because it suggests substantially raised risks and so is not incompatible with Gardner"?

A. No, it does not suggest substantially raised risk. It itself does not have substantially raised risks, but it is compatible with raised risks. There is too much uncertainty in the Dounreay study. The numbers are too small to be certain.

Q. So the Dounreay cohort study does not contradict Gardner because it is compatible with....?
A. It is compatible with Gardner, yes.

A

Q. With substantially raised risks?
A. That is right.

Q. And so compatible with Gardner?
A. Exactly.

Q. MR. LANGSTAFF: Professor, plainly I think I may not have asked you the question sufficiently clearly because I had understood your answer to relate, not only to the cohort study, but also to the case control study?
B
A. Yes.

Q. I see you are nodding.

Q. MR. JUSTICE FRENCH: This applies to the Gardner case control study as well?
C
A. No, we are referring to the Dounreay case control study as well.

Q. Considering Dounreay and its impact on Gardner, so if Dounreay cohort study does not contradict Gardner, for the reason given, then the same will apply to the Dounreay case control study as to its impact on Gardner?
D
A. Yes.

MR. JUSTICE FRENCH: Yes, where are we off to now, Mr. Langstaff?

MR. LANGSTAFF: The fourth report of Prof. Evans, my Lord.

E

MR. JUSTICE FRENCH: Would you just allow me a moment, Mr. Langstaff?

Q. MR. LANGSTAFF: Professor, have you located your fourth report?
A. I think it is sitting back in my case. Ah, yes, right at the back of this one.

F

Q. Having hunted for that, I wonder if you might also take, Professor, Prof. Howe's report, which includes as an appendix the report of McLaughlin. Professor, can you keep your fourth report open and turn, in Prof. Howe's report, to his appendix, where he exhibits the McLaughlin report.

G

Q. MR. LANGSTAFF: Can I turn you to the summary of the report on the second of those pages? My pages are not numbered, Professor, but if you look at the beginning of the McLaughlin Report - do you have that?
A. Yes.

MR. JUSTICE FRENCH: Is that the one that starts, "Atomic Energy Control Board Information Bulletin '92"? Does it look like <u>that</u>?
H

MR. LANGSTAFF: My Lord, yes, it does. It is a few pages further on where there is what appears to be a covering sheet, the right-hand side of which has "Research Report" at the bottom.

MR. JUSTICE FRENCH: Sorry, say that bit again.

MR. LANGSTAFF: My Lord, it is about four pages further on.

MR. JUSTICE FRENCH: "Research Report" at the bottom right?

MR. LANGSTAFF: My Lord, yes. That I think is the first page. One can then turn over the page and begin with the text.

Q. Professor, I think this is a report which you have recently looked at in order to comment upon for the purposes of your fourth report.

"SUMMARY

An epidemiologic study was performed to determine whether there was an association between childhood leukaemia and the occupational exposure of fathers to ionizing radiation prior to the time of the child's conception. The study focused on the effect of exposures received during employment in the nuclear industry, particularly in the period before a child's conception.

The study employed a case-control design, whereby children with cancer ("cases") and children who did not develop cancer ("controls") were compared with respect to their prior exposure history. The case series consisted of children (ages 0-14) who died from or were diagnosed with leukaemia and born to mothers who, at the time of the child's birth, resided in the vicinity of an operating nuclear facility in Ontario. Cases occurring from 1950 to 1988 were identified from the Ontario Cancer Registry. The residence of parents at the time of each case's birth was determined from birth certificates.

Eight controls per case were identified from birth certificates. Control children were those who had not developed leukaemia by the time the index case was diagnosed and were matched to a case according to date of birth and mother's residence at the time of birth.....

Data pertaining to occupational radiation exposure of the 1002 fathers were obtained by a computerised record linkage with the Canadian National Dose Registry (NDR) and subsequent examination of the employer records. Links to the NDR were identified

> for 95 fathers: of these, 52 were reactor workers, 31 were uranium miners, 10 worked in other industries, one was a medical worker and one had an unknown job class."

Then it sets out the obtaining of radiation doses in milliSieverts, noting:

> "....largely due to gamma radiation and, in addition, (a) tritium dose (in mSv), which is the most common type of whole body internal exposure received by Canadian nuclear reactor workers, and (b) for uranium miners, internal exposures to the lungs due to radon and radon progeny (in working level months). Total whole body dose was calculated for each father by summing the external whole body dose and tritium dose."

And then the radiation exposures are set out in the various periods. It sets out in the middle of the next page, beneath the punch-hole:

> "The primary focus of this study was on the effects of radiation exposures occurring prior to a child's conception. There was no evidence of an elevated leukaemia risk in relation to any exposure period (lifetime, six months or three months prior to conception) or exposure type (total external, or internal dose). For example, the odds ratio for any exposure to radiation (total dose > 0.0 mSv) during a father's lifetime prior to conception was 0.87...."

It sets out then the confidence interval:

> "....which was based on the exposure of fathers of six cases and 53 controls. For any whole body exposure to radiation during the six-month period prior to conception, the odds ratio was 0.96 (95% CI = 0.34-2.77), based on the exposure of fathers of five cases and 41 controls. Also, there was no apparent gradient of effect with increasing radiation dose."

And it then justifies that from the findings. :

> "Paternal exposures up to the time of a case's diagnosis or death were also considered and found not to be associated with the occurrence of childhood leukaemia.
>
> The radiation doses that were reported by Gardner et al to be most strongly associated with leukaemia risk were specifically considered in this study. None of the cases in this study had fathers with either a lifetime preconception dose of 100 mSv or greater (whereas five controls fell into this category), or a six-month preconception dose of 10

> mSv or more (compared with nine controls). The prevalences of exposure to these radiation doses were similar among the fathers of controls in this study and in the study by Gardner et al. The fact that relatively high preconception doses occurred among the fathers of controls but not cases emphasised that the dose-response relationship reported Gardner et al did not occur in this study."

Can I, having read that just quickly, if I may, take you, Professor, to page 21 of the report - it is numbered at the top, my Lord, in the middle of the page.

MR. JUSTICE FRENCH: There are little Roman numbers and then....

MR. LANGSTAFF: It is Arabic numerals, 21.

MR. JUSTICE FRENCH: Then Arabic goes on. Where we have a table?

MR. LANGSTAFF: And it is what one might have described in another context as a "starry-sky" approach, I think. One sees there the diagram of the cases and controls which McLaughlin et al were looking at, and it is possible to read off this chart, just for comparison with the doses that you were later to consider, the doses now agreed for the Gardner study, the maximum dose would appear to be in the region of 190 mSv to one control, and we can see there is another control in something of the same region, and all the other controls and cases appear to have received a lifetime dose of less than 110 mSv:

Q. Is it the case, Prof. Evans, that when you were considering the Gardner doses, as agreed, for the purpose of re-analysing the study, there were in excess, I think, of ten cases and controls who had received more than 250 mSv?

A. I think that is so, but I could not tell you the exact number off-hand. Certainly the pattern is noticeably different.

Q. Can I return you, then, to (ii)? :

> "The largest, but also the least stable, relative risk estimates seen in this study referred to uranium miners, with an odds ratio of 7.27 ...."

and it then gives a confidence interval of 0.59 to 88.7. What is meant by an unstable relative risk?

A. It simply means it has a very wide confidence interval.

Q. What can one say about the width of the confidence interval there for the uranium miners?

A. It implies a risk that could either be that uranium mining reduces your death rate by 40% or increases it by a factor of nearly 90, so the uncertainty is enormous.

Q. Do you know from your study of this report the category of worker in whom the highest doses were recorded?
A. I believe it is the uranium miners.

A

Q. MR. JUSTICE FRENCH: Perhaps it is not necessary to know, in which case you will say so, but why is the confidence interval so wide in relation to uranium workers?
A. Because there are so few miners involved, like two or three, I think, is my recollection.

B

Q. MR. LANGSTAFF: I think you are told, Professor, at the bottom of (ii) and the top of (iii) there are five matched cases and controls, and plainly that does not tell you how many of those five cases and controls are actually uranium miners.
A. I think in the text of the tables it does tell us at some point.

C

MR. JUSTICE FRENCH: I am content not to take time pursuing it unless you think we should.

Q. MR. LANGSTAFF: The study then goes on, in relation to the finding about uranium miners, at the top of page (iii):

D

> "Given that (a) statistical significance was not achieved, (b) the majority of radon dose ...."

- that would be the dose that uranium miners would have, would it?
A. I could not say. I mention that is, but I do not know whether that is the only dose they have.

E

Q. "(c) a previous ecologic study found that the mining region did not have an excess of childhood leukaemia, it is concluded that the observations pertaining to uranium miners were a chance finding due to random variation associated with small numbers."

Then it deals in the paragraph after the next:

F

> "It is concluded that there was no association between childhood leukaemia and the occupational exposure of fathers to ionizing radiation prior to the time of conception. This conclusion applies in particular to radiation exposures arising from employment in the nuclear industry in Ontario. No association was detected for external whole body dose, tritium dose or radon exposures, or for any of the preconception or prediagnosis periods of exposure. Odds ratios were close to 1.0 for all radiation dose categories and occupations except for uranium mining, which had a larger, but not statistically significant odds ratio.

G

H

> The findings of this study in Ontario are not consistent with the hypothesis that childhood leukaemia is associated with the occupational exposure of fathers to radiation prior to conception, as was found in the case-control study at Sellafield in the United Kingdom by Gardner et al. The results from Ontario provide evidence against the existence of such an association for exposures to either whole body external radiation or tritium."

You say, and I take you back to your report, having shown you what is said about the McLaughlin study and the summary of the findings, to what you say about the quality of the report, and you accept, I think, that it was carried out to a high standard but you have some concerns ....

A. Yes, especially as it was sponsored by the Atomic Energy Control Board of Canada.

Q. You have some concerns about it, I think. Your first concern is the selection of controls. Can you explain what you had in mind here as an important problem with the selection of the controls in the McLaughlin Study?

A. I think it is important in that if there is the possibility that some of the controls had developed cancer, which is quite unlikely because the numbers of people doing so should be very small, but one would have thought that they would, like Gardner, have expected to exclude anyone who might have had a radiation induced disease from among their controls. If they have failed to do that, and they actually found such a thing, and such a person was in the study, then the study would be totally invalidated. I think that is very unlikely but I think that it is a bad methodological point not to exclude from your controls those who might be having a disease that is caused by radiation.

Q. You say that there is a possibility of bias if the controls had developed cancer?

A. If that were so, yes.

Q. MR. JUSTICE FRENCH: Do we know one way or another whether people suffering from a disease were included?

A. No, we do not. They specifically say that they could not have leukaemia or have died. Those are the only two exclusion criteria essentially.

Q. So it leaves open the query, were the exclusion criteria wide enough?

A. That is right.

Q. If they were doing their job sensibly then it would be wide enough?

A. I would have hoped that they would say, "We will exclude anyone who got a cancer from being a control". It is one thing to have them as cases and it might be argued that it is sensible to only look at leukaemias, which is what

they have done, but there may be somebody with non-Hodgkin's lymphoma that they would argue is not caused by radiation but they have actually included them among their controls.

Q. If they were doing their job sensibly wouldn't they say, "We can't have him, forget him"?
A. Exactly, and then I would have expected them to have written that in their report. It leaves open a question. I do not think I would want to say this report is rubbished as a result of that but it raises a question in my mind.

Q. Exclusion of - dare I use the expression "confounding categories", "biasing categories"?
A. Exclusion of possible cases, I would call it, simply.

Q. Exclusion of possible cases not spelt out in the methodology?
A. Yes, I think that is right and I think particularly in the light of the fact that Gardner's methodology spelt that sort of issue out very clearly and they have obviously designed and carried out their study subsequent to Gardner, and make a lot of reference to it. A lot of their methodology is similar and in this respect they have done something different, and it leaves me with some slight degree of uneasiness.

Q. Exclusion of possible cases not spelt out in the methodology, contrary to Gardner; this admits the possibility that a potential case may have been included?
A. Yes, among the controls, that is the point, that they have not excluded people from the controls who in another study might actually have been cases.

Q. So I should say exclusion of possible cases from the controls is not spelt out, and this admits the possibility that a case may have been among the controls?
A. It is a possibility, a logical one at any rate - very unlikely.

Q. I am not sure if this is not getting close to the Bristol exclusion?
A. No, I think it is a very different sort of issue because this is a design issue that says I am going to include as possible controls people who might have a disease that is caused by radiation and I am possibly going to include them in my controls, and if I do and I find somebody, let us say for the moment that we go back to that diagram on page 21, if you were to learn that one of those stars at 190 mSv had got non-Hodgkin's lymphoma, and this is being used by them as evidence against, you would say there is something funny going on here. I think it is very, very unlikely but as a methodological point, if they had been the first to do the study I would not have had the problem because then you could say they had not thought of that as an issue, but given that Gardner was so specific on the issue they ought to have been as well, in my view.

Q. Yes, I follow how you put it.

Q. MR. LANGSTAFF: If there were, for instance, five cases of leukaemia in the cases, and let us say, purely for the sake of example, five cases of non-Hodgkin's lymphoma amongst the controls, and the study was looking at the two separately, there would appear then to be no risk from radiation in respect of the leukaemias, whereas if it was legitimate to put the two together, the leukaemia and the non-Hodgkin's lymphomas, your accurate study might have had ten but your study of leukaemia would have had five and no non-Hodgkin's lymphomas ....

A. If all your five controls were non-Hodgkin's lymphomas, which is just so exceedingly unlikely, you would now have an infinite relative risk because you would have ten cases and nought controls, and not five and five.

Q. I asked the question in extremis simply to elucidate the point.

A. Yes. It is not likely to be a problem but is an aspect of the design from the beginning that could lead to bias, whereas the exclusion of case 106 I do not think leads to bias or inclusion. I do not think it is either way, provided you do it all at the beginning.

Q. You then turn to the power of the study.

MR. JUSTICE FRENCH: Shall we turn to the power of the study tomorrow morning, Mr. Langstaff?

MR. LANGSTAFF: My Lord, I would be obliged.

(The Court adjourned until the following morning at 10.30 a.m.)