IN THE HIGH COURT OF JUSTICE

QUEEN'S BENCH DIVISION

1990 R No 860
1989 H No 3689

ROYAL COURTS OF JUSTICE
THE STRAND
LONDON

Friday 27th 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)

From the Notes of J L HARPHAM LIMITED
Official Shorthand Writers
55 Queen Street, Sheffield S1 2DX

INDEX TO TRANSCRIPT

FOURTEENTH DAY'S PROCEEDINGS

FRIDAY, 27TH NOVEMBER, 1992

STEPHEN JAMES EVANS Recalled

Examined by MR. LANGSTAFF (Continued)

Q. Prof. Evans, I was asking you yesterday evening when we broke about your fourth report, the second point which you were making about the McLaughlin study. So what you should have in front of you is your fourth report and a copy of the McLaughlin study which, as we know, is annexed to the report of Prof. Howe. Professor, if you would turn to page 32 of the McLaughlin study?

A. Yes.

MR. LANGSTAFF: Your Lordship will recall that we went through the summary of the report, the Canadian study into six facilities in Ontario, and Prof. Evans had made a comment about the exclusion of cancers, or the non-exclusion of cancers from the controls, and the second comment I was about to ask him about when we adjourned was the second comment which he has put at page 2 of his fourth report, dealing with the power of the study:

Q. You were referring there, Professor, to page 32 of the McLaughlin study, so if you would have that open. Let me ask you about it in this way: first of all, underneath the heading F.3 on page 32 the authors set out what the statistical power of the study is, and you were explaining yesterday and telling us that principally it is a function of the size of the numbers involved in the study?

A. Yes.

Q. The second paragraph deals with the study in particular and says this:

> "The proportion of controls with a total whole body dose greater than zero prior to conception was lower in this study (6.0%=53/890) than in the case-control study by Gardner et al (14.5%=40/276 among local controls)."

A. Yes.

Q. "Nevertheless, the sample size of this study (112 cases), which included more than two times the number of leukaemia cases than the Sellafield study (52 cases)..."

I think in the Sellafield study there were an additional 22 cases of non-Hodgkin's lymphoma taken into account?

A. That's right.

Q. "...was sufficient to provide more than 80% power to detect a true odds ratio of 2.5 or greater. For this exposure category, Gardner et al. reported an odds ratio of 1.4, whereas an odds ratio of 0.87 was found in this study."

I am going to ask you about the meaning and significance, in lawyer's terms, of this. Where it says that the sample size of the McLaughlin study "was sufficient to provide more than 80% power to detect a true odds ratio of 2.5 or greater", what do the authors mean by a true odds ratio of 2.5 or greater?

A. What they mean is that if in truth radiation exposure, that is, a total whole body dose prior to conception more than zero, they mean that if radiation exposure multiplies essentially by 2.5 your risk of getting leukaemia, then the study should be able to detect that. If one imagined doing a large number of studies twenty percent of them would fail to find the effect to be significant, but 80% of them would find it.

Q. We know it is conventional, when you are assessing the possibility of a chance result, for statisticians to use a 95% confidence level, a p value, as we know, of 0.05 or less. Is this 80% figure the conventional figure for power or is there any conventional figure?

A. Eighty percent is the sort of power I would typically use as the minimum power. You would not expect to design a study with less than 80%. You might hope to have a power of 90%, and I believe that my colleague, Dr. MacRae, always argues for a power of 95%, but I personally design many studies with a power of 80%. This entirely reasonable.

Q. MR. JUSTICE FRENCH: Now before we proceed, Prof. Evans, I would just like to record for my own purposes, in extenso, the answer you gave beginning with the words, "If in truth..." Can you reproduce that?

A. I will try. If in truth radiation exposure multiplies the risk of getting leukaemia by 2.5 or more, then 80% of studies of this size and this rate of exposure should find a statistically significant effect. I think that first paragraph there under F.3 I find to be very clear, but perhaps that is because I know what it is meant to be saying, but it is very clear. It makes it clear that the power of the study has in fact - I try to simplify things - four things going into it. Firstly, the sample size; secondly, the size of the relative risk; thirdly, what p value you use, and we use 0.05, which is analogous to talking about 95% confidence intervals. That is the other side of the coin. The last one is the proportion of the population that is exposed to the factor. I think that is a very clear description.

Q. Yes, they are listed in the second sentence of F.3:

"The power of a study is a function of its sample size, the size of the relative risk, the prespecified alpha probability..."

Need I concern myself with "alpha" as opposed to any other probability?

A. We conventionally just talk about the probability of failing to find a difference as what we tend to call a type 2 error. We give that a beta probability. Another way of talking about power is saying you have a beta probability of 0.2 - a 20% probability of failing to find a difference. It is just an entirely conventional thing of saying alpha and beta, and it has nothing to do with alpha and beta radiation. It is just the conventional statistician's use for statistical significance.

Q. MR. LANGSTAFF: You went on in the earlier answer to say that the minimum power you would look for in the study was 80%, and there have been suggestions from other statisticians that ideally the power should be higher?

A. Yes.

Q. MR. JUSTICE FRENCH: You specified Dr. MacRae as using 90% or 95%?

A. Well, I have heard him on several occasions argue for using much higher powers, but I think that life is not quite as easy as that and we have to be content with 80% power in a lot of the studies we design.

Q. MR. LANGSTAFF: If a study has 80% power to detect a true odds ratio of 2.5 or greater, what will its level of power be for an odds ratio which was less than 2.5?

A. The power will similarly be less.

Q. Less than 80%?

A. Less than 80%.

Q. MR. JUSTICE FRENCH: Is this right? If an odds ratio of less than 2.5 be adopted...

MR. LANGSTAFF: My Lord, I think it would be found, because the odds ratio, of course, is the product of the study.

THE WITNESS: True odds ratio, that is the point. You don't know what the odds ratio is. We never know. Only God knows. What we say is if the true one is 2.5 then we have a power of 80%. If the true one is only 2, we will have a power that is substantially less than 80%.

Q. MR. JUSTICE FRENCH: If the true, but unknown odds ratio, in fact be less - is that right?

A. If the true odds ratio was in fact less.

Q. In fact be less than 2.5, then the power will be substantially less than 80%?

A. Yes. It will depend on how much less than 2.5 it is.

Q. Will be pro rata less than 8%?

A. Yes, pro rata. There is a complicated formula.

Q. MR. LANGSTAFF: We see in this paragraph the authors are comparing the power of the Ontario study to detect true odds ratios of the sort reported by Gardner for the same dose categories at Sellafield. We see in their last line, having said that their study is 80% powerful to detect true odds ratio of 2.5 or greater, that for this exposure category Gardner reported an odds ratio of 1.4. What are the implications of that odds ratio - 1.4 - being less than 2.5 so far as the applicability of the Ontario findings to the Sellafield results are concerned?
A. I think the Ontario study does not have a very strong chance of finding an odds ratio of 1.4.

Q. So far as this category of dose is concerned, therefore, can you say that the two studies, the Ontario study and the Sellafield study, are necessarily inconsistent?
A. No.

Q. MR. JUSTICE FRENCH: You can or cannot say they are necessarily inconsistent?
A. I would say that they are possibly consistent.

Q. MR. LANGSTAFF: If you keep your finger at page 32, Professor, and turn back to page 18, we see a table, Table 8, which sets out the results in some detail. The result that we have been examining in that paragraph comes under the heading "External Whole Body Dose", in mSv, "Before Conception". The category greater than 0.1 produces an odds ratio of 0.87?
A. That is right.

Q. If one then goes immediately to the right of 0.87, we are then in a column which is headed "95% CI".

Q. MR. JUSTICE FRENCH: That is confidence interval?
A. Exactly so.

Q. MR. LANGSTAFF: We see that the 95% confidence interval extends from 0.32 to 2.34?
A. Yes.

Q. What are the implications of that band?
A. It suggests that this study is compatible with true risks in the range 0.32; that is, reducing the risk of leukaemia by 70% to 2.34, which means more than doubling the risk of leukaemia.

Q. MR. JUSTICE FRENCH: Yes. When you say 70%, is that rounding up the 68?
A. That is rounding up the 68, yes.

Q. Yes, and equally more than doubling, is approximating to 2.34?
A. Yes.

Q. MR. LANGSTAFF: Does it follow that if the true relative risk were 1.4, that it would be well within the bounds of compatibility shown by that range?

A. Oh, very clearly well within the bounds.

Q. Could I take you back now to page 32, asking you to keep a finger in page 18? Let's look at the third paragraph where the authors turn their attention from the dose categories they have examined to the high radiation doses? Page 32, the third paragraph, where it says:

> "The proportion of controls exposed to a high radiation dose prior to conception (eg lifetime preconception dose of greater or equal to 100 mSv) was more similar between the two studies, being 0.6% in this study and 1.1% in the Sellafield study. For a rare exposure such as a preconception dose greater than 100 mSv which was present in 0.6% of controls, this study had more than 80% power to detect excess risks of 7.6 or greater. Therefore, for high preconception radiation doses, this study had sufficient power to detect only very large relative risks."

Let me ask you about that. If the true relative risk were in fact less than 7.6, would this Ontario study be able to detect such a risk at a level of 80% confidence or above?

A. No. I think if you look in page 2 of my fourth report, I did an approximate calculation and found the power to be 50% to detect substantial risks such as ones of 5.

Q. MR. JUSTICE FRENCH: Before I go to your fourth report can I record your answer?

A. My answer is that the power to detect a risk that is noticeably less than 7 will be pro rata less than 80% power.

Q. That is the power of the McLaughlin study?

A. That is the power of the McLaughlin study.

Q. MR. LANGSTAFF: We will see in due course, Prof. Evans, the relative risks that you found on your re-analysis. Of course, what the McLaughlin authors were considering were the risks that Gardner had found on his analysis of the data as presented and considered by him. Can we just for the moment turn back to page 18 and do the same exercise in relation to the 7.6 figure as we did in relation to the other dose category?

A. I think we need page 19 to do it.

Q. Can you point us to the appropriate figure?

A. The appropriate figure is not exactly given, but if we again go to the middle of the table, the external whole body dose prior to conception. That is in the middle of the page there and it has a row that begins zero for the paternal exposure and 106 cases and 837 controls. We see that above 50 mSv dose the observed odds ratio was 1.29, but the 95% confidence interval was 0.23 to 7. They don't in fact give a row for greater than 100 mSv, which is the equivalent to Gardner.

Q. The text explains that is because of the inadequate numbers in the study?
A. That is because of the inadequate numbers. We see that the data are compatible with a risk of 7 beyond 50 mSv, which is clearly compatible with Gardner's study.

Q. MR. JUSTICE FRENCH: Is it a risk or a confidence interval?
A. Well, the confidence interval goes out to 7, and that is the upper limit, if you like, that you would think that these data are compatible with, for the value of the relative risk. That 7 is a value of relative risk.

Q. So one conceives a confidence interval as being the upper and lower limits of the risk?
A. Yes, it is a very difficult concept.

Q. Thank you for saying that! Now table 9 gives a confidence interval of 0.23 to 7. This is for doses up to and including 50 mSv?
A. No, it is 50 mSv and above, is the 1.27.

Q. I get fooled by the diminuendo sign in music. It is the other way round?
A. It is the other way round in mathematics, I'm afraid.

Q. Doses of 50 mSv and greater. There is no line for 100 mSv and greater?
A. That is right. We do know that the controls would be 5 out of 890 from the text on page 32. I think we know that the cases will be zero. I would not wish it to be thought I am trying to say they are being wicked in not putting in that category, but you can see it is an illustration of where you choose your boundaries makes life difficult. You can end up confusing or hiding things, but in this instance I don't think they are. They would not be able to calculate directly a confidence interval, very easily at any rate.

Q. There is no line for a 100 mSv, but the controls being 5 out of 890 and the cases being zero, the calculation is impossible?
A. It is not impossible, but using the methods I suspect that they have, it would not work. I think that would be true.

Q. The calculation would, you believe, be impossible?
A. It would not be possible using the methodology they have used.

Q. "The calculation would, I believe, be impossible if they were using the methodology which I believe they did"?
A. Yes, I think that is true. It is not a terribly important point at that stage.

MR. LANGSTAFF: My Lord, if it would be helpful, I could ask Prof. Evans to demonstrate the concepts of confidence interval and the confidence limits and the

confidence level by using the overhead projector and a graph because, I confess for my own part, I found a graphical representation the easiest way of beginning to grasp the way that a statistician uses the concept.

MR. JUSTICE FRENCH: Yes, I would be grateful for help in this field, certainly.

Q. MR. LANGSTAFF: Professor, do you have a spare transparency and a marker?
A. Yes. This is not what I had come prepared to do.

Q. Can I ask you to draw, first of all, an X and a Y co-ordinate?
A. Yes.

Q. And can you show the sort of normal distribution curve that you might expect from data, given the random effects of chance?
A. I think you are asking me to do something that is not appropriate.

Q. I am sorry. In that case, would you like to explain graphically the use of confidence levels and intervals?
A. If you want me to try and explain the idea of the confidence interval on a relative risk, I will try and do that.

Q. Would you, please?
A. Right. If we have the idea that there is - we will draw in this direction relative risk, and it could be, particularly in regard to case control studies, also odds ratio, and the terms may be used interchangeably. We have the idea that, at this value of 1, if we are looking at, let us say, the effect of radiation or it could the effects of something else, that a relative risk of 1 means no difference. There is no risk associated with it. There is no benefit if we are thinking of it in terms of a treatment.

Q. Can I just interpose there? That would mean that, for every 100 cases you examined against 100 controls, you would expect exactly the same incidence in each?
A. You would expect the same incidence of disease.

Q. And so if it was....?
A. Well, no, wait a minute. You are talking now about cases as if they were people exposed. What you would expect to find is that, for every 100 people exposed to radiation and every 100 controls, you will find the same incidence of leukaemia.

Q. The same number of cases?
A. The same number of cases.

Q. And so it will be 1 over 1 or 5 over 5?
A. Exactly.

Q. And hence you get a figure of 1. Thank you.
A. What happens is that, if this value - we normally actually plot this on a scale which is asymmetric. So we plot this on a scale that, let us say, has 0.5 here, because that is a halving in risk, and we plot it on a scale that has 2 there because that is a doubling in risk because, in that way, they are symmetrical.

Another way of doing that would be to plot this on a logarithmic scale, which has exactly the same effect, and we plot things in that way.

Now, a particular study may find a relative risk, let us say, of 0.87, and I will say, even though I am not very good at it, that that is 0.87 at that point. That is what we call in statistical terms a "point estimate". We acknowledge that there is uncertainty in all that we do and that that uncertainty will be largely dependent on how many people we have studied. So we can then say let us look at a 95 per cent confidence interval on this relative risk and, just going by memory, it went down to 0.32 and up to 2.34 or something of that kind, and so we say that, although that is our best estimate of the risk, we think that other values within this range are compatible with it and, as they move further out, they become less compatible pro rata.

So that a value of 0.87 with this as a 95 per cent confidence interval is really very compatible with a risk of 1, pretty compatible with a risk of 1.4, still compatible with a risk of 2, but it makes it slightly less likely, and right out here we start to say it is less compatible. It does not mean that the risk is not out here. The risk could be out there and we have an unusual finding.

Similarly, it could be that we have a value out here that is very large and we have a confidence interval here that goes down there and goes up to some enormous value in that direction because, on this scale, this interval will be symmetric. It is not symmetric on the numerical scale because this 0.32 is only 0.52 below 0.87 - all right - and 2.34 is more than one unit above it. So the confidence interval is symmetric on this scale.

So we may have a very large relative risk here that just includes 1 and so, if it includes 1, we say that the difference is not statistically significant and, if it excludes 1, then it is, and so a risk that is just there, that is like that, is regarded as not statistically significant, whereas a risk that is there, virtually the same risk with a slight difference, ends up being less than 0.05 and some people believe there is a substantial difference between them and I do not.

Q. Let me just ask you a little bit more about that. The arrows on your graph show the band within which there may be compatible results?
A. Yes.

Q. And that is a band, is it, which is dictated by the percentage to which you wish to be sure of compatibility or the reverse, the incompatibility?
A. Yes.

Q. And you use the expression there 95 per cent confidence interval. Does that mean that the arrows you have drawn show the range within which you cannot be more than, if I use the expression, 95 per cent certain - I hope you use it for present purposes - that the result is incompatible with that which you have found? Let me rephrase that. By establishing a 95 per cent confidence interval, are you ensuring that what is beyond the limits of that interval is less than 5 per cent likely if chance alone is considered?
A. Loosely, yes.

Q. But there is a difference, if we were going to be strict in language about it, between the confidence limits and the confidence interval?
A. No, they are used interchangeably.

Q. They are used interchangeably, but the limits are the ends of the scale?
A. The limits are the end, yes. The limits are the two values and the interval is the range between, yes.

Q. And the confidence interval is arranged between?
A. Yes.

Q. When you use the expression 95 per cent confidence interval, you mean the interval which is established if you are looking for the exclusion of chance to a 95 per cent extent?
A. Yes.

Q. So that where the relative risk, the true relative risk, that you have drawn on your graph is 0.87, and you show us the range above and below, does that mean that you would expect 95 per cent of all results to fall within that range?
A. It is philosophically a little bit difficult, but what it means is that, if I were to do this study a large number of times, 95 per cent of the time I would include the true value within those limits and so I could, if you like, run a computer simulation of these results with various true values and I would find values that lay like this, like this, like this, like this, if I were to do it a large number of times, and I would find that the true value would be included within those limits 95 per cent of the time. 5 per cent of the time the true value would be outside those limits. So I might have a series of studies like that, ignoring this one down here for the moment, and it is very clear that values between there and there, values in that range, are compatible with all of the studies.

Q. Yes, and that would reflect, would it, that the greater the amount of data you have, the more certain you can be about the band within which the true result is likely to fall

A. Absolutely.

Q. The limit in such a case would be much narrower than where you have sparse data, when the limits have to be very widely placed.

MR. JUSTICE FRENCH: I think I have grasped it. Whether I shall retain it is another matter:

Q. Is there anywhere in the documents, or in any document that one can be confident of obtaining, an expression of what you have just illustrated which might be within general comprehension?

A. I think one of the good places is in Prof. Howe's report.

Q. I mean, I have seen exegeses on these lines, which have seemed to me to be clear, but I do not recall precisely where they were. You think Prof. Howe has a good one?

A. I think within those documents, my recollection is that Prof. Howe has some good descriptions. I think Dr. MacRae has some quite good descriptions.

MR. ROKISON: My Lord, I was going to suggest the first report of Dr. MacRae does explain this.

MR. LANGSTAFF: My Lord, I think that is right and, at the risk of self-advertisement, the opening itself has a passage which may be helpful.

MR. JUSTICE FRENCH: So let us consider MacRae, Howe and Hytner/Langstaff.

MR. HYTNER: Mainly Langstaff on that particular point. If it is any comfort to your Lordship, that is now about the twelfth time that I have grasped the concept of the confidence interval and limit. My Lord, at the moment I retain it, but the other 11 times, my Lord, it went!

MR. JUSTICE FRENCH: I will have a look at those again, thank you.

THE WITNESS: May I be allowed to remark that I am terrible grateful for your remark about diminuendo. It explains, I think, why so many of my medical students have difficulty with that very thing themselves. I had never thought of it before. Thank you.

Q. MR. LANGSTAFF: Can I return you, Professor, to your reports and to page 32 of the Howe report?

A. Do you mean the McLaughlin report?

Q. Sorry, I beg your pardon. You are quite right, the McLaughlin report. We dealt, I think, with the second

and the third paragraphs under F3 and you told us the power of the study and your view that that study was, nonetheless, possibly compatible with the Gardner findings. You say, at page 3 of your fourth report....

MR. JUSTICE FRENCH: Before we move on, I just want to make sure. Yes, the answer that you have just referred to - correct me if I am wrong, Mr. Langstaff - is that 1.4 is, therefore, well within the bounds of compatibility with the Gardner study.

MR. LANGSTAFF: My Lord, I thought I had also gone on from there to ask Prof. Evans about the higher risk category. Certainly I had intended to and, if I have not done so, let me ask him again.

MR. JUSTICE FRENCH: You go on to say, McLaughlin, page 19 and Table 9 gives a confidence interval of 0.237. This is for doses of 50 mSv and greater. There is no line for 100 mSv and greater, and then there is an explanation as to why there is no such line, so I have not recorded the answer you have just summarised

MR. LANGSTAFF: My Lord, let me put it again in case it is my recollection that is in error:

Q. Do you regard a risk of 7.6 or greater as being incompatible - sorry, let me rephrase the question. On the basis of the information provided by the McLaughlin study at page 32, did that study have sufficient power to detect the relative risks that you discovered on your re-analysis of the Gardner data?

MR. JUSTICE FRENCH: On the basis of the information provided by the McLaughlin study at page 32, the study did/did not have the power to detect the relative risk....

MR. LANGSTAFF: Produced by your re-analysis of the Sellafield data.

MR. JUSTICE FRENCH: Is this Gardner or Gardner re-worked or Gardner re-worked with the....?

Q. MR. LANGSTAFF: Let me ask you in relation to each of those. We will come to the exact figures in a moment or two, when I think it will be plainer. So far as your analysis on all data, the most complete data, on the agreed dose figures?

A. I think that I would want to remind people that each of the studies done has some uncertainty in them and that, if we emphasise those point estimates and say are the data compatible with a particular point estimate in another study, we have to remember that that study also has some uncertainty. However, if we say that the most recent re-analysis of all the data - and what I think is our best estimate of the effect at Sellafield is on page 11 of my third report. Table 17 has a value of relative

risk for above 100, greater than or equal to 100, of 6.8 for local controls and total preconceptional dose.

A Q. In relation to area controls, that is Table 19, I think?
A. And that is 6.46.

Q. Those risks being less than 7.6. What follows in relation to the power of the McLaughlin study to detect risks of the magnitude that you show in those tables?
A. The power is likely to be down towards 70 per cent.

B Q. MR. JUSTICE FRENCH: So, "On the basis of the information provided by the McLaughlin study at page 32, their study did have the power to detect a relative risk produced by my analyses at Tables 17 and 19, but only to 70 per cent"?
A. About that. I have not done the arithmetic, but that is....

C Q. "My analyses at Table 17, page 11 of Evans 3, but only to a power of about 70 per cent." Is that right?
A. That is correct.

Q. MR. LANGSTAFF: In layman's language, perhaps stating the obvious, that means that, in three cases out of 10, it would not detect such a level; in seven cases
D out of 10, it would?
A. That is right.

Q. The Gardner paper itself - I do not ask anyone to turn to it, but I will remind you of the relative risks shown by it once I have found my own copy of it....

MR. JUSTICE FRENCH: Are we going to Gardner or
E not?

MR. LANGSTAFF: My Lord, I do not think it is necessary for your Lordship to turn it up. I shall, I am sure, be corrected if I get the figures wrong:

Q. The relative risks for a total dose before conception of greater than 100 mSv was given as 6.42 in relation to
F area controls and 8.3 in relation to local controls. That is both leukaemia and NHL and, in respect of leukaemia alone, the relative risk is given as 6.24 in relation to area control and 8.38 in relation to local controls.

MR. JUSTICE FRENCH: Need I write that for the
G purpose of your question?

MR. LANGSTAFF: My Lord, I think not:

Q. It would follow, would it, that the McLaughlin data would be more than 80 per cent likely to detect the results shown by Gardner in relation to one set of controls, area controls, and about 70 per cent likely to detect the
H risks in relation to the local controls?
A. I think you may have that the wrong way round.

Q. Yes, I think I have. Let me put it this way then: that in relation to one of the relative risks produced by Prof. Gardner for the highest dose categories, there
A would be a greater than 80 per cent likelihood of detecting such an effect; for the other, about 70 per cent?
A. Yes.

Q. You say in your fourth report, and this is returning then to your fourth report, that:

B "A more informative comparison would be to compare regression slopes for the two studies."

A. Yes.

Q. "If this study had carried out such an analysis the two slopes may well have been consistent with each
C other."

You go on then to say, as you have pointed out before:

"....the regression slope analysis is a far better way of considering trend than categorisation into different dose groups. In calculating the power of the study to detect the risk in the Gardner study
D McLaughlin et al have used the same dose categories. In doing so they have assumed that the dose distribution within the high dose category is similar to that in the Gardner study and it may not be."

Professor, I am going to ask you, if you would not mind, to return to the overhead projector and to explain to us
E what is involved in regression slopes?
A. What I am going to do is talk about regression in the context that we usually use regression, and I am now going to use overheads that, I believe, Mr. Rokison has copies of.

Q. Professor, before you begin with your telling us of these regression slopes, can I ask you a few questions to put
F it into the context that I might be more familiar with, and it may be helpful as an introduction to your telling us of regression slopes. Where you have results shown by a study, comparing two variables, you will end up with a random scatter of points which can be plotted. Is that fair?
A. Yes. It is not always random, of course.

G Q. And you are here showing us a plot of blood pressure as against age in years?
A. That is right.

Q. That scattergraph would indicate that somebody just under the age of 20 years was examined and found to have a systolic blood pressure of about 118, somebody at the age
H of 40, 120, somebody at 70 had 180, and throughout the range there are random results?

Q. MR. JUSTICE FRENCH: The systolic being the upper level?
A. The systolic being the upper level.

A

Q. MR. LANGSTAFF: If you wanted to know whether there was a correlation between age in years and systolic blood pressure, if the older you are the more likely you are to have higher blood pressure, for whatever reason, simply having points on a scattergraph would not give you the information very clearly, would it?
A. No, it is not sufficient to just look at the points.

B

Q. The ideal would be to draw a line if one could to demonstrate the relationship?
A. Yes.

Q. Is it right that you could draw a line by eye, looking at those points, and you would end up with something like that? Would that be an accurate way of doing it?

C

A. It would in some circumstances be quite a good way of doing it but it is not very reproduceable and you would not get agreement between different people doing it.

Q. In some cases, if it were a case of the miles travelled against the cost of a ticket, and if you knew that the transport authority charged 10p a mile, there would be a pretty obvious straight line?

D

A. The points may well lie exactly along the straight line.

Q. But where there is not such an exact correlation you cannot expect the points to lie on a straight line?
A. No.

Q. Can you demonstrate how you would go about mathematically establishing the straight line?

E

A. What we usually do is that we have the idea that if we draw a particular line that the points will obviously vary from that line, and we are interested in a sense in trying to predict what we would expect somebody's blood pressure to be, given their age, so we are interested in saying, "If you are aged 60 we may well expect that your systolic blood pressure is likely to be 162", or something of that sort.

F

Q. Of course, you would need to know that in order to detect whether they were unusually high or unusually low, and what clinical consequences may follow?
A. You may be wishing to do that as a standard or in some instances to find out whether there is a relationship. We then say, if we look at the deviation of these points from the line, some of them are above the line and some of them are below and in mathematical terms these have a positive deviation from the line and these have a negative one. We then add up all those deviations having squared them to get rid of the negative sides.

G

Q. MR. JUSTICE FRENCH: I do not understand how squaring something gets rid of a negative?

H

A. When we multiply minus 1 by minus 1 we obtain plus 1. A way of looking at that, that is obviously again in itself a difficult concept, multiplying minus 1 by minus 1 leads to plus 1, but a way of looking at it is imagining, if I change my scale here that this is nought and here is plus 1, that, if you like, when I am saying that I have got minus 1 I am doing something in the opposite direction. So if I go to another overhead to try and explain that particular point, though I do not think it is a vital one, if we have a number scale here and here is nought and there is plus 1, and we accept the idea that minus 1 is just there, we can say that going from this point we are going in the other direction. So if we have minus 1 and we multiply it by minus 1 it is a bit like changing direction twice, so that we go from here, we change direction when we go negative, and then we change direction and go back again to be positive, so a negative times a negative is positive. It is a bit like saying to somebody, "About turn", "March one pace, about turn", and that is negative. So when we multiply minus 1 times minus 1 that equals plus 1.

Q. Judges sometimes remark in these circumstances, "I hear what you say"! (Laughter)

Q. MR. LANGSTAFF: Perhaps a simplistic ....
A. I do not think that it is a key point to the argument. The really key point, if I may, is that mathematically then we are able to obtain ....

Q. Can I just ask you to hold there for a moment, Prof. Evans, and can I ask you a few supplementary questions? Is perhaps a simple way of putting it, I hope not too simplistic, to say that where you are working out the deviation of points from a line that if you are to make sense of the line mathematically you need to lessen, so far as you can, the total deviation of the points from the line, to fit the line as best you can to the points?
A. Exactly.

Q. And for that purpose it does not matter whether you have minuses or pluses, and minuses would only complicate the matter mathematically?
A. Yes. The point is that we need to have some arithmetical way of obtaining a line that is as close as possible to all of the points and this way, we call it least squares, is one of the ways of doing it.

Q. I was going to ask you, we see sometimes in the texts of various of the reports that we look at, we hear of the method of least squares, and that is ensuring mathematically that the distance between the individual points and the slope that you draw is as little as possible?
A. Yes.

Q. Least has an obvious interpretation and squares is simply because mathematicians in order to work out the

distance use the squares of the value to avoid the minus signs?
A. That is right.

Q. MR. JUSTICE FRENCH: Can I put in a question here which might assist me if I get the answer I hope for? Is another way of looking at it, I appreciate perhaps a workmanlike way rather than one acceptable to a mathematician, is what one is seeking to do with one's regression slope to strike the average of the variables but trying not to be diverted by wild cards, as it were, by wild variations? Does that express the concept at all?
A. Yes. The problem with least squares is a wild observation can affect it when there are small numbers.

Q. So you do not try to avoid your wild deviant?
A. No, you try to take all of it into consideration.

Q. Is what you are seeking to do to strike an average, a line which accommodates the average between the various points?
A. Absolutely. We are looking at the average blood pressure at ages but we have not just divided them into those between less than 20, 20-40, 40-60 and 60-80.

Q. So as a working concept the way I put it will do?
A. Yes.

Q. MR. LANGSTAFF: Can you tell me this, suppose for the moment, Professor, that there was absolutely no correlation between the two variables that you were examining?
A. You will end up with a horizontal line.

Q. So if it was the price of teabags in Moscow compared to the number of commuters from Kent, and you plotted them, if you were able to do so, on a graph, you would end up, you would expect, with a completely straight line?
A. I suspect so but I can envisage a relationship between them, if you wish.

Q. So the significance of a slope is that it shows there is, or the data indicates, a relationship?
A. Yes.

Q. Following on from that ....

Q. MR. JUSTICE FRENCH: When you are saying the existence of a slope, are you including or excluding a slope that looks like a zig-zag?
A. If you were to plot a line through all of the points exactly then indeed you would obtain a zig-zag but the usual assumption is that a lot of these points are showing some source of variability that may be measurement error, may also be variability because of individual characteristics ....

Q. Or whether somebody has just had a cigarette or whether they have just run upstairs?
A. Yes. You hope that you have measured everybody after they have sat down for ten minutes so that you do not end up with that sort of problem, but you simplify things and you usually simply draw a straight line. Occasionally you will find that it is not a sensible thing to draw a straight line but that is the simplest and that is where you will begin.

Q. It is still a regression slope if you finish up with a curve?
A. It is still a regression slope in some senses if you finish up with a curve. A zig-zag, no, but a curve, yes.

Q. The existence of a slope, which may include curve?
A. Which may include a curve.

Q. Indicates a relation between the variables?
A. Yes.

Q. A horizontal line indicates no relationship?
A. It indicates no straight line relationship. There could be a relationship such that they all lay on a circle, and if you then looked for a straight line through there you would have to draw a horizontal line because the points lay on a circle.

Q. MR. LANGSTAFF: But for all practical purposes ...?
A. For all practical purposes, yes.

MR. JUSTICE FRENCH: A horizontal line for all practical purposes indicates no relationship.

Q. MR. LANGSTAFF: You were going to overlay, I think, onto that succession of dots, a line and I was going to ask you, having got from you that the existence of a slope is indicative of a relationship between the two variables, I am now going to ask you about the measurements and coefficients of the slope. Can I first of all ask you this in general terms: if you have a slope does the degree of slope in fact matter?
A. The degree of the slope depends on the units that you have measured it in.

Q. Just by way of example ....

Q. MR. JUSTICE FRENCH: The degree of the slope depends on the units of measurement?
A. That is right.

Q. MR. LANGSTAFF: On the example which is on the board at the moment, if instead of taking age in years you substituted age in months and each of the intervals at the bottom of your graph were months instead of years, your scale at the bottom would be 12 times - I am sorry, I was going to say 20 months, 40 months, 60 months and so

on - your points would then be plotted much wider apart and the slope would be very much less steep?
A. Yes.

Q. So it really is a function of the intervals that you use either along the horizontal or the vertical axis as to what steepness, if I can use a layman's term, your slope will have?
A. In virtue of its numerical form, yes.

Q. In order to express the coefficient of a particular slope how do you go about it?
A. What we simply do is say, how far along here do we need to go, we can calculate the slope by looking at a difference between this point and this point and saying we have gone along 40 units and gone up 38 units, and so our slope then is 38 over 40, which is 0.95, and that is how we get this particular number. So the interpretation of that is that your blood pressure on average goes up with 0.95 of a millimetre for every year of age.

Q. MR. JUSTICE FRENCH: First of all, I may think I know what coefficient is but I would rather be confident. Would you tell me what a coefficient is?
A. The slope is also termed the regression coefficient and what we say there is, this is the change in blood pressure for one unit change in age, and here where we have measured age in years it means for the change of one year in age. Had we measured it in months this coefficient would have had a value that would have been one-twelfth of that and it would have been the change per month. So it is just the change in blood pressure per year change in age.

Q. Yes, I can see that is the practical result of applying the label "coefficient" to that exercise but at the moment it does not help me to understand what a coefficient is viewed as a concept?
A. Coefficient is something that you just multiply something else by.

Q. A coefficient is a unit?
A. It is something like the cost of living index; that is a coefficent.

Q. MR. LANGSTAFF: Professor, instead of a unit you might use the word "number", I think, mightn't you? It is a number?
A. It is a number which we multiply something else by generally.

Q. MR. JUSTICE FRENCH: By which something else may be numbered, or is numbered?
A. Is multiplied by it; that is usually what we refer to a coefficient as.

Q. By which something else is multiplied.

Q. MR. LANGSTAFF: In order to produce a measure?
A. In order to produce a measure.

Q. MR. JUSTICE FRENCH: E.g., the cost of living index?
A. Yes. So we might multiply the cost of living index by the salaries of professors one year ago, to try and obtain the estimated salary of professors this year. We might be disappointed! (Laughter)

Q. I was going to suggest the massive amount of the increase! So in the example you are giving the coefficient which gives the change in blood pressure for the unit change in age, that coefficient is 97 plus 0.95?
A. No, it is just the 0.95 is the coefficient.

Q. MR. LANGSTAFF: Can I get you to explain the 97? Blood pressure must start somewhere because anyone alive has some blood pressure, so no matter how young you go there will always be some blood pressure?
A. Yes.

Q. And in order mathematically to describe a straight line you need to know two things, I think, first of all where you are starting from and then the degree of slope of the line after that?
A. That is right.

Q. MR. JUSTICE FRENCH: You can go down to the 60s? I mean some athletes go down into the late 50s, don't they?
A. Yes. I would not wish you to draw too much from this particular diagram, used for teaching purposes. It is usually used for an audience of young medical students where I am the oldest and so the amusement is usually in the other direction! You are quite right, systolic blood pressure for some people is in fact really very low.

Q. Yes. I will take on trust the 95.

Q. MR. LANGSTAFF: So that figure for the blood pressure is simply the starting point and from that starting point you add so much per year?
A. Yes.

Q. It is 0.95, and you are given your coefficient 0.95 per year?
A. I would not wish this particular set of data to be used in evidence in the sense of blood pressure.

Q. MR. JUSTICE FRENCH: No, I understand it is purely a teaching tool?
A. Teaching medical students.

Q. MR. LANGSTAFF: Professor, when you are looking at the blood pressure and age in years, both are obviously measurable, blood pressure goes down and up, and so does age in years. If you are comparing the risk of getting leukaemia, or any disease for that matter, against an

exposure, it is likely, I suspect, that the exposure will be measurable in intervals but the risk of the disease is really only one of two possibilities, isn't it? You have either got the disease or you have not. Can you tell us how you fit this sort of analysis to a situation where you are not examining one of the variables, in terms of a range of possibilities, but only a yes and a no?

A. This is quite a difficult concept but in simple terms we can have something that may look like dose, and we then have disease, if you like, in this instance, classified as yes and no and we can, for arithmetical purposes, give that the value nought and that the value 1. So we can plot people who have varying doses along there, and then we can plot people who have got the disease with their doses along there. Though this looks a little strange, mathematically we can form a relationship that will have some sort of curved form of that kind. It will not be exactly a straight line because you cannot go out of the range there. You cannot have less than no disease and you cannot have more than yes of the disease, and we would then call this the probability of having the disease. So we would suggest that for a particular dose the probability that somebody has the disease is so much. The probability cannot fall below zero or go above one, so the curve that we have cannot be a straight line other than at perhaps some simple points, the whole range of doses.

Q. MR. JUSTICE FRENCH: Is that properly called a regression slope?

A. It is still called a regression slope and that is where we have the idea of what we call logistic regression, and that is a way in which we convert these numbers between nought and one into something that will then look like a straight line in certain circumstances.

Q. As you said yesterday, one must not get confused with, for example, military logistics?

A. Nothing to do with military logistics at all. It really ought to be called "log it" regression and then it would sound weird and convey its nature.

Q. Yes, and would also steer one away from a confounding factor?

A. Absolutely.

Q. MR. LANGSTAFF: You say, and here I am bringing you back to your report - you need not have it in front of you at the moment but the rest of us might like to have page 3 of your fourth report open, and you can leave the projector on for the moment - that a regression slope analysis is a better way, a far better way, of considering trend than categorisation into different dose groups. So you are considering an exercise done mathematically on the basis of the concepts you have been outlining as being a far better way than grouping. Why is that?

A. If, for example, I were to look at systolic blood pressure with age in years, then almost any grouping that I chose there would show a trend of blood pressure and age. I would find it very difficult to put the line in such a way that wherever I drew it I would find a trend. However, if I drew the trend, for example, just there I would find that the average for this group would be there, but if I had chosen the line, instead of just there if I put my line in a slightly different place, by including that point I could actually make my average value be a little bit less because this value, being lower than the rest, will alter the average there. So by judicious choice of the boundary I can affect the result. It may be that I do that with good intent or with bad intent, but I will end up with something that is partly dependant on where I happen to put the value. I could still do a regression analysis on the averages within those and I could look for a trend, if you like, between my three green points here, having set my boundaries there, and I could essentially do a regression line just using my new modified points, which are the group data, and that is analogous to the score test that was used by Prof. Gardner, given that he has a group. However, when you have small amounts of data it is rather better to use the original values and to use a full slope if you can, but the communication of that is usually a little more difficult to the ordinary audience.

Q. MR. JUSTICE FRENCH: What did you call Prof. Gardner's method?
A. He used in his ....

Q. What was the label you put on it?
A. Score test.

Q. Thank you. So you say regression is better than Gardner's score test?
A. Yes, though in most circumstances they will give you similar results.

Q. MR. LANGSTAFF: The score test you are referring to there is a reference to that which Prof. Gardner has given in his statement?
A. In his statement.

Q. MR. JUSTICE FRENCH: Yes. It is what in other circumstances I think we have been calling a categorisation of doses, isn't it?
A. It is a little more subtle than that. It is categorising the doses but then rather than just saying, is this value raised above the lowest value, which is just looking at the relative risk in that group alone, it is saying, is there a tendency for relative risk to rise with doses within those groupings. So that is better than just concentrating on the high dose group, the greater than 100 mSv group.

Q. So grouping would be a better word to choose than category?

A. Grouping would be a better word to choose but there is a way of analysing the data where you just look at the data in groups. The next best method is to look at the data in groups and see if there is a trend, but I would contend with sparse data the best method of analysis would be to look at a slope, a regression slope, using all the individual data.

Q. MR. LANGSTAFF: Let me ask you about that which you then say at page 3 of your fourth report. I remind you of your words, and you may be able to demonstrate this for us. You say, having said the regression slope analysis is a far better way of considering trend than categorisation into different dose groups, you say this:

> "In calculating the power of the study to detect the risk in the Gardner study McLaughlin et al have used the same dose categories. In doing so they have assumed that the dose distribution within the high dose category is similar to that in the Gardner study and it may not be."

Can you explain to us what you mean by that?

A. If I group people by age there I could have an age group, and I am going to say that that happened to be aged 55 for the moment, but if I group people above age 55 and I have a particular group of people, it could be that the majority of those people in one particular grouping were between 55 and 60 and only very few under 80; whereas another group of people, there might be only a few people between 55 and 60 and a large number of people over 80. The group labelling would still remain the same. If I were to try and say what their average risk was it would depend not just on the genuine relationship of age with the systolic blood pressure, but also on whether most of those aged over 55 were close to 55 in which case the average would be down here, or whether I was dealing with people in an old folks' home, shall we say, and the average age was much closer to 80. Therefore, the same group may have an average blood pressure that is just <u>there</u> or just <u>there</u>, depending on the age distribution that I have <u>there</u>.

Similarly, with dose distribution. If I have a category that says "over 100 mSv", it depends on whether there are just one or two sitting close to just over 100, or whether they go out from 100 to 150, 200, 400 and so on.

Q. MR. JUSTICE FRENCH: Why is it you can use the word "category" and I can't?

A. Because I use "group" and "categories" in interchangeable ways and you are more precise, my Lord! In this instance!

Q. MR. LANGSTAFF: Before we leave this can I, at the risk of howls of protest, complicate the matter a little

further? In due course when you come to tell us the results of your own re-analysis of Prof. Gardner, you not only provide us with the coefficients of the slopes, but you tell us that those particular slopes have certain p values. I am going to ask you about what gives a particular slope a particular p value. Let me ask you in this way: going back to the example I used earlier of mileage against cost in a transport authority where there is a price per mile which is applied consistently, you would expect most of the fares for the distances travelled to fall on or about the straight line. Maybe someone travelling one and a half miles would pay for the two mile ticket and so there may be a little variation over and above the line.

In such a case you would have a straight line indicating the correlation between distance travelled and the price of travel, but you would still have one or two points a little above and a little below the line?

A. Yes.

Q. To a layman it might be suggested that you could plot any distance along one of the co-ordinates and be able to estimate the price with virtual certainty simply by reading off the straight line graph?

A. Yes.

Q. Would that be the same as saying that that line had a low p value?

A. That would have an exceedingly low p value.

Q. To what extent does the p value depend upon the degree of variation of the individual points that you plot on your scattergraph and the line you attempt to draw between them?

A. It makes a good deal of difference. The larger the variation the larger the p value would be.

Q. Larger p values are less certain. Smaller p values are more certain?

A. That's right.

Q. MR. JUSTICE FRENCH: The question was: what gives a slope a p value? Answer?

A. Answer: three things. Number one, the variability. So in the railway example there is very, very little variability about the line, the points all lie on the line. The more the variability the more the p value. It goes up from 0.001 to 0.2 to 0.4 and so on.

Q. This is still item 1, is it?

A. This is still item 1. As variability increases so the p value itself increases and its significance decreases. The second item, and perhaps the most important one, is the sample size.

As the sample size goes up the p value - everything else remaining the same - will come down. Other things being

equal, if we had a certain set of rail fares and distances we would need a rather smaller sample size to show that there was a relationship between rail fare and distance to travel, than we would between age and systolic blood pressure where the scatter of the points around the line is rather greater. So age and blood pressure we will need a reasonably large number of points before we become convinced there is a genuine relationship.

Q. Yes. Number 3?
A. The third one is the size of the slope.

Q. By "size" you mean length rather than degree?
A. No, I mean degree.

Q. You mean degree? I thought you could juggle the degree simply by altering the numbers?
A. Every time I juggle the degree I would juggle the units I have got measured by variability. So it is degree and variability measured in the same units. I put all three of those things into a formula and then at that point it doesn't any longer make any difference what the units are.

Q. Three is the degree of the slope?
A. Three is the degree of the slope, and so thought that may change when I change age in years to age in months, so my variability of this, relative to the line, will also change.

Q. The p value is the probability of it being a true relation?
A. Yes. Strictly it is the probability of getting a relationship this big when the true one is zero.

Q. Is the probability of finding the slope in fact produced?
A. The probability of finding the slope in fact produced when the truth is there is no relationship.

Q. Or to express it slightly differently, the improbability. Is it the odds against or the odds on?
A. It is the odds against, yes. It is the improbability.

Q. So it is really improbability?
A. Yes.

Q. MR. LANGSTAFF: Professor, you can return to your report. We dealt with the McLaughlin study, now let us turn and look at the second of the studies additional to those which you considered in your first report, produced since Prof. Gardner, and this is the one which is produced for the purposes of these proceedings by Dr. Wakeford in a draft form, and annexed to his report.

MR. JUSTICE FRENCH: Is this covered in Evans's report?

MR. LANGSTAFF: It was covered in the fourth report, my Lord. It is called "Parker et al", page 3.

Q. What I would like to do, if I may, Professor, is to take you to the preliminary draft of the report, which I think is annexed to Dr. Wakeford's report.
A. It is a statement of Dr. Wakeford.

Q. Yes, I think that is the same as the report. For practical purposes there is no difference. If you turn to the back of that you should find a document headed "Preliminary Draft".

MR. JUSTICE FRENCH: At the very back?

MR. LANGSTAFF: My Lord, I think it is. I may not have the report in quite the same form as your Lordship has it.

MR. JUSTICE FRENCH: Yes, the very back document is "Second statement", but I think it is the penultimate.

MR. LANGSTAFF: It is between the two, I think. Mine is in the same typeface. My Lord, there is no secret about this. It is a report that has come in, as inevitably happens, a shade late in the day, and I have it in the same typeface, therefore, as the statement from Dr. Wakeford, but your Lordship should find something which is headed "Preliminary Draft" and underneath that, "12th November, 1992."

Q. Professor, this is a preliminary draft dated 12th November, 1992, of a paper written by Louise Parker and others; amongst them Dr. Wakeford?
A. Yes.

Q. And that is what you are looking at?
A. Yes.

Q. Its subject is "Childhood leukaemia and occupational radiation exposure: the geographical distribution of preconceptional radiation exposure associated with fathers employed at Sellafield Nuclear Installation, West Cumbria for births during 1950 to 1989." The paper deals, by way of introduction, with Sellafield and its particular position and Seascale on page 2; page 3 with the causes of childhood leukaemia:

> "Ionising radiation is an established cause of childhood leukaemia, but this, and other known causes, can account for less than a quarter of all incident cases. Several etiological hypotheses...have been proposed to account for the majority of cases, including it being the result of an infection which is especially effective following the mixing of previously isolated communities, and the unusual immunological response to a delayed exposure to antigens. Clearly the proximity of

> Seascale to the Sellafield nuclear installation has excited much speculation as to the relationship between the Seascale childhood leukaemia cases and radiation exposures arising from the operations at the installation."

It deals with Black and COMARE and on page 4 it turns to the Gardner report and cites at pages 4 and 5 what the Gardner report says.

A. Yes.

Q. Then the central paragraph on page 5:

> "This paper explores this implication..."

That is the Gardner hypothesis:

> "...further by examination of the geographical distribution of this putative risk factor for childhood leukaemia (ie paternal preconceptional radiation exposure) in Cumbrian children born between 1950 and 1989 to fathers employed at Sellafield, using a database assembled for that purpose."

It then deals with the data and the methods:

> "A database of the Cumbrian children of Sellafield employees, born during 1950-1989 was compiled. 1950 was taken as the start of the period of interest since it was then that nuclear operations commenced at Sellafield."

At the top of page 6:

MR. JUSTICE FRENCH: If that is strictly correct, isn't that when the piles were under construction? They started in 1951? Or have I got that wrong?

MR. LANGSTAFF: My Lord, yes. It was 1951/52 that the piles went into production.

MR. JUSTICE FRENCH: Pile 1, 1951; pile 2 1952?

MR. LANGSTAFF: My Lord, yes.

MR. JUSTICE FRENCH: But I need not worry about the one year?

MR. LANGSTAFF: My Lord, that is what they did. They took 1950 as the starting date. My Lord, I am told that nuclear operations - Mr. Rokison has been kind enough to say - were built up to during 1950, may have started during 1950, although the first pile wasn't in production until 1951.

MR. JUSTICE FRENCH: Was there radiation before 1951? That is what is important.

MR. LANGSTAFF: My Lord, may we come back to that? We may be in a position to tell your Lordship the definitive answer after the short adjournment:

Q. The top of page 6:

> "All children born in the geographical region currently defined by the county of Cumbria (except for xxxx for the period 1974-1989, which was in Cumberland up to 1974 but is now in Yorkshire and has approximately xx births per year) during the period 1950 to 1989 were identified by means of the live birth register..."

So all children born identified. Then the next paragraph notes:

> "The majority of births of the children of the Sellafield workforce...would have taken place in West Cumbria, although a number will have occurred in the remainder of Cumbria and the compilation of the birth register for the greater area would maximise the identification of children with Sellafield-employed fathers."

The third paragraph:

> "All information...entered into a database constructed for the purpose at the University of Newcastle..."

Then it sets out the computer system used and the fourth paragraph:

> "The residential address at birth of the mother of each child, as reported on the birth certificate, was postcoded..."

Page 7 sets out the link between Sellafield employees and Cumbrian born offspring as recorded in the birth register. It records that only three men opted out and in the last paragraph on that page:

> "Each person employed at Sellafield by BNFL or the UKAEA since 1950 has been given a unique works number and this as well as their name, sex and employment dates, and in some instances a residential address, is included in a computer database (the Personnel Datafile) held by BNFL at Sellafield for epidemiological purposes...It was this Personnel Datafile, as it existed in 1988, that was used by Gardner et al to link case and control fathers to employment at Sellafield."

At the top of the next page:

> "The Cumbrian-born children of Sellafield employees were identified by linking the parent details from

the birth register with the employee details held in the Personnel Datafile and employee dossiers."

It sets out the stage of the matching procedure. We can go to page 9, dealing with the chase-up of information. The third paragraph on that page:

"A validation of the matching process was performed in which postal questionnaires were sent to 1,000 current and 1,000 past Sellafield employees...The questionnaires enquired about the date and place of birth..."

The bottom of the page deals with the radiation doses which were used:

"Annual external whole-body ionising radiation dose summaries were accessed for all workers who were identified as being fathers: those who had been positively matched to a child on the Cumbrian birth register. Dose summary were obtained from the BNFL computer database which is maintained for epidemiological purposes. The dose summaries include radiation doses recorded while employed other than by BNFL and/or the UKAEA at Sellafield. These annual dose summaries are the only dose data which it is currently practicable to use for such a large number of individuals, and the database has been audited, on a sample basis, by the National Radiological Protection Board. This database, as it existed in 1988, was used in the study of Gardner et al."

A. Yes.

Q. Let me interpose there. When you had a database for the purposes of your re-analysis of Gardner, was that identical to the 1988 database that Gardner had first used?

A. I am led to believe that the doses have been re-calculated and in addition some linkage information between the file of doses and Gardner's data had been brought up to date and improved.

Q. Radiation doses received by fathers were calculated and it sets out why and notes that those were the two periods used by Gardner and determined for part years by directly proportioning the relevant annual doses as Gardner did, and categorising doses in the same way as Gardner used, using the four bands: 0, 1-49, 50-99 and over 100. Page 11:

"The collective paternal preconceptional doses for any particular areal unit were calculated by summing the total and 6 month paternal preconceptional doses, respectively, for all those matched children located (by maternal residential address at birth) within that areal unit. Children of the same father were located separately. The geographical

> distribution of those doses was generated using the mapping package ARCINFO running on a SUN sparkstation. In particular each Sellafield employee-child pair was allocated to either within or outside Seascale civil parish depending on the location of the grid reference of the maternal residence at the birth of his child. Digitised boundaries for civil parishes...were obtained from Ordnance Survey. Maternal residential address at the time of the birth of the child was a matching parameter in the case-control study of Gardner et al, and was used to locate geographically paternal preconceptional dose.

So by "collective paternal preconceptional dose for an areal unit", what do you understand the study to have been doing?

A. The study is grouping units and saying what is the average dose within each of those units, by geography.

Q. The "Results":

> "The Cumbrian birth register contains details of approximately 270,000 live births registered within Cumbria over the 40 year period 1950-1989. 15,308 of these children were inked to xxx males employed by BNFL and/or the UKAEA...The children of the Sellafield workforce were born throughout West Cumbria, as can be seen in Figure 2."

Let's just have a look at Figure 2. It is three pages from the back of this particular report. It shows a map of that which you recognise as West Cumbria, surrounded on the left hand side by white which is the sea and on the right hand side by a line which indicates the boundary between West Cumbria and the rest of Cumbria or Yorkshire, as it may be?

A. Yes.

Q. If you keep your finger in Figure 2 and turn two pages forward towards the front of the report, you see a more conventional map with the names of various places on it that we can recognise?

A. Yes.

Q. The standard map, if I can call it that, the one with the names on, enables us to locate the existence of the heavy black dots on the map of distribution of births, does it not?

A. Yes.

Q. We can see where Seascale is located, just in from the coast, a black dot and a black square which, as it were, is cut diagonally along the coast line on that map?

A. Yes.

Q. The black square to the south, one single black square surrounded by various others, that is Millom?

A. Yes.

Q. If one goes north, north-east from Seascale, there is a black section of three squares in the shape of an inverted "L"?
A. Yes.

MR. JUSTICE FRENCH: North-west?

MR. LANGSTAFF: My Lord, yes. I am sorry, but my sense of direction was badly expressed there:

Q. That corresponds with Egremont?
A. Yes.

Q. Along the same line, roughly, north north-west the large black blob on the coast is Whitehaven?
A. Yes.

Q. Does it appear that the two black dots immediately to the north of Egremont on the diagonal are approximate to the position of Cleator Moor?
A. I presume so.

Q. So that would indicate where the greatest number of births during the period were, as we can see by the legend at the bottom left-hand side of the figure. May we go back then to the wording of the report at page 12:

> "The children of the Sellafield workforce," it is said, "were born throughout West Cumbria, as can seen in Figure 2, although the majority were born in the settlements to the north of Sellafield. Of those 15,308 children, 8,886 have a paternal total preconceptional dose, and 7,244 have a paternal 6 month preconceptional dose."

A. Yes.

Q. "So many child-employee potential matches remain outstanding," etc.

"Table 3," it says, "describes the geographical and temporal distributions of births to the Sellafield workforce and the associated preconception radiation doses."

Table 3, if I can just take you to that, is again towards the rear of the report and three pages in front of what one might describe as the political map of the area. There are three pages to it, the first Table 3 in writing:

> "The distribution of the numbers of births, collective dose (person Sv) and mean dose (mSv), between Seascale civil parish, West Cumbria Health District outside Seascale, and Cumbria outside West Cumbria, for Cumbrian-born children with fathers employed at Sellafield before conception, born between 1950 and 1989, and the breakdown into the

four decades 1950s, 1960s, 1970s, 1980s and various dose categories, for (a) total .... preconceptional .... dose and (b) 6 month .... dose."

A. Yes.

Q. So, if we look at Table (a), it is total preconceptional doses and we can see the three geographical groupings that the study has used - Seascale, in comparison with West Cumbria outside Seascale, in comparison with Cumbria outside West Cumbria; the doses, the number of births, the collective dose in person Sieverts and the mean dose measured in thousandths of Sieverts, milliSieverts, underneath.

So the procedure, as you understand it, is that the total preconceptional exposures of the fathers in each of the three areas were added together and that gives one a total collective dose in person Sieverts?

A. Yes.

Q. And "mean" is another word for "average", is it?

A. Yes.

Q. So we can see, by looking at the table, the total amount of preconceptional radiation given to fathers within an area and the average that each of those fathers would have received?

A. Yes.

Q. Back to page 12, summarising the results:

"The collective paternal total preconceptional dose associated with these children is 514 person Sv, a mean dose of 58 mSv per exposed...."

MR. JUSTICE FRENCH: Sorry, where are you reading?

MR. LANGSTAFF: Sorry, my Lord. It is page 12.

MR. JUSTICE FRENCH: Whereabouts?

MR. LANGSTAFF: Half-way down.

MR. JUSTICE FRENCH: Thank you. "The collective paternal...."

MR. LANGSTAFF: My Lord, yes:

"The collective paternal total preconceptional dose associated with these children is 514 person Sv, a mean dose of 58 mSv per exposed child,"

it says, but I think it means father of a child:

"The collective paternal 6 month preconceptional dose...."

MR. JUSTICE FRENCH: Sorry, can we pause there? I am not sure I have grasped the concept of 514 person Sv.

Q. MR. LANGSTAFF: Let me ask you, Professor, so we have it as your understanding and I am sure, if this is wrong, it will be corrected in due course by the author of the study. The expression "Sievert" we know of, I think, Professor?
A. Yes.

Q. And "person Sievert" is, I think, described in the report, is it?
A. Yes.

Q. What do you understand by "person Sievert", "so many person Sieverts"?
A. I am trying to find their exact use because it is not something that is generally used in the field in which I work. I am just trying to find the page in the report where they explain it and I think that is the best place to go rather than having me do it. I thought it was early in the report. I now cannot find it. It may be in the discussion, is it? Dr. Wakeford, an author, not able to find it either.

Q. I think you will find it in paragraph 16 of Dr. Wakeford's report itself?
A. That is right. Yes, it is in his....

Q. I knew I had seen it somewhere and I am grateful to Mr. Read for indicating.

MR. JUSTICE FRENCH: Did you say page 12 of Wakeford?

THE WITNESS: Page 7 of the preliminary bit of the report, Wakeford's own statement.

MR. LANGSTAFF: My Lord, page 7, paragraph 16.

THE WITNESS: So it is simply, as far as I understand it, if we have 10 people, the person Sieverts is simply the sum of all the doses that those 10 people have received. It is not in any way averaged. It is simply the sum of the doses there. So if we have 10 people in the locality, we add up all the doses that those 10 have received.

Q. MR. JUSTICE FRENCH: I see how the exercise then is performed, but I do not at the moment see how it is useful?
A. I tend to share your view.

Q. Perhaps we will discover?
A. We will discover. I think it is most useful where you do not have individual data on individuals. You only have data on totals for a particular area and then, if you know the total dose and you knew totals, but could not

follow up what had happened to any individuals, then I can see that that can be very useful.

A

Q. Well, whether useful or not, it is the best you can do?
A. It is the best you can do.

Q. MR. LANGSTAFF: Perhaps you have answered it, but if you were examining a supposed link between radiation exposure and the likelihood of leukaemia or other malignancy in the children of those exposed, which would you regard as a preferable method of study - a method approaching it in this way or a case control study of those identified cases?

B

A. I think, if you are interested in particular risk factors, a case control study will be more useful than this sort of study.

Q. The report, just so that we can see what it says before I go to your more detailed comments upon it, page 13 summarises at the paragraph just above Discussion:

C

> "In summary, the fractions of collective total and 6 month paternal preconceptional doses associated with the births within the civil parish of Seascale between 1950 and 1989 are 7% and 6% of the respective collective doses for births in West Cumbria, reflecting the proportion of all births which occurred in Seascale (6%)."

D

Sorry, I am invited, and, of course, I do so, to read the bottom of the previous page. I did not read it, it is quite right. Let me do that so that we have that. The bottom of page 12:

E

> "The collective paternal total preconceptional dose associated with these children is 514 person Sv, a mean dose of 58 mSv per exposed child."

I think I read that, but did not go on:

> "The collective paternal 6 month preconceptional dose is 43 person Sv, a mean dose of 6 mSv per exposed" - again it says "exposed child. For the 819 children born in Seascale, the collective paternal total preconceptional dose is 34 person Sv (7% of the entire collective total dose), a mean dose of 48 mSv per exposed child. Similarly, the collective paternal 6 month preconceptional dose allocated to Seascale is 3 person Sv (6% of the entire collective 6 month dose), a mean dose of 4 mSv per exposed child. For children falling within the highest total and 6 month dose categories, 6% and 5% of the respective collective doses are associated with Seascale."

F

G

I have read the rest and dealing then with the Discussion:

H

"A possibly causal association between paternal preconceptional radiation exposure and childhood leukaemia (and NHL) was postulated by Gardner et al following their case-control study. ..... It was suggested that the excess of haematological malignancies in children in Seascale could be effectively explained by the radiation doses received by their fathers in the period prior to the case child's conception during the course of their employment at Sellafield. If this inference is correct then the geographical distribution of the putative risk factor for these childhood malignancies (i.e., paternal preconceptional radiation dose) would necessarily reflect the distribution of the disease excess, and be concentrated within Seascale to a substantial extent.

The results show that 6% of Sellafield employees' children were born in Seascale civil parish in the 4 decades from 1950. These births were associated with 7% of the collective paternal total preconception dose and 6% of the collective 6 month dose.

These proportions can be compared with the fraction of the putative excess risk which may be derived from the case distribution to be concentrated in Seascale so as to substantiate the suggestion of Gardner et al that the excess cases in Seascale are 'explained statistically' by their paternal preconceptional doses. Since it is an approximately tenfold case excess that is to be accounted for, then most, if not all, of the leukaemia (and NHL) cases born in Seascale must be attributable to these radiation doses. Of the" - and it says here "5" - "leukaemia cases born in Seascale, 4 are known to have a paternal preconceptional radiation dose. Consequently, these 4 cases (or, at a minimum, 3 of these 4 cases) must be attributed to their doses to account for the excess of leukaemia cases in Seascale. Similarly, the 1 out of 2 NHL cases born in Seascale who has a paternal dose record must be attributed to his/her preconceptional dose.

Of the 8 leukaemia (and 2 NHL) cases born and diagnosed in West Cumbria and known to have a paternal preconceptional radiation dose received at Sellafield, the relative risks given by Table VI of Gardner suggest that, overall, 5 leukaemia (and 1 NHL) cases might be attributable to these doses."

Thus, by subtraction, I think, leaving four:

"It would seem reasonable to attribute those cases with the highest doses to this putative risk factor, and this is compatible with the argument concerning the Seascale cases presented above.

> The geographical distribution of these excess leukaemia (and NHL) cases may be used to infer the proportion of the putative risk which would necessarily have to be located in Seascale to be consistent with the interpretation of Gardner. If 4 of the 5 .... leukaemia cases are from Seascale, then 80% of the excess risk...."

It appears to be talking there in terms of the excess cases over that which one would normally expect:

> "....due to paternal preconceptional doses would be assigned there...."

and it gives the confidence interval:

> "If 3 of the 5 attributable leukaemia cases are from Seascale, then 60% of the excess risk due to paternal preconceptional doses would be located there. Similarly, 5 out of 6 .... gives 83%, and 4 out of 6 .... 67%."

Then it says this, which I think may be the nub of the study:

> "These figures are clearly incompatible with the 7% of collective total, and 6% of the collective 6 month, paternal preconceptional radiation doses of West Cumbrian offspring of Sellafield workers being located within Seascale. Even if all 10 leukaemia and NHL cases with paternal preconceptional doses are assumed to be attributable to these doses, giving 50% of the excess risk assigned to Seascale, the marked incompatibility remains."

I do not think, unless I am asked to do so, that I need read on, except perhaps to take you to page 19, the second paragraph on that page:

> "This study has generated the group of all children born in Cumbria to fathers employed by BNFL and/or the United Kingdom Atomic Energy Authority at Sellafield and receiving an occupational radiation dose before conception, and has used the same, or very similar, pertinent sources of data as those used in the case-control study of Gardner. It has shown that the suggestion that the paternal preconceptional doses of children born in Seascale are sufficient to explain the excess of childhood leukaemia cases in the village is incompatible with the absence of any indication of a similar excess in the much greater number of children with such doses born outside Seascale.
>
> It is concluded that it is highly unlikely that the Seascale childhood leukaemia cluster is due to paternal preconceptional radiation exposure and this must cast further doubt on the directly causal

> interpretation of the statistical association between paternal preconceptional radiation exposure and childhood leukaemia reported by Gardner et al.
>
> The Seascale childhood leukaemia cluster remains an enigma."

Let me take you to what you say about that in your fourth report. Page 3, under the heading "Parker et al". First of all, you caution that it is an early draft and you would, therefore, be wary about making too much of it. Do I take it that that goes both in criticising it as much as in accepting it?

A. Absolutely, yes.

Q. You look at the quality of the data, and the first point I think you have already made, that the data, as far as you are aware, has since been updated. Can I deal with the next point? You say:

> "The study is incomplete in terms of the follow-up of leukaemia cases."

You note that the study relies entirely on cases identified by Gardner:

> "....in doing so excludes cases that may have been diagnosed outside West Cumbria and also those cases that have developed after the end of the time period examined by Gardner but are within the period examined by this study."

What is the point you are making there?

A. When you do a case control study, you are interested in ascertaining a set of cases and a set of controls who are as similar as possible and, in some senses, provided you have done the same thing to the cases as the controls, geography and other aspects do not matter too much. So Gardner is not really as interested in geography as this study should be. This study seems to be looking at things within certain areas and is looking at a geographical type of study that one could perhaps do from national statistics, although they have data on individuals, and I am a little confused at what their objects are. I can understand that they wish to try and undermine Gardner in it, but it seems a little strange approach and I still have not got my mind round this study fully. It is not a conventional way of approaching data.

Q. Then the top of page 4....

Q. MR. JUSTICE FRENCH: Could it be, Prof. Evans, that it is designed to cast light or darkness or whatever on an enigma within an enigma, which is why so many at Seascale?

A. Yes, I think that there is something of relevance in it. That is, that there are paternal high doses elsewhere in

West Cumbria, and high doses to other Sellafield employees, but....

Q. This is purely speculative on my part. Perhaps it is best to wait for cross-examination and then we will perhaps learn whither it is tending.
A. But one would have expected to say, "Let us look at all the children very carefully elsewhere." Rather than just looking at the Gardner case control studies, I would try and look at a different method of ascertainment of the cases, but it is not terribly clear.

Q. We will wait and see about that.
A. There are 1,000 current and 1,000 past Sellafield employees who had a questionnaire sent to them, but there is no mention of any response rate to those questionnaires or, indeed, any data from them, and that sort of thing makes me think it is preliminary and, therefore, I am hesitant in being too critical or accepting it either.

Q. Yes, it is labelled "Preliminary", is it not?

Q. MR. LANGSTAFF: If you look at your next comment upon it, so far as you can comment on a preliminary report, you note the use of grouped data as opposed to individual data?
A. Yes.

Q. You make the point, in the second sentence:

> "An analysis using individual data is to be recommended since grouping the data might mask a risk associated with preconception radiation exposure. One cannot predict what the results of the study would be if an analysis was carried out using individual data but on the other hand I am not convinced by the conclusions drawn by the authors from analysis of grouped data."

Why is that?
A. I think they have over-interpreted their data because they do not seem to have looked at the most powerful way they could have of looking at the individuals in that data. That is the basic problem. If you group person Sieverts and you look at the dose to an area and then say, "What has happened to it?" it is as if you were assuming that the same dose was spread over all the individuals in that area rather than looking at the individuals. While for a very important risk and for a disease that was fairly common, that might be a reasonable approach because the numbers that you would get might be very large - that would be the intuitive way that I have of approaching that - whereas doing it in this way, we are looking at something very rare and then we are spreading it out. We are apportioning the dose over a whole area rather than to the individuals and then saying, "What is the apparent effect?"

I think it provides some evidence - it undoubtedly provides some evidence - against the idea that preconceptional doses alone are the explanation within Seascale, but the idea that preconceptional doses has no effect....

Q. Stop there, Prof. Evans.

Q. MR. JUSTICE FRENCH: It provides some evidence that preconceptional doses alone do not account for the excess, but - I think you were going to say "but...."?
A. But they do not provide strong evidence that preconceptional dose is not important anywhere.

Q. What, as an element in aetiology?
A. As an element in aetiology.

Q. Yes, I missed out a verb. You said, "I think Parker et al have something their data"?
A. I think that they have dealt with their data and spread it around, I think was the....

Q. This was, I think, the very first phrase you used.

MR. ROKISON: The word was "over-interpreted", my Lord.

THE WITNESS: Over-interpreted, sorry.

Q. MR. LANGSTAFF: You were, I think, making the point, or beginning to make the point, which you address at page 4 (c) in your fourth report, where you deal with the conclusions that can be drawn from the Parker study?
A. Yes.

Q. You say you are not in agreement with them?
A. I am not in agreement with their overall conclusions.

Q. And then you go on to examine the incidence of leukaemia in Seascale, so far as it is revealed by this particular report, and you look at the numbers, I think?
A. Yes.

Q. "Professor Gardner's 1987 birth cohort study examines the incidence of cancer in the children born in Seascale. 1,068 children were born in the village between 1950-83. From the Parker report it is apparent that approximately 630 of these" - we have just seen the figure - "had fathers who received preconception radiation exposure. It is known that all the five leukaemia cases that were born in Seascale had fathers who were exposed to radiation prior to their conception."

You say:

"This means that the incidence rate of leukaemia amongst children born in Seascale whose fathers who

had worked at Sellafield prior to their conception is approximately 15 times the national average. By contrast," you say, "no leukaemia cases occurred in the remaining group of 438 children who were also born in Seascale but whose fathers were not exposed to radiation prior to their conception."

Let me just take you to those figures. 1,068 children, I think, are born between 1950 and 1983 and the Parker report takes you up to 1989, in terms of births, and so there is a further six years there. Were you able to estimate the number of children born in that period from any data?

A. I am sorry, I missed the thrust of your question.

Q. I was just asking you to explain this. 1,068 children are born up to 1983?

A. Yes.

Q. The Parker report takes you to 1989?

A. Yes.

Q. A further six years?

A. Yes.

Q. Are you able to say from any of the available data how many, or roughly how many, children were born in Seascale in those six years?

A. I cannot give you that straight off, no. It is a little bit confusing. Table 3 gives us the distribution of people who were employed at Sellafield.

Q. Yes?

A. But I do not think that they give us the distribution in those extra six years that I can recall, so I cannot tell you out of my mind what the number is.

Q. In any event, you are making the point, are you, there that the children who the study reveals to have leukaemia in Seascale, whose fathers had preconception doses, appear to be 15 times roughly more than average likely to have leukaemia and, if one examines those children of workers who were not exposed to radiation, there appear to be no leukaemias?

A. No.

Q. So, if you were going to draw a conclusion from those two facts set one against the other, what conclusion would you draw as to any significance of parental preconception exposure?

A. I still think that parental preconception exposure is likely to explain some of the increase in risk.

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

MR. JUSTICE FRENCH: Yes, certainly. Two o'clock.

(Luncheon Adjournment)

Q. MR. LANGSTAFF: Prof. Evans, if you return to your fourth report, page 5, we dealt this morning with the first of the reports additional to those that you considered in your first report and we now come to the last of the additional reports, and that is the report from Draper et al, 1992. You will find that, Professor, in the bundle P4 at page 30. Would you turn first to page 29, simply to note, I need not read it out, the second paragraph of the letter there sent out from the Childhood Cancer Research Group as to the use, for the purpose of the release of this draft of the report. It was with that in mind, Professor, that you have taken this report, looked at it and drawn some conclusions from it. Looking at page 30 of the report, we see the authorship of it, and at page 31 the abstract, the objective:

> "To reappraise the epidemiological findings reported by the Black advisory group concerning a possible excess of malignant disease, particularly of childhood acute lymphoid leukaemia together with non-Hodgkin lymphomas (NHL), in the vicinity of the Sellafield nuclear installation, and to determine whether any excess of malignant disease had occurred among persons aged 0-24 years in the area in the years following the Black report."

A. Yes.

Q. "i.e. from 1984 to 1990."

- seven years covered. Design and method:

> "Calculation of incidence rates using data from population-based cancer registries and special surveys."

It says the subjects, the outcome measures and then:

> "**Results** Previous reports of an increased incidence of cancer, and especially of leukaemia, at ages 0-24 years in Seascale during the period up to and including 1983, are confirmed. For the period 1984-90 there is evidence of an excess of total cancer for the age group 0-24 years. This is based on four cases: these include two cases of NHL but none of leukaemia."

A. Yes.

Q. "There is an increased, but non-significant, incidence of 'other cancers', based on two cases (one pinealoma ....

- that, I think, is a form of brain tumour, is it?

A. I am not an expert in that field.

Q. "... and one Hodgkin's disease) occurring in the upper part of the age-range (i.e. 15-24 years), in this period. This is not observed in the younger

age group or in previous years. For the immediately surrounding area, i.e. the county districts of Allerdale and Copeland, excluding Seascale, and in the remainder of Cumbria, there is no evidence of an increased incidence of cancer at ages 0-24 in either period.

Conclusions During both the periods 1963-83 and 1984-90 the incidence of malignant disease, particularly lymphoid leukaemia/NHL, in young people aged 0-24 in Seascale was higher than would be expected on the basis of either national rates or those for the surrounding areas. Although it seems that this increased risk is unlikely to be due to chance the reasons for it are still unknown."

While dealing with the dates, Professor, may I say that my information in relation to the 1950 date that was mentioned this morning is that it was October, 1950, that the piles became operational and plainly there would have been radioactive material present before October, 1950.

MR. JUSTICE FRENCH: Yes, but presumably not material itself under the influence of radionuclides?

MR. LANGSTAFF: My Lord, I think beyond saying that there must have been radioactive material emitting radioactivity ....

MR. JUSTICE FRENCH: Yes, the mere fact that it is there will emit some but presumably none through the stacks or any of the other sources with which we are familiar.

MR. LANGSTAFF: My Lord, they would have been testing it, I think, in 1950.

MR. JUSTICE FRENCH: So there might well have been some through the stacks.

MR. LANGSTAFF: There might have been some, through the pile stacks.

MR. JUSTICE FRENCH: Yes, pile stacks, I am sorry I keep saying stacks when I ought to be more precise.

MR. LANGSTAFF: I think, my Lord, the fairest thing is to say this is supposition on our part, it is a reasonable supposition, it would be unfair to say that this is a certainty - collectively we do not know but this is the best we can offer your Lordship.

MR. JUSTICE FRENCH: Yes, thank you.

MR. ROKISON: My Lord, if your Lordship wants more accurate information on that ....

MR. JUSTICE FRENCH: I only want it if anybody thinks it important. If it is agreed not to be important then please do not bother.

Q. MR. LANGSTAFF: Then I think the report deals with the introduction ....

MR. JUSTICE FRENCH: Just one moment, I am sorry, Mr. Langstaff - can I put Wakeford away?

MR. LANGSTAFF: My Lord, yes:

Q. Returning to the Draper study, page 32, it sets out the conclusions about the increased risk in Seascale being unlikely to be due to chance and then goes on to set out much of the material that we have become familiar with over the day-and-a-half. It sets out the "Methods" at the bottom of page 33:

> "... the analyses would cover both total malignant disease around Sellafield and also a number of individual diagnostic groups defined as follows ...."

and it sets out the diagnostic groups. One sees at (i) lymphoid leukaemia and non-Hodgkin lymphomas going together and other and unspecified leukaemias separately, Hodgkin's third, brain and spinal tumours fourth, and all other malignant diseases fifth, and it says:

> "Diagnostic group (i) was chosen in the light of discussions in the COMARE report on Dounreay ... together with the conclusion of the working group that acute lymphoblastic leukaemia (ALL) could be adequately distinguished from other leukaemia in the present data."

"Areas to be Analysed", bottom of the page:

> "(a) Seascale ward;
> (b) Allerdale and Copeland ...
> (c) Cumbria county (without Allerdale and Copeland)."

"Calendar Periods" is at page 35, the "Case Ascertainment" sets out the sources, "Population Data" sets out the source of that; at the bottom of page 36, "Incidence Rates", annual rates per million; page 37, "Comparisons with National Data" and then we get "Results" at page 38. "Cases of Cancer in Young Persons in Seascale since 1953", listed in Table 3 it says. Page 39, "Cancer Incidence at Ages 0-14, 1963-90", in Table 4, and 15-24, Table 5, and leukaemia and lymphomas in Table 6. Let us just have a look at those tables, if you would, Tables 3, 4, 5 and 6. Table 3 is on page 53. There one sees cancer among persons, giving their age at diagnosis from 1953 onwards, and the nature of the cancer under the heading "Diagnosis", which is the column third

from right, fifteen cases from 1953, setting out the various details. Table 4, and here, Professor, we come upon another statistical term, I think. The columns, if you look at Seascale Ward and the columns underneath Seascale Ward, we have first of all the number, and that obviously speaks for itself, the number of cases considered by the study. Then we have ASR - what does that stand for?

A. It stands for "Age Standardised Rate".

Q. How does one interpret a number such as that given in respect of 1984-90 at 511.2? What would that convey to a statistician?

A. That on its own conveys the fact that one has made allowance by age standardising for any difference in age distribution in the people who were living in Seascale Ward, in this instance the children.

Q. Can you explain why age standardising may be necessary to get valid statistics?

A. We know that the most important predictor in general of a death rate, notwithstanding our earlier graphs, is age, that as your age goes up your death rate on the whole also goes up, but also, as it happens, in regard to children, in the age group 0-1 death rates are very high, very much higher than at other times until much later in middle life. So a different distribution of ages within different areas would lead, just because of that difference in age, to different death rates. Age standardising attempts to remove any effect of a different age distribution in different areas.

Q. MR. JUSTICE FRENCH: Different, not geographical areas, but areas of research?

A. No, different geographical areas.

Q. MR. LANGSTAFF: So that you can make a proper comparison?

A. Exactly.

Q. MR. JUSTICE FRENCH: Age standardisation is designed to reduce - would this be a bias, a confounding factor, or what?

A. Yes, age would exactly in this instance be a confounding factor, and it is getting rid of age as a potential confounding factor.

Q. To reduce the confounding factor of age - is that sufficient to describe the function?

A. That is exactly it.

Q. MR. LANGSTAFF: How does one interpret a figure, an age standardised figure, of 511.2 in relation to the period 1984-90?

A. It suggests that for every million hypothetical children aged 0-14 who might be living in Seascale you would then expect to find, having adjusted for age, that if they had the same age structure as the rest of the United Kingdom

that 511 of them would have a leukaemia or non-Hodgkin's lymphoma for every year, so it is an incidence rate per year. This is the number of new cases in each year.

MR. JUSTICE FRENCH: You pick 1984-90, Mr. Langstaff. Is there any reason for doing that, as opposed to taking the first figure, 1963-83?

MR. LANGSTAFF: My Lord, yes, because that was the additional data this study looked at over and above that which had been examined by Gardner - Gardner, of course, not dealing with age standardised rates.

MR. JUSTICE FRENCH: I quite follow that, so what you are underlining is that this is a post-Gardner phenomenon?

MR. LANGSTAFF: My Lord, a phenomenon which continues.

MR. JUSTICE FRENCH: Yes, but post-Gardner?

MR. LANGSTAFF: That finding is, my Lord, yes.

MR. JUSTICE FRENCH: So let me note the answer:

Q. The figure of 511.2 indicates that per million of population aged - is it 0-14 or 1-14?
A. 0-14.

Q. 0-14, there will be 511.2?
A. That is correct.

Q. 511.2 leukaemias or NHLs per year?
A. Yes, though the 511.2 is a spurious accuracy.

Q. Yes, that figure may be challenged but that is what is suggested by the table?
A. Yes.

Q. And you are going to proceed to challenge it, are you?
A. No, I am just going to point out there is a lot of uncertainty in it and so saying 511.2 as opposed to 510 is a little bit over the top.

Q. So the figure of 511.2 indicates that per million of population aged 0-14 there will be 511.2 leukaemias and NHLs but the figure of 511 has uncertainties - what are you saying, which render such precision inappropriate?
A. Yes. I would not want you to try and make an emphasis on 511.2 as though that was the point. The point is that it is 500 and not 30.

Q. MR. LANGSTAFF: Are you saying that the importance is in comparative analysis?
A. The importance is to compare it with the rest of Cumbria and Allerdale and Copeland Ward.

Q. One can see dramatically how the areas alter in the incidence?
A. Yes.

Q. MR. JUSTICE FRENCH: The figure of 511 has uncertainties in it. A broader comparison, i.e. 500 as against 30, Allerdale and Copeland minus Seascale, would be more appropriate?
A. Yes, well, it is not that there is anything wrong with that. I was worried that you were picking on 511.2 as if ....

Q. I was only picking on it because it was there!
A. Because it is there, yes, but its precise value is not the important point.

Q. I will simply add that precise values are not of the essence?
A. Exactly.

Q. MR. LANGSTAFF: Can we turn to the text, where it deals with Table 4 - page 39 in the bundle - and see the summary of that comparative exercise in the second sentence:

> "The rates of malignant disease and, specifically, of lymphoid leukaemia/NHL for children in Seascale are substantially higher than those for the remainder of Copeland/Allerdale, Cumbria or England and Wales."

and, of course, England and Wales does not appear in the table but there we have it in the text, that that is the fact. I am sorry, Table 2 sets out England and Wales, where by comparison one can see that the age standardised annual incidence rate per million - this is page 52 - is 35.5 for 1969-83, and sadly increasing to 39.6 for 1984-87, aged 0-14, and a thankfully lower rate for those in the older age groups.

If I can return you then to the tables and ask you to go to Table 7 at page 57, the table of the "Observed Numbers of Cases at Age 0-24 in Seascale 1963-90 and Poisson Probability of Observed or Greater Number of Cases, Calculated from Estimates of Incidence Rates for England and Wales as given in Table 2" and here we see the likelihood of that number of cases being due to chance?
A. Yes.

Q. In 1963-83, five cases, lymphoid leukaemia and NHL in Seascale, one of other cancers, and the probability values, the P values, 0.816 for other cancers, 0.0242 for all malignant, and for lymphoid leukaemia 1.61×10^{-4}, so we would have to put a point and three noughts, then 161, would we?
A. That is correct.

Q. So it is a P value of 0.000161?
A. Yes.

A Q. A 1 in 10,000 or 1.5 in 10,000 chance of it being due to chance?
A. Yes.

Q. For 1984-90, the number of cases in Seascale, we see two lymphoid leukaemia and NHL and the probability under that, again expressed mathematically, 7.02×10^{-3}, so that would be 0.00702, would it?
B A. It would.

Q. And that would be 7 chances in 1,000 of that being a chance finding?
A. Yes.

Q. Similarly, for the number of other cancers within that period 8.5 - I am approximating - 8.5 chances in 100 of
C that being a chance result?
A. Yes.

Q. And for all malignancies again we would put two noughts in front of the three, 0.00335 and that would be 3.5 cases roughly in 1,000?
A. Yes.

D Q. The discussion in the paper, based on that data, begins at page 11, page 41 of the bundle:

> "Two principal questions are considered in this paper. First, do the findings of the Black report relating to the period up to and including 1983 remain unchanged now that more comprehensive data sets and analyses are available? Secondly, did the
E excess incidence of childhood leukaemia in Seascale found in the various analyses summarised in the Black report persist in later years? The present report covers the periods 1963-90..."

It sets out the children:

> F "...and 1984-90 for leukaemia and lymphomas in adults. As explained in the Introduction, the diagnostic groups, age groups, calendar periods and areas to be analysed were agreed in advance of the analyses being carried out.
>
> The conclusions of the Black report are confirmed insofar as they relate to malignant disease
G occurring in young persons between 1963 and 1983;..."

So up to the period covered by Gardner, there is a confirmation here of the conclusions of the Black report?
A. Yes.

H

Q. It goes on:

> "...on the basis of the six cases included in Table 3 we conclude that the excess in Seascale is unlikely to have arisen by chance."

Do you agree?
A. Yes.

Q. "All of the six cases are included in the report by Craft et al. As explained above, we have omitted from these analyses case 15 in Table 3, since this person had an address in another part of Britain which was regarded as his area of residence for the purposes of the National Cancer Registration Scheme. Inclusion of this case would have strengthened our conclusions concerning the period 1963-83..."

MR. JUSTICE FRENCH: Is that Edinburgh?

MR. LANGSTAFF: My Lord, no. That, I think, is Bristol.

MR. JUSTICE FRENCH: That is Bristol.

Q. MR. LANGSTAFF: For the purposes of this study Dr. Draper has excluded that particular case?
A. That is what I believe to be so.

Q. "For the period before 1984 our analyses rely on much the same evidence as the Black report, though more complete registration data are now available. There is, however, no way of overcoming the objection that analyses of Seascale data for this period are not amenable to any rigorous statistical evaluation because the area, age group and types of disease to be studied were selected as a result of the observed 'cluster'."

I think that is something which we may have touched on before. Is it a matter of importance when you are looking at the evaluation of the results of a statistical survey, that you should specify your study object in advance?
A. It is preferable to do so, without any doubt.

Q. Is it preferable to specify the groupings of data that you are likely to use in advance of having the data to group?
A. Yes.

Q. What is the risk if you have the data first and then choose your groups?
A. There is a risk that you will have over estimated, or at least found far too small, a P value for anything you then carry out an analysis on.

Q. Is this making the same point you made yesterday, when you said that what was - and I am paraphrasing - impressive from your point of view in considering the Seascale results were that they had been analysed in a number of different ways, in a number of geographical periods, from a number of different data registries by a number of different statisticians and produced similar results?
A. Yes.

Q. MR. JUSTICE FRENCH: Isn't the point which the writer of this paper is making this, isn't it referring to the risk you yourself mentioned of any set of doctors getting their heads together and finding an explanation or a connection between cause and a disease? Isn't that what this sentence is about?
A. Yes. I think in particular this sentence is about, shall we say, the media approach to things, where you notice something interesting and you look for every bit of evidence in favour of it and choose your boundaries in that way.

Q. Unless you are very rigorous and objective in your approach it is liable to affect the study?
A. Yes. When you said that it is liable to affect the study, I think it will particularly affect any P values that are calculated, that is the point. It has a dramatic effect, potentially, on the P values.

Q. Tell me if this is a proper way to express it? A preconception as to causal relation will affect P values?
A. Yes. If beforehand you have an idea, and you then go and collect data, that will be reliable. If, on the other hand, somebody has told you that there is an excess somewhere and you go along and say, "Ah, there is an excess there, let me look at the P value for that", that is a dangerous thing to place too much reliance on the P value. It doesn't mean there isn't a genuine excess, of course, but it may mean the excess was there because you already knew it was there. The fact that you knew it beforehand will affect your P values.

Q. Is the word "preconception" inappropriate? How would you alter it?
A. A prior hypothesis, having a prior hypothesis.

Q. The existence of a prior hypothesis is liable to affect the P value placed on any findings?
A. Yes, I am slightly afraid you have misunderstood. If you have a prior hypothesis and then, and only then, collect the data, the P value is reliable.

Q. Yes.
A. I was slightly worried that you were saying the prior hypothesis undermines the calculation of the P value. The prior observation of data undermines the P value.

Q. I don't think I am there yet.
A. Being very specific in regard to Seascale and Windscale, the TV programme found an excess. If you then ask: what is the probability of giving that excess, assuming that everything was uniform, you will find automatically that that is an unlikely event because you already know from the data you have got there are several cases there. On the other hand, if you then wait and say, "Let's see what is happening in this area in the future", and say, "What is the probability of excesses?" then your P value for that study becomes very reliable. So, if you like, what I am saying is that in Table 7 on page 57, the P value calculated for 1963 to 1983 is open to criticism. The P value for 1984 to 1990 is not open to criticism in the same way at all.

Q. Yes. I must start again. The P value of Table 7, page 57, is liable to criticism as regards 1963-83, but that relating to 1984-90 is not? Is that - again please put me right if I am getting it wrong - is that analogous to the advantages of a cohort study which is carried forward in time rather than viewed from a past date and then carried forward to the present?
A. I would say no.

Q. In the case of a cohort study which begins, let us say in 1960 and comes forward to the present time, you have all sorts of imponderables like recall bias which might be people shunning the disease or trying to establish a connection with the disease and various other things, misremembering how much seafood you ate. Whereas if you carry it forward you can observe what the people are actually doing and what actually happened?
A. Yes, there is some slight analogy, but the main point is whether you know about the findings, in some senses, beforehand. Now the difficulty - and I can see that in some senses with the cohort study, yes, that is...

Q. There are elements...
A. There are elements in common, but it is not the key issue in a cohort.

Q. The key issue is whether you know that which the study may, if it comes out a certain, produce?
A. Yes.

Q. I was calling that a preconception as to what it might be.
A. It is an acceptable word, but I would...

Q. You would prefer to express it how?
A. I think what you mean by preconception is that you have already peeked at the data?

Q. Yes.
A. All right, that would be a way. It is peeking at the data beforehand.

Q. Yes, a preview of the data?
A. A preview of the data.

Q. MR. LANGSTAFF: Is it perhaps, to an extent, making the data fit the result which you know to be the case, rather than looking at the data and seeing objectively what result they in fact produce?
A. No, I don't think that that is the point.

Q. MR. JUSTICE FRENCH: Well, what I am going to write down, and tell me if this is anywhere near the mark: a preview of the data may render the P value of the study subject to question?
A. Absolutely.

Q. MR. LANGSTAFF: Draper goes on on page 42 to say this:

> "This criticism cannot be applied to the results for 1984-90. Even the case from this period that was included in the Black report (with the year of diagnosis wrongly given as 1983 rather than 1984) was diagnosed after concern had been raised about the high incidence in Seascale. For the age group 0-24 there is an excess of malignant disease which is highly unlikely to have arisen by chance (Table 7). These more recent data therefore strengthen the suggestion that there is an increased incidence in Seascale for the age group 0-24 years though, while the original findings related mainly to lymphoid leukaemia at ages 0-14, there were no leukaemias and only one case below age 15 during 1984-90. Of the four cases found in this period two had NHL, one had Hodgkin's disease and one a pineal tumour; the excess is mainly attributed to NHL. We have excluded from these analyses case 14 of Table 3 since this case occurred beyond the period specified in planning the analysis (see Introduction)."

That is an example of rigorous statistical methods, that you plan your analysis first of all and if the case falls outside the period you exclude it?
A. Exactly.

Q. "The occurrence of this case does however strengthen the conclusion that there is an excess of lymphoid leukaemia/NHL at ages 0-24 in Seascale."

Can I ask you to look at Table 3 on page 53, case 14 there was a male born in 1975, diagnosed in 1991 and therefore outside the period of study of Draper and his colleagues, who was suffering from ALL?
A. Yes.

Q. And we see not included in the present analysis?
A. Yes.

MR. JUSTICE FRENCH: So we are having a look at it only firmly to reject it?

A MR. LANGSTAFF: My Lord, I think so. The authors of the study have looked at it and simply said they draw strength and comfort from it.

MR. JUSTICE FRENCH: Yes. You are entitled to look at it after the study to draw comfort, although you cannot look at it for the purposes of the study?

B THE WITNESS: I think particularly for calculating P values, that is the really key issue. You should not now calculate a P value on the basis of saying, "Well, we will just extend it to 1991." It would be quite reasonable to begin another study which had a larger time period and perhaps to look from 1984 to 1995, or something of that kind, and then it would be entirely correct to include it.

C

Q. MR. JUSTICE FRENCH: Oh, yes, if you do a new study. I can understand that.
A. You can then calculate the P value.

Q. However, one is entitled to look at events that occur outside the study period for your P values?
A. Provided you don't use it to calculate a P value, you can do it. That would be my view.

D

Q. For what purpose do you look at it?
A. Because you are interested in the science and not just the P value. The P value is of limited value in the scientific sense. I think the questions the authors would have is: have we got yet another unusual event? They say, "Well, we don't thinks so, because lo and behold here is yet another cancer when we wouldn't have expected any at all to have occurred." That is just part of a more general scientific approach rather than trying to calculate P values on.

E

Q. Is it analogous to looking at another paper to say, "Well, it is consistent with..."?
A. Yes, exactly. It is that sort of thing.

F

Q. So you cannot alter the P value because in the light of a case which arises outside the study period as an index of general consistency?
A. It is an index of general consistency.

Q. It may, however, be an index of general consistency.

G

Q. MR. LANGSTAFF: Having dealt with that, they say this at the end of that paragraph on page 42:

"As regards other cancers in this age group there is a small, non-significant excess..."

H

That is using "non-significant" in the statistical sense?
A. That is right.

Q. "...during 1984-90, but no overall excess if the whole period 1963-90 is considered.

There is no evidence that the raised incidence in Seascale extends to the two county districts nearest to Sellafield or to Cumbria generally."

Page 43, the authors of the study look at the hypotheses that might account for the findings presented:

"First, it is possible that the results are simply due to chance since a search for 'clusters' is likely to reveal some spatial aggregations of cases even if there is no causal explanation: this is particularly true if the age groups, areas, calendar periods and diagnostic groups to be studied are not specified in advance. When claims were originally made concerning a cluster at Seascale it seemed quite possible that this was the explanation. The accumulation of further data since the original reports and the analysis in Table 7 suggest that this is not the correct explanation."

To what extent do you agree with that?
A. I think that is very clear and I agree with it entirely.

Q. "Secondly, the most obvious suggestion is that the cases are caused by the direct effects of environmental radiation on the child or foetus. The results of calculations based on estimates of environmental discharges and on modelling of risks attributable to such radiation suggest that the doses delivered to the child or foetus were far too low to explain the 'cluster' unless either the discharges were considerably underestimated or the assumptions made in computing the risks were grossly incorrect."

What do you say about that?
A. I am inclined to agree with that.

Q. "Thirdly, Gardner et all, in their case-control study of leukaemia and lymphoma diagnosed during 1950-85 among young people in West Cumbria, concluded that the excess occurred among children whose fathers had high levels of exposure to radiation before the child was conceived, but perhaps particularly in the preceding six months; they suggest that some cases were the result of paternal germ cell mutations, and that this could explain the excess in this geographical area. Again, the level of risk implied by this explanation seems inconsistent with the dosimetry and previous estimates of genetic risk. It has been suggested

that the measured dose of external radiation may in fact be a surrogate measure for internal exposure to radionuclides or to chemicals; such alternative explanations are still open to the objection that there is no generally accepted human data to support them."

Can I just ask you this: in the study you have seen and the information you have reviewed in relation to Sellafield and Seascale, to what extent does it appear to you that any specific chemical can be implicated in the etiology of the leukaemias?

MR. ROKISON: Could we ascertain what material has been seen in relation to that? I think there is none referred to, but I may be wrong.

Q. MR. LANGSTAFF: Let me put it this way: are you aware of any suggestion that any specific chemical might be responsible for the leukaemias?
A. Leukaemias in Seascale?

Q. In Seascale.
A. No, I am not aware of any suggestion.

Q. It goes on:

> "...such alternative explanations are still open to the objection that there is no generally accepted human data to support them. The present analysis includes the geographical area covered by Gardner but follows it too closely in time to provide data to test his findings; only cases 12-14 in Table 3 (one NHL, one leukaemia, one Hodgkin's disease) were diagnosed after the period covered by the Gardner study and moreover all three were conceived before the parents moved to Seascale.
>
> The only published study that can be directly compared with the Gardner report is that by McLaughlin et al..."

Well, we dealt with McLaughlin and we see there that the authors of this report note the similarities and differences which are set out in text between those two studies. It deals overleaf with other researches and deals then with the theory that a virus might have been responsible for the excess at Seascale.

Above the first punch hole:

> "The high incidence in Seascale has occurred over an extended period and it is not clear to us whether this could be explained by Kinlen's hypothesis."

The viral hypothesis:

> "A number of studies, see, for example, Draper, have suggested that childhood leukaemia is more common

among higher socio-economic groups and it has also been suggested that the risk of childhood ALL is doubled in isolated towns and villages, but the excess in Seascale is too large to be accounted for in these ways."

To what extent does that accord with your understanding?
A. I would agree with what that says.

Q. "In conclusion, we confirm that there is good evidence for an increased incidence of lymphoid leukaemia/NHL among young people in Seascale though we are unable to identify the cause of this increase nor can we say that the new data and analyses presented here either support or detract from the conclusions of Gardner et al."

Now, could I ask you, having looked at that report, to return to your fourth report, and what you say about the Draper study, page 5 of your report? When you say there:

"...this study is further convincing evidence that the excess of childhood cancers in Seascale must be genuine."

what do you mean?
A. The fact that from 1984 to 1990 an excess has been found, when this had a prior hypothesis and the data have not been known beforehand, is to me very, very convincing indeed and that P value in the second row of Table 7 of Draper is, to me, very strong evidence that the excess in Seascale during that period, 1984-90, is not due to chance. It also, therefore, lends support to the fact that the earlier period was also not due to chance, so this building evidence one brick upon another.

Q. You then note in words that echo the report's own conclusion:

"The study is compatible with preconception radiation exposure playing a causal role in the cancer excess although this is not directly addressed in the study because there is no data on paternal occupational exposures given."
A. Exactly.

Q. Can I return then to your first report? Page 30. It is underneath the heading "Overall Conclusions". You come to the first of your conclusions:

"It is quite clear from the studies I have considered that some aspect of living in the vicinity of nuclear plants is causing the excess levels of leukaemia. There can be very little suggestion that all the excesses are due to chance."

Now in summary, what do you base that on?

A. What I based that on in June was the combined reports of Black and COMARE, of the further subsequent studies that had been done looking at Seascale in a variety of ways, and at that time my judgment was that it was unlikely that the excesses were due to chance.

Q. To what extent have your views of the Seascale and Sellafield excess been strengthened or weakened by looking at the subsequent reports that we have referred to?

A. Very strongly strengthened by Draper, in the report that we have jut looked at.

Q. You examine, Professor, the possible causes, chance then being excluded, from pages 27 to 29 in your report. Can I take you back to page 27. The possible explanations you look at are statistical artifact or alternative explanations and the alternative explanations are viruses, car pollution, chemicals and pollen. That is around nuclear plants generally, I think, that you are dealing with there?

A. Yes.

Q. Let me deal with each of those. So far as Seascale is concerned, do you regard the excess of leukaemias and lymphomas as solely due to a virus?

A. I think that is very unlikely.

Q. Why do you say that?

A. I think, if it had been due to a virus, we would have expected to have found the clustering that we discussed yesterday and in Draper's 1991 report. We would have expected to have found clustering in space and time to be rather common. If we apply those sort of methodologies to other diseases that we know have a viral cause, we find that the clusters are identified all over the place and we find that same sort of patterning happening even with such simple viruses as food poisoning.

Q. How consistent do you regard the findings of the studies that you have looked at with the hypothesis that a viral infection was the sole cause of leukaemias and lymphomas around the Sellafield plant?

A. As I say, if it were a viral cause, I would expect to find that the patterns of disease were via some sort of transmissible agent and so you would expect to find throughout the country clusters of leukaemias in space and time that, on the whole, we do not find.

Q. You deal at paragraph 80 with that. I think you say at paragraph 80:

> "....if such a viral mechanism were operative it would not rule out a radiation linked cause. The Greaves' letter (in response to Kinlen's .... paper) is a concise summary of how his hypothetical viral mechanism could be combined with a radiation linked

pathway to explain the Sellafield and other 'nuclear installation' excesses."

When you said that, if a viral mechanism were operative, it would not rule out a radiation linked cause, what did you have in mind?

A. What I mean is that, for most cancers, as far as we are aware, there are multiple events that have to happen in order for the cancer to appear in a clinical form and it is as if there were a chain reaction. For some cancers, it appears that there are four or five perhaps things that need to happen in order for the cancer to become clinically evident. So it is possible that leukaemia is also of this form. I am not an expert in the field of how many particular stages there might be but, given my general knowledge of cancer, it is possible that a virus, coupled with radiation, might perform two of those steps in the chain reaction.

Q. You go on to deal at j2 with statistical artefact as a cause and I think, putting it shortly, you reject it?

A. Yes.

Q. At paragraph 85 you deal with your overall conclusion as to what, in your view, is the most likely cause of the excess leukaemia cases in the vicinity of Sellafield. What, in the light of all the further information that you have received and considered and been asked about in Court, do you consider now to be the likeliest culprit as a cause of the leukaemias around Sellafield and Seascale?

A. I think that radiation is the most likely cause.

Q. Why do you say that?

A. The next sentence says, in my report:

> "Sellafield has the largest leukaemia excess in its vicinity and also has higher radiation levels both inside and outside the plant than any other plant in Britain."

I think that we are talking about something around Sellafield. We have high occupational exposures and we also have high environmental exposures, and I think it is possible that the interaction of those two is an explanation. Whether that is the correct explanation or not, radiation seems to me to be the most likely culprit.

Q. So far as the two cases themselves are concerned, going from the general to the particular, to what extent do you consider that radiation is, or may be, a cause of the leukaemia of Dorothy Reay?

A. My own judgment is that that is very likely.

Q. And what is your judgment in respect of the non-Hodgkin's lymphoma suffered by Vivien Hope?

A. I think the evidence is slightly weaker but, nevertheless, is still a likely, and at the moment the most likely, explanation.

Q. You have given us your present opinions, Professor, and you have referred us to the opinions that you expressed on 1st June, 1992, when you said, at paragraph 85:

> "Without doubt the most significant work concerning a possible mechanism for the excess around the Sellafield plant has been that carried out by Prof. Gardner and his team, ... particularly the case-control study."

Have you, since 1st June, conducted your own re-analysis of all the data relating to the Gardner cases?

A. I have.

Q. And did you produce a third report - we already have it in evidence - dealing with that re-analysis?

A. Yes.

Q. Let me ask you this. Before you began the mathematical calculations leading to your re-analyses, did you have any discussions with anyone from the Defendants' side as to the methodology that you would employ?

A. Before the third report, I did, yes.

Q. Who did you speak to?

A. I spoke to Dr. Wakeford and I am not sure, I think it is Mr. McElvenny, or maybe Dr. McElvenny.

Q. Did you reach an agreement as to the approach to be taken to the data?

A. As far as I understand, yes.

Q. Do you understand it to have been suggested since your third report that there may be a suggestion that a different approach to calculating P values might have been employed by you?

A. I understand there has been an objection raised.

Q. Was it ever suggested to you before you began your re-analysis that any method of calculating the P values, other than that which you used, should be used?

A. No, those had appeared in my secondary report as well that was dated before that meeting.

Q. MR. JUSTICE FRENCH: Can we pause there a moment? You say that you saw Messrs. Wakeford and McElvenny?

A. I did.

Q. Before undertaking your re-analysis?

A. Yes. My final re-analysis.

Q. Your final re-analysis. Did you or did you not discuss with those gentlemen your method of approach to the P factor?

A. Yes, I believe I did.

Q. No criticism was then made?

A. No.

Q. It must follow that, if your belief be a mistaken one, then there is nothing in the point?
A. Entirely. Can I....?

Q. Just add something in a moment, please. Yes, Professor?

MR. LANGSTAFF: May I just follow up that last....?

MR. JUSTICE FRENCH: I think he wanted to add something.

THE WITNESS: I was going to say just in paragraph 16 of my second report, which has been overtaken largely, and, in some senses, my third report is merely an update of the second report, and the second report was done at a stage where agreement on the doses had not been achieved is my understanding. At paragraph 16 of my second report that Dr. Wakeford and McElvenny were familiar with and made comments on the fact that our tables were nearly the same, though not identical, that that methodology was stated there.

Q. MR. JUSTICE FRENCH: Paragraph....?
A. Paragraph 16 on page 3 of my second report.

Q. So the last answer is qualified by the fact that those gentlemen would be well aware of paragraph 16?
A. I would hope so, yes, and they certainly commented on the tables from that.

Q. So that whether you specifically presented them with it, the point you are making now is, there it was for them to see?
A. Yes.

Q. "I consider whether I mentioned it or not...."?
A. I believe that I did mention it.

Q. I know. You have said as much.
A. Yes, sorry.

Q. "But I consider whether I did or did not tell them, they must have known my method by reason of paragraph 16 of Evans 3." Evans 2?
A. Evans 2.

Q. MR. LANGSTAFF: What was the purpose of your meeting in advance of doing the analyses for Evans 3?
A. The purpose in my meeting was that we all make mistakes on occasions and the idea was that, to avoid wasting the Court's time over discussion of trivial details, we would exchange copies of the tables that we each produced. There had been a comment made that our numbers did not necessarily exactly agree and I found that I had made minor mistakes in my second report - failure to link the right person correctly - and I hoped that we would be able to exchange tables and check that the numbers that appeared in those tables were in agreement before we arrived in Court.

I requested that I should be able to communicate that directly to Dr. Wakeford rather than through lawyers and he to me, but I understood that that request was refused in the end.

Q. I think that, to be fair, Prof. Evans, was a matter between the solicitors, about which no objection at all is raised, nor, of course, ought to be raised by the Plaintiffs.

MR. JUSTICE FRENCH: Yes, it is something that is part of lawyers' mysteries that laymen often find incomprehensible.

MR. LANGSTAFF: My Lord, indeed:

Q. If I can then take you, Professor, from the lawyers' mysteries to the scientific ones, I think, in your third report. The intention of your third report is set out at paragraph 3?

A. Yes.

Q. Was it the intention of your third report to repeat the Gardner analysis to confirm its veracity, making slight modifications to allow for a more accurate estimate of dose than was available to the Medical Research Council team?

A. Yes.

Q. The data you produce from that analysis is known as "using original dose records"?

A. Yes.

Q. Secondly, to create a complete re-analysis using the agreed doses. By "agreed doses" - I lead on this - do you mean the doses agreed between the parties for the purpose of these proceedings?

A. Yes.

Q. Thirdly:

> "A re-analysis including the 39 extra cases and controls who could not be traced for Gardner's 1990 report but were intended to form part of his original analysis and have now been traced."

A. Yes.

Q. And, fourthly:

> "An analysis using 'internal doses' for both the workers who formed part of the original study and including those subsequently traced."

A. Yes.

Q. You will continue with a comparison of the results of those analyses with the Gardner analysis, Table VI, that we have seen?

A. Yes.

Q. You note at (6) that:

> "The analyses in this report are based on the computer file provided by the Defendants following agreement of the doses."

Is that a computer file of data relating to individuals and their doses?

A. Yes.

Q. You set out your method and, paragraph 8, you note you have been provided with a file giving internal doses, which Prof. Gardner did not have.

Paragraph 9, you have examined the two time periods used in the case-control study: preconception in total and six months prior to conception.

Can I ask you this? Prof. Gardner got his results for the six month preconception period by taking the appropriate year into which the six months fell and dividing the annual dose by 2 to get the six month period. Did you approach that in the same way?

A. No, I was given the doses. I did not do the actual work myself, but Dr. Dennis, I believe, and the Defendants' own experts looked at the month or, at least, period by period dose for each individual badge, as far as I understand, so that, as far as was possible, the exact monthly doses were incorporated in those six months.

Q. I think, just so there is no secret about it, I can say that Gardner did not have any doses other than the annual doses to work from and it is no criticism of him, as a statistician, that he only had those as annual doses?

A. No, nor of British Nuclear Fuels in the matter.

Q. You had the advantage that further work had been done to analyse the six months' accurate data?

A. Yes.

Q. In paragraph 11 you note the difference between area and local controls and that:

> "Some of the Defendants' experts argue that the Area controls are not as good as the Local controls in that an excess is already known about in the local population...."

What do you say about the relative advantage, whether one is better than the other for the purpose of analysis?

A. I think it is very difficult to say that one is in all circumstances better than another and I find that having the two lends weight to any conclusions that I draw if they are in agreement.

Q. Paragraph 12, you set out the three diagnostic groups used - leukaemia on its own, non-Hodgkin's and Hodgkin's - and you have pre-specified, you say, that you would look at leukaemia and NHL combined for all analyses?
A. Yes.

Q. Why do you use the word "pre-specified"?
A. Because I did it before I looked at any of the data.

Q. You note that that combination was objected to by some of the Defendants' experts, Prof. MacMahon in particular. You think there remain good grounds for combining them. What is your understanding of the good grounds for combining them?
A. I think that in Draper in 1992, he also explains why he combines them and I am not sufficiently expert on the medical background to talk about the exact distinctions between sub-divisions of leukaemia or between leukaemia and non-Hodgkin's lymphoma. I certainly understand that, for some of the periods under study in Gardner's data, there could sometimes be a mistake made in the classification of individual cases between leukaemia and non-Hodgkin's lymphoma and I know well from my general experience in medical research that diagnoses are not always precise.

Secondly, it becomes very tedious to look at leukaemia and non-Hodgkin's lymphoma separately and combined. It means doing three analyses where one would do and I am all for a simple view of things where it is possible.

Q. MR. JUSTICE FRENCH: So there are good grounds for combining them. First, because of the reasons given by Dr. Draper?
A. Yes.

Q. And, two, because it becomes tedious to do three analyses?
A. Yes.

Q. As would be necessary if you look at leukaemia and NHL together and then individually?
A. Yes. If I might be allowed to elaborate slightly on the emphasis on the pre-specification?

Q. Yes.
A. It means that the P values that I then obtain, I am slightly more confident about them rather than having three possible P values from each of the three separate analyses and then selecting the one that is most significant, or least.

Q. "I then have only one P value instead of three." Does one need to say more than that?
A. No.

Q. A thing that I find a little strange - perhaps it is a question of semantics, I do not know - it seems to a non-scientist rather odd to find as good ground for not doing an exercise that otherwise might be appropriate that it would be tedious to do it?
A. I think if I had unlimited time, then that would not be a good reason. It is partly that it is tedious, but the issue of the P value is also there. I think it is also overwhelming to look at vast numbers, three times the number of tables. I do not think it provides extra evidence in regard to the case.

Q. MR. LANGSTAFF: Can I ask you this as well, Professor, in a moment? How many non-Hodgkin's lymphomas would one have been looking at if one had analysed non-Hodgkin's lymphomas entirely separately?
A. At most, 22.

Q. What would be the power of a study looking at such numbers?
A. The power of the study will be very much less than looking at leukaemia on its own with 52 cases, at most, and even less power than looking at 74 cases combined.

Q. To what extent would you, as a statistician, attempt, if you could legitimately, to avoid having to study small numbers?
A. If you can avoid it, you tend to try and do so.

Q. Paragraph 14:

> "As part of the analysis for Table VI in the published paper" - that is the Gardner paper - "case and control fathers were divided into three groups: those who could be positively linked to the Sellafield workforce file, those who were negatively linked to the Sellafield workforce file, and those who be neither positively nor negatively linked (the 'linkage not possible' group). The analysis for Table VI was performed entirely on those individuals whose fathers could either be positively or negatively linked to the Sellafield workforce file...."

and you say you had repeated that in the re-analysis using the "agreed doses":

> "For all the analyses on the agreed dose data all cases and controls have been included."

Q. MR. JUSTICE FRENCH: Those lines are ruled out in my copy?
A. Yes, those two sentences are contradictory.

MR. LANGSTAFF: Sorry, the line has slipped on my page. It is underlined.

Q. MR. JUSTICE FRENCH: For all the analyses....?
A. Yes, that sentence should be deleted.

Q. Down to "included"?
A. Yes.

Q. Is that all that need be deleted?
A. Yes.

Q. MR. LANGSTAFF: You go on, after the deleted part, to say:

> "These cases and controls for which linkage was not possible have been counted as having zero occupational dose as on the files from BNFL."

A. Yes.

Q. So you treated the "linkage not possible" as having no occupational dose and included them in the study as such?
A. The remaining ones for whom linkage was not possible.

Q. That was, you say, as you proposed in your affidavit on 8th May?
A. Yes.

Q. You deal with the data file at paragraph 15 and we have, I think, already noted the second to last sentence and the last sentence there:

> "The data on the extra 39 workers revealed that ten, one leukaemia case and nine controls had doses of gamma, seven of whom had neutron and internal doses. Of the twenty-nine there were two leukaemia cases, one of Hodgkin's lymphoma and twenty-six controls."

Paragraph 17:

> "The matching has been taken into account using conditional logistic regression, with an additive risk model, done with the package EGRET, which was the statistical program used by Gardner and his team to perform the conditional logistic regression and obtain odds ratios in a matched analysis."

Let me ask you about that. By "matching" what are you referring to?
A. What I am referring to is that each case was identified and then the Gardner team went to the birth register and looked for controls who were similar to that particular case, and so each control could be linked to a case to which it was matched in regard to, in some instances, exact parish of birth; in other instances, a rather wider area of birth and, in all instances, on age or, at least, on date of birth.

Q. And sex?
A. And sex.

Q. So that is what you referred to by matching and you took that into account, you say, using conditional logistic regression. Now, you have described to us a regression slope, and is conditional logistic regression the method of seeing whether you get a regression slope?
A. Yes, particularly when dealing with match sets, that is what the conditional bit means. The conditional means that you are looking for a slope, effectively within each set, of a case and its controls, and so if you fail to take that into account you would not put in conditional logistic regression, you would use ....

Q. Let me deal with it in this way. If asked to explain the subtleties of conditional logistic regression more than you already have, and if asked to explain such things as the difference to be made using an additive risk model, or a multiplicative risk model, you will be happy in due course to do so?
A. Yes.

Q. Let me ask you this: was the method you used an appropriate method to analyse the type of data that you had?
A. Yes, it was the method used by Gardner and by McLaughlin.

Q. And by McLaughlin?
A. Yes.

Q. You referred to additive risk models and multiplicative models. A layman might understand the difference between addition and multiplication, and hence the derivation of the words. Can I simply ask you this: what difference does it make whether you use an additive or a multiplicative model for this particular data?
A. Almost no difference at all to the overall conclusions.

Q. Have you checked your results by the other method?
A. Yes, I have.

Q. So you set out there, so that your results can be scrutinised by any other statistician coming to them, the method you have used and you say in the middle of the paragraph that the model you have used is exactly equivalent to the linear risk model described in the report of Duncan Thomas, and again can I simply ask you this: if asked to explain that you are prepared to do so?
A. Yes.

Q. I shall not ask you any more about it at this stage. You say that all P values quoted have been derived from likelihood ratio tests. Were those used by McLaughlin?
A. Yes.

Q. You say:

> "It is noted in the EGRET manual and is well known among statisticians that the likelihood ratio tests

are more reliable and robust, even in small data sets, than either the score tests or other methods based on standard errors."

Score tests we have come across before?
A. Yes.

Q. Was that the test that Prof. Gardner referred to in his statement as having used on his data?
A. Yes.

Q. How compatible are your data produced by your method of analysis with his score tests?
A. They give very, very similar answers.

Q. Now your "Results". Tables 1-9, you say, have not altered in much detail, and turning to paragraph 20, to the "Trend Analyses Using Actual Doses Rather Than the Grouped Doses", you have already explained to us what the importance of this is and let me then take you to Table 10 where you summarise the regression slopes produced by the re-analysis. If we were to turn to page 12 and Table 20, do we see there a table which compares the regression coefficients that you get from the various different sets of data that you were looking at?
A. Yes.

Q. Let me then ask you about Table 20 as being an easy comparison. When you analysed the original data, as you describe it, and looking for the sake of these questions at the local total, you have a coefficient of 0.019 for your regression slope?
A. Yes.

Q. Would that on its own tell us anything in particular?
A. Not very much.

Q. If one casts an eye across to the right-hand side, under the table headed "P Values", one sees a local total 0.019 P value for that?
A. Yes.

Q. That suggests, does it, that there are 19 chances in 1,000 of producing as little variability as the regression slope from the original data would suggest?
A. Yes.

Q. When you analysed, using the agreed doses but excluding the additional 39 cases, does the table show what results you got?
A. Yes.

Q. The local total, the regression slope, 0.013, how similar is that to 0.019?
A. It is very similar.

Q. When you turn to the "All cases (agreed dose data)", what do you say about 0.017?

A. That is also similar.

Q. Is that similarity of any significance to you?
A. Yes.

Q. What is the significance?
A. The consistency in those indicates to me that there is more likely to be a real effect.

Q. Why is that?
A. If there were no relationship then the regression slopes would be unstable. They would vary a great deal from one analysis to another, particularly when for the first two rows we are dealing with 66 cases in the analysis and then we, in the last row, deal with 74 cases in the analysis, we would expect if there were no genuine relationship some rather greater instability in there.

Q. The P values we see go from 0.019 with the agreed dose excluding the 39, 0.04, and all cases using the agreed dose data down to 0.018, I think is the lowest of the P values. Do you draw a conclusion from the consistency of inconsistency of those P values?
A. I would expect to find that the P value would be related to the sample size and so I would expect to find, given the same circumstances, the second and third rows to show the difference they do, that in the third row the P value would be smaller, but again the fact that those P values are consistent is something that to me is the strength of the evidence.

Q. Does the effect then of your re-analysis, using the agreed dose data and including all the additional case material that you know of, does that strengthen or weaken your original June conclusions as to the causation of the Sellafield and Seascale leukaemias?
A. It considerably strengthens it.

Q. Professor, by way of direct comparison with Gardner's published paper, can we look back at pages 10 and 11, and this is including all the data from the additional 39 cases, you prepared four tables which replicate Table 6 of Gardner?
A. Yes.

Q. In the important respects, and do they show there the relative risk for all cases looking at six month cases, as against local controls ranging from 1.07 in the 1-4 mSv category, going up through 3.34 in the 5-9 mSv, to 3.82 in the over 10 mSv?
A. Yes.

MR. JUSTICE FRENCH: This is a milliSievert table?

MR. LANGSTAFF: My Lord, yes:

Q. Table 17, the total pre-conceptional doses, 0.73, 0.61 and 6.8, and 6.8, I think one notes in relation to the

figure we were looking at earlier from the McLaughlin, the 80% power to detect 7.6?
A. Yes.

Q. As compared to area controls, the relative risks again are those shown in the last line of your tables?
A. Yes.

Q. And those are the figures directly comparable with the same results from Gardner's Table 6?
A. Yes.

Q. Page 13, do you report in a similar way on internal doses, this information having become available to you in a way that it simply just was not when Prof. Gardner did his analyses?
A. Yes.

Q. Can I take you straight to paragraph 36, where you say this:

> "What is important from Table I5 is that there is now some evidence that there is a genuine trend with increasing internal dose."

A. Yes.

Q. Is there a hesitation about the use of the word, "some"?
A. Yes. The P values for the local and area six months are both statistically significant, and while I would not wish to over-emphasise that the local and area total data do not show such a strong effect.

Q. You set out the regression slopes and we see what they look at and you say at paragraph 37:

> "these regression coefficients are very large because the measured internal doses are small. I would not place too much reliance on the individual coefficients but the general pattern is quite clear."

A. Yes.

Q. That is the effect of the data, is it?
A. Yes. Those slopes could, of course, be zero or negative values, in theory at least.

Q. But did you find that?
A. I did not find that and so that is where the consistency is.

Q. You say at 38:

> "An analysis of a 'total' dose formed by adding the external and internal doses together ... left the regression slopes given in Table 20 virtually unchanged."

and you say this:

"The P values were fractionally reduced ...."
A. Yes.

Q. What would you expect to happen to a P value as you add more data if the relationship is a real one?
A. I would expect the P value to go down.

Q. MR. JUSTICE FRENCH: Yes, it is rather difficult to envisage something going down and yet being more probable but that is the gymnastics we have to do?
A. That is unfortunately so.

Q. MR. LANGSTAFF: You summarise the regression slopes, agreed doses and internal doses, all cases included, at the Table I6. Your conclusions, I think all of them we have effectively dealt with in your evidence, Professor. You say this at 46:

> "The re-analysis confirms the overall conclusions of Gardner in regard to the case. The extreme values of relative risk in the highest dose groups have been reduced slightly but the trends shown by regression analysis are both similar and more consistent with previous knowledge. The most complete data with the agreed dose levels now shows firm evidence from both local and area controls that paternal radiation exposure is associated with childhood leukaemia."

Do you regard it as affecting the conclusions that you had earlier reached that the extreme values of relative risk in the highest dose groups were reduced slightly on your analysis?
A. Yes.

Q. How does it affect your conclusions?
A. I think that the first findings of Gardner are likely to be, even in the presence of a genuine effect, slightly larger than the true effect, and to do a re-analysis which has reduced the apparent association makes the comments made by Draper and others that the doses that were received were not sufficient to explain the excess, the doses become more nearly able to explain those effects, and that one is moving towards previous dose models - not to be exactly the same as them but one is moving towards it.

Q. MR. JUSTICE FRENCH: What do you mean by "previous dose models"?
A. Black and everybody else have used data from radiation exposure ....

Q. You are talking about earlier UK studies of Black, COMARE ...?
A. Well, the work reported by them and I imagine it is largely the atomic bomb data and generalisation from animal experiments and that sort of thing. It is a fairly vague statement and it is not my own expertise in that area.

Q. MR. LANGSTAFF: You emphasise the trend shown by regression analysis. You describe the evidence as firm. Does that remain your view as to the force of the evidence, having considered all the reports that have been put to you during your evidence so far?
A. Yes, my view is the evidence is firm.

Q. Are your conclusions, the conclusion that you reached at the end of your earlier report, any stronger or any weaker as a result of that re-analysis?
A. They are somewhat stronger as a result of the re-analysis.

Q. Finally, Professor, let me ask you this: do you regard it in any way as irresponsible of Prof. Gardner to have published the study that he did of the leukaemias and lymphomas around Seascale and Sellafield, and his findings in respect of them?
A. No ....

MR. JUSTICE FRENCH: Has anybody suggested it was?

MR. LANGSTAFF: My Lord, yes.

MR. JUSTICE FRENCH: All right, then he can answer.

MR. LANGSTAFF: My Lord, would your Lordship take the ....

MR. JUSTICE FRENCH: Never mind, if it has been suggested it has been suggested and he can answer.

THE WITNESS: I would take almost the contrary view, that having conducted a study as well as one could do in the circumstances, to have found those results and to have suppressed the publication would be entirely unethical.

Q. MR. LANGSTAFF: I wonder if you can find the report of Dr. Selby?

MR. JUSTICE FRENCH: Is this the "irresponsible" point?

MR. LANGSTAFF: My Lord, yes.

MR. JUSTICE FRENCH: I have accepted it has been made.

Q. MR. LANGSTAFF: It is all right, Professor, you need not, I think, find it. Do you consider that the public in Cumbria would be unduly alarmed by the publication of such a study?

MR. JUSTICE FRENCH: This is a public relations man question, isn't it?

THE WITNESS: That would be exactly my point ....

MR. LANGSTAFF: My Lord, I shall not pursue it any further. It can await cross-examination in due course. Thank you, Prof. Evans.

Cross-Examined by MR. ROKISON

Q. Prof. Evans, as you know I represent British Nuclear Fuels and I want to ask you some questions about your evidence and a few other things besides. I think you were in Court where I told my Lord that I would not be in a position to cross-examine you for the moment in relation to your re-analysis and I regret that unless my cross-examination goes on even longer than I estimate I will have to ask you to come back. It is because I am reserving my cross-examination in relation to that, that I would like to have further clarification from you in relation to one area of that.

MR. ROKISON: May I be permitted simply to ask one matter? My Lord, my learned friend referred to paragraph 17 of Prof. Evans' third report and said, "If anybody would like you to explain what you have done, in terms of that paragraph, would you be delighted to tell them?" and Prof. Evans very courteously said he would. I am wondering whether because I want to reserve my position, I would like him I would like him to explain if he would some parts of that paragraph, and I hope I may be permitted to ask that without embarking further on cross-examination on this part of the case, my Lord?

MR. JUSTICE FRENCH: Yes, you must take your own course, Mr. Rokison. I understand the problem.

MR. ROKISON: But your Lordship is quite happy I should simply ask for clarification of this and then reserve my position in relation to further cross-examination?

MR. JUSTICE FRENCH: I do not see why on earth you should not. It is not uncommon, in other fields of litigation, to do that simply in order to close off avenues.

MR. ROKISON: My Lord, I am very grateful.

MR. JUSTICE FRENCH: By all means take your own course. We are looking at Evans 3, page ...?

MR. ROKISON: It is Evans 3, page 6, and it is paragraph 17.

Q. It may be that the questions which I ask you or the way in which I ask them may demonstrate my current ignorance on this matter. You refer to the fact that you are dealing with matched cases and as I understand it what happened was that each case had its own matched controls?
A. Yes.

Q. You explained to my Lord how the conditional logistic regression had taken that into account?
A. Yes.

Q. You refer to the fact that you used conditional logistic regression within an additive risk model. I think what an additive risk model means, does that mean that the result that you get, for example if we look at Table 20, where you get, "All cases (agreed dose data) - local six months, 0.152", does that mean that there is an additional risk and it is 0.152 per milliSievert? Is that how it works or not?
A. It is not quite as simple as that.

Q. I feared not. Could you explain as simply as possible, please, what it shows?
A. I would be happy to do so but it is a very complicated formula in many senses and I would have thought that your own experts would be better placed to explain that to you most gently, but I will attempt to do so. The simple ....

Q. MR. JUSTICE FRENCH: Why don't we do this? Why don't we give, as it were, Mr. Rokison, a raincheck on that until Monday?
A. If he would really like me to do that, I would like to have some overheads and do the same exercise and have some prepared data to show you.

Q. Mr. Rokison can always, having consulted his experts, then put such further questions to you as he wishes, having perhaps clarified both his own mind and the questioners.

MR. ROKISON: Very well, I am happy to do that:

Q. But you say it is not as simple as the way in which I put it to you?
A. No.

Q. And that is a matter which I will investigate with my experts and come back to you maybe on Monday or maybe I will leave it over. You say that it was the statistical programme used by Gardner and his team to perform the conditional logistic regression and obtain odds ratios and a matched analysis, but as I understand it they did obtain odds ratios or relative risks in relation to the various categories?
A. Yes.

Q. But they did not carry out, as I understand it, a regression analysis such as that which you have carried out?
A. That is right.

Q. So could you explain what you mean here? Are you saying that they used EGRET in order to --- are you saying any

more than that they used EGRET in order to do the exercise which they did?
A. Yes.

Q. That is all you are saying?
A. That is all I am saying.

Q. I see. What had confused me, we ought to put a comma after "team" and then that is clear, is it, am I right? That is what had confused me about that. It was not the statistical programme used by Gardner to perform the conditional logistic regression but it was the package which was used by Gardner that you have used to perform the conditional logistic regression, is that correct?
A. We both used it to do conditional logistic regression. We both used it to obtain odds ratios. He used it only on the group data. I did it on the individual points.

Q. Very well, that has clarified it, thank you very much.
A. It was exactly this point that I thought we had discussed with Dr. Wakeford, and we discussed it down to the detail of what version of the programme we were actually using and we exchanged exactly what version. There are only a limited number of alternatives that one can have with this programme and we discussed ....

Q. Let me just say in relation to that, and it may not matter, that there is a difference of recollection, unfortunately, Prof. Evans, in relation to that, but I hope that it will not become a matter of importance, and I do not think that in the context of the case as a whole it is.
A. I can't see it having any importance, personally.

Q. Now, it is simply this, and I am wondering whether you can explain this to me and to my Lord. This morning you very helpfully explained to us by reference to your blood pressure example the way in which you would explain it very clearly to your students what a regression slope is, and effectively what it tells you. Can you explain how you do such an exercise where the points that you are putting into your analysis are themselves points which relate to a relative risk with a wide or narrow confidence level? How do you carry it out? Or is it simply a question of feeding it into the computer and it churns the result out the other end?
A. To somebody who didn't know what it was doing, yes it is doing that. However, what you are doing is that you feed into the computer the data on every individual in your study. All right? So if we just turn on two pages to, say, table 11, at page 8, if I may, we have there 455 individuals, and we have 66 cases and we have 389 controls who are linked to those cases.

Q. Yes.
A. We feed in the data for each individual, all 455, and the relevant information we give it is first of all whether

each individual is a case or a control, whether they had leukaemia or not; secondly we feed in what dose that they had; and thirdly we feed in what case a control is linked to, and that is all that we do.

Q. Yes?
A. We then say what is the relationship between dose or in this particular instance if we use the program to calculate a relative risk for being 1-4 mSv, we will end up saying what is the relative risk of being a case or rather the relative risk of getting leukaemia if we have a dose of 1-4, compared with having no dose at all, and we use the zero dose as our reference. And we do that taking into account what set they are in and EGRET gives us the number 0.90, and it will give us that number whether we use an additive model or a multiplicative model.

Q. Well, I think I understand that as far as table 11 is concerned, where what it is doing is giving you a relative risk in relation to those dose categories.
A. Yes.

Q. And it will also in relation to each of those relative risks give you whatever confidence factor you ask it to, whatever confidence levels you ask, will it?
A. It will do so in different ways according to whether you ask for an additive model or a multiplicative model, because the confidence intervals are calculated in different ways.

Q. And what did you ask it to do in relation to confidence levels?
A. If we go back to my report at paragraph 17, page 6, and the last sentence of paragraph 17, that is what you have been discussing:

> "... confidence intervals using likelihood methods are more reliable than those based on simple standard errors, but they are not available from EGRET and the standard error based intervals have been quoted for the grouped data for comparative purposes."

Q. Is that not relating to your regression slopes and your P values for your regression slopes?
A. No, that is relating to group data for comparative purposes. I have calculated no confidence intervals at all for the regression slopes.

Q. You have calculated no confidence levels at all for your tables either, have you?
A. I haven't presented any there. I presented them where I wish to compare with Gardner in my report number 2.

Q. Yes but your report number 2 has to a large extent been overtaken by your report number 3, to a large extent, has it not?

A. Yes, but Table 9 has not changed. Table 9 is where I have quoted confidence intervals.

A Q. And there you quoted confidence limits where you are comparing the exercise which you have done, which we find in your third report, is this right, at paragraph 18? It is referred to in paragraph 18, and you set out your confidence limits there, comparing them with those which were found by Prof. Gardner?

A. Yes. And in paragraph 19 I say:

B

> "Table 9 which gave the 95% confidence intervals calculated using standard errors by EGRET for the highest dose categories in all the tables, 1-8, used a multiplicative model for the calculation of confidence intervals. Since the likelihood based intervals are not available in EGRET, the additive mode based intervals are not hugely sensible."

C Q. I see, so that is why it used the multiplicative model for those?

A. Yes. You would actually obtain quite easily, confidence intervals that would include negative values for the relative risk in those tables, which is complete nonsense.

D Q. Yes, I see. So did you do a similar exercise in relation to your two re-analyses, one using the agreed dose data and one using the agreed dose data plus the 39 additional workers?

A. I did something - what do you mean by similar? Did I do confidence intervals for the dose groups and so on?

Q. Yes.

E A. No, I didn't.

Q. So you have not even looked at them, you do not know what they are?

A. No, because I don't think that, if you are asking me to do my analysis, I don't think that the grouped analysis is the best analysis to do.

F Q. Well, you may not think it is the best analysis to do, but you nonetheless do it, and you do it on the basis of the agreed doses and you do it on the basis of the agreed doses and the 39 additional cases?

A. Yes.

Q. And indeed you were making the point that the work that has been done by McLaughlin is compatible, and you were

G suggesting that Urquart's study was compatible, because they were within what I might call common confidence limits?

A. Yes.

Q. Now, what I do not quite understand is why you have not even done those calculations, or if you have done them

H why you have not presented them in this document?

A. I haven't done them because I don't think that they are terribly helpful.

Q. Well, they may not be very helpful, and that may be a reason why we would like to see them.
A. If you would like I will produce them for you within 30 seconds here. I have my computer and I can produce it for you.

Q. Well, perhaps I will not ask you to do it now in Court, but perhaps that might be a matter that you could do for us by Monday?

MR. JUSTICE FRENCH: Is this a convenient moment to break off your cross-examination? By all means complete the line you are on at the moment.

MR. ROKISON: Well, that finishes that particular point that I wanted to ask about, my Lord, yes.

THE WITNESS: Can I just make it clear what you would like me to do? That is calculate confidence intervals for the highest dose categories, or for all the dose categories?

Q. MR. ROKISON: For all of them for each table, so that they are comparable with other documents which we see, not only the Gardner study, but also the Canadian study, and I think every other study that we see where one has relative risks that we also find confidence intervals set out. So perhaps you would be kind enough, if you would....
A. Can I then ask you why Dr. Wakeford and those who have access to EGRET and the same set of data couldn't do it for you themselves? I had understood as a result of our meeting together that there would be exchange exactly of these tables to avoid wasting the Court's time with trivial details.

Q. Well, you see, that is another matter on which your understanding does not to be the same, and that is exactly the reason why those who are instructing me thought that it was prudent that everything should be sorted out between solicitors and be done in writing, lest there were any disagreements of differences of recollection as to what may have been discussed orally, but the position is that I would like you, if you would would, to do that exercise, Prof. Evans. Whether it is an exercise that either could be done on our side or has been done on our side is, with respect, not a matter that I want to discuss with you. If you would be kind enough to do it, then I would be very grateful.

Q. MR. JUSTICE FRENCH: I understand, at least I hope I understand, it is not something terribly onerous, though it may be rather irritating.
A. No, it is not terribly onerous.

MR. ROKISON: Well, I apologise if it is irritating.

MR. JUSTICE FRENCH: Well, it is only irritating on one view of the facts.

MR. ROKISON: Yes, my Lord, that is right.

MR. JUSTICE FRENCH: And I do not begin, it is no issue of mine ....

MR. ROKISON: No. And I apologise if it is tedious, and I know you do not like doing work that is tedious, but perhaps you have between now and Monday.

MR. JUSTICE FRENCH: Now, that perhaps was unnecessary, Mr. Rokison?

THE WITNESS: Can I just be clear? You wish to have confidence intervals not just on the highest dose categories?

Q. MR. ROKISON: Not just on the highest dose categories, please.
A. But on all of the dose categories?

Q. Indeed, if we may?
A. In tables 11-14, and tables 16-19?

Q. Yes, please.
A. Right, so you are asking me to do something that I think is scientifically unnecessary?

Q. Yes, I am asking you to do something ....
A. Thank you very much.

Q. And I understand that you think it is scientifically unnecessary.

MR. JUSTICE FRENCH: It is getting late on a Friday afternoon. I think perhaps things will look a little different on Monday, at least I hope they will.

Q. Dare I say this, Prof. Evans? If you could give me, not every instance of a regression slope, but at least in one or two instances, a regression slope done on a nice piece of graph paper instead of figures, in a column, I think it would help me to visualise it. Is that a chore?
A. In relation to these data?

Q. In relation, for example, to Table 10?
A. I will try.

Q. If it is going to involve great labour, don't bother.
A. If I am to do what Mr. Rokison has asked that will occupy a good deal of my spare time this weekend and I do not know that I will be able to produce any nice graphs for

you then, but if it sounds as though I am going to be recalled then I will undertake to provide them by the time of a recall.

Q. Yes, that would be helpful, thank you. I am sorry it is going to take a lot of your weekend.

Q. MR. ROKISON: I genuinely am sorry as well but there are reasons why I want to ask you to do it. I am not just asking you to do something just because I want to be petty about it, I promise you.

MR. JUSTICE FRENCH: Very well. 10.30 on Monday, please.

(Court was adjourned until Monday, 30th November at 10.30 a.m.)