GENERAL MEDICAL COUNCIL

FITNESS TO PRACTISE PANEL
(applying the General Medical Council's Preliminary Proceedings and Professional Conduct Committee (Procedure Rules) 1988)

On:
Friday, 10 August 2007

Held at:
St James's Buildings
79 Oxford Street
Manchester M1 6FQ

Case of:

JAYNE LAVINIA MARY DONEGAN MB BS 1983 Lond
Registration No: 2826367
(Day Four)

Panel Members:
Mrs S Hewitt (Chairman)
Mr J Brown
Ms J Goulding
Dr M Goodman
Mr R Grey QC (Legal Assessor)

MR I STERN, QC, and MR S SINGH, Counsel, instructed by Clifford Miller, Solicitors, appeared on behalf of the doctor, who was present.

MR T KARK, Counsel, instructed by Field Fisher Waterhouse, Solicitors, appeared on behalf of the General Medical Council.

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INDEX

Page

FITNESS TO PRACTISE

ELLIMAN, David, continued
Cross-examination by MR STERN (continued) 1

THE CHAIRMAN: Good morning. In terms of timetable for next week, looking at your list you are very likely to be on your feet still on Monday, are you not?

MR STERN: I will be, yes.

THE CHAIRMAN: Then you have got the gap on Tuesday?

MR STERN: As I see it, and as you will be aware, being very experienced, estimates of counsel are always inaccurate, but doing the best I can I am hoping to conclude the first report today. Whatever time I conclude today I would like to finish to day and then revisit my cross-examination on the second report to see if I can reduce it significantly. That will obviously save a lot of time. If that is right, then I hope to conclude the second report on Monday, some time in the morning, possibly lunchtime, maybe earlier.

Thereafter there may be some issues that we need to determine or at least seek the view of your learned Legal Assessor. Then I believe that will be the end of the case in relation to the General Medical Council – they have no other witnesses. Thereafter, of course, it will be the case of Dr Donegan. Obviously, I would not wish to start Dr Donegan on Monday if, as I assume, we are not sitting on Tuesday. That would not be fair to her, in my submission. What I would wish to do then is to start her evidence on Wednesday and as to how long that will take, I am hoping, having been through the papers in this way that I will not need to do that again. Obviously, what Mr Kark does, I do not know; he may want to cross-examine on the papers.

This, as you will appreciate, is rather tentative, and you will see how it goes. That means that we may finish the evidence by the end of next week. Final submissions on Monday the following week, and thereafter I will not ask how long you will be.

THE CHAIRMAN: That is very helpful. Any observations?

MR KARK: Only, I suspect, that we will use Monday fairly fully because once Mr Stern has finished cross-examining I am likely to have some re-examination and, of course, there may be Panel questions.

THE CHAIRMAN: As far as today goes we will have a short coffee break and then we will try and wind up at ten-to one, five-to one.

DAVID ELLIMAN, recalled
Cross-examination by MR STERN (continued)

Q We are going to start with Hib, as I am going to call it (as I think it is colloquially known). I think we can deal with Hib fairly quickly because your first point, which you noted on page 27 of your report and corresponds with page 37 of Dr Donegan's report. The comment is in the third paragraph down. The part that needs to be looked at is the whole of that paragraph, essentially:

> "The incidence of invasive disease caused by the encapsulated forms (A-F) of H. influenza have been risking since the 1960s which is also the time that mass vaccination was introduced and antibiotics started

being prescribed so liberally."

Your comment in the middle of page 27 is:

> "The implication is that there may be a link between these events, otherwise why mention them. Dr Donegan produces no evidence to support a causal link. On the other hand, there is evidence that, in general, recipients of vaccinations do not suffer an increase in invasive infections."

That is your point?
A It is, yes.

Q Can I just ask you, please, to have a look at the Harrison's 11th edition, which you do not have yet but you are about to be given? *(Same handed)*

THE CHAIRMAN: I think that is D11.

MR STERN: Can I draw your attention to the relevant paragraph so we can save a little time? Obviously at page 268 it is the Hib section; over the page at 269, obviously, Dr Elliman, I will not keep repeating the point I have made to you on a number of occasions. If there is something I have missed out you will obviously help the Panel by filling them in. On the right-hand side of page 269, under "Epidemiology", the first part:

> "[It] infects only humans and primarily in the upper respiratory tract. It can be recovered from the nasopharynx of up to 90 percent of healthy individuals with the frequency of infection related inversely to age. The colonization rate of type b organisms averages 5 percent."

Then the point, more directly, is in the final paragraph of that section:

> "The incidence of systemic H. influenzae b diseases has increased fourfold during the past 3 to 4½ decades, and more adults are being affected. The basis for this increased attack rate is not understood but improved diagnostic laboratories and diminution in the prevalence of type-specific immunity due to excessive use of antibiotics have been suggested as possible mechanisms. Changes in antigenic composition and/or virulence of the organism and the prevalence of cross-reactive antibodies also may be responsible for this change."

That is the point?
A Yes.

Q Can we move then to the second point, which I can deal with even more shortly? Page 38 of Dr Donegan's report and the top of page 28 (if we take the point shortly) of your report:

"Dr Donegan states that the two Hib vaccines with the highest efficacy are not available in UK. She gives no reference to support this."

A Yes.

Q Two things: first of all, although there is no reference there would you expect a general practitioner to look at the BNF, being the British National Formulary?
A I would not expect a general practitioner usually to look at the BNF when he is giving immunisations because the supply of immunisations comes direct from the Department of Health, so it is not like prescribing some drugs.

Q It is my fault – I expressed it badly. Would you expect the vaccinations that are available to be in the BNF?
A Yes.

Q Sorry, that is the point I wanted to make to you. I think, in fact, you gave evidence in relation to these two vaccinations the other day, indicating that PRP OMP was not available in this country?
A It certainly is not currently – it is HbOC and HbTT.

Q Sorry, I was asking about PRP OMP first of all?
A Yes, it is not available currently, no. It is not used currently.

Q I think you were asked – again, I have not got the exact passage to hand but I am sure we can find it, if necessary – about it and you indicated that it was not available at the time?
A I hope I said I thought it was not. I was not definite.

Q You may not have been definite. So far as HbOC, I think you said that it had been available intermittently?
A Yes.

Q That was not your exact word but that was the effect of what you said?
A Yes.

Q So although there is no reference to support it, it is, on the face of it, accurate?
A As you can see from my report, I talk about the significance of what is quite a minor difference.

Q So far as your third point, I will just draw attention to it though I will not go to the paper. The third point you make in relation to Hib is this. At page 30 of your report and page 39 of Dr Donegan's report, this is a reference to *Pulse*, is it not, and you have made a comment about that?
A Yes.

Q Obviously, that is it. It is *Pulse* and there it is – there is not much I can ask you about that. Can we go now to menningococcus C, which begins at page 31 of your report? I am very grateful to Mr Singh, who has drawn my attention – for anybody who

wants the reference, it is day 2, page 26. Mr Kark said:

> "Can we just deal with those last two references. Without going please into the technicality of it, are those vaccines that have been used in the UK?"

Your answer:

> "There are different varieties of Hib vaccine. The PRP-D vaccine..."

which, I do not know if that is the same?

A No, that is a fourth variety that has never been used in this country.

Q That is exactly what you said:

> "...has never been used in the UK, because most people felt it was not as effective as the other three. The HbOC vaccine has been used on and off in the UK."

A Yes.

Q For anybody's reference, that is D2/26B. Menningococcus begins in Dr Donegan's report at page 41 and 31 in your report. There is nothing on page 41 of her report; your comments begin in relation to page 42 of her report and the third paragraph down beginning "Looking at possible reasons". Page 42 of Dr Donegan's report and page 31 of your report. The comment made by Dr Donegan is this:

> "Looking at possible reasons for a weakening of people's immune systems over the last ten years or so which would make them more susceptible to invasive disease it is certainly the case that children are having a much larger number of vaccines and at an earlier age than in the past."

I do not think there is any untruth in that. Your comment, over the page at page 32, is that Dr Donegan should have mentioned, I think, the surveillance factors (if I can summarise it)?

A Yes. My response to this one was not enormously detailed but one of the issues is the changes in diagnosis of this disease, which is what I am referring to quoting Dr Ramsay and others.

Q Dr Donegan's point in looking at possible reasons for a weakening of people's immune system, you cannot be so averse to criticism of the vaccine that that is not an acceptable comment?

A It is an assumption, because it says "Looking at possible reasons for a weakening", which implies you start off from there is a weakening there and you are looking for reasons for it. I would not start off from that premise. If you are looking at possible reasons, you might look at all sorts of things, and then you would dismiss them. One of the ones you would dismiss is the load of immunisations, as I provided some papers

previously to show there was no evidence for that. Of course, we have already talked about the difficulties of ascribing causal associations in time and for menningococcus disease there is a cyclical pattern as well – which I can produce a graph if you want.

Q I am sure you are right, but we are not talking about including absolutely every point. All she is making is a perfectly reasonable point, in my submission, that there are possible reasons for the weakening of people's immune systems over the last ten years or so that will have made them more susceptible to invasive disease. Is that not a reasonable point?

A I have two problems with it. One, as I have said, it almost implies a premise that there is a weakening, for which there is no evidence; then it is talking about looking at reasons for and it does not mention that the one about immunisations has actually been dismissed by a lot of scientific research. So it is raising it as a possibility but not the other possibilities and the conclusion that most people drew from the possibility.

Q Can we look at the paper – Dr Donegan's reference is 73. We have now moved to the second bundle of references, so you can put away the first bundle if you wish, or at least put it to one side. It is 73 in Dr Donegan's bundle, so we have finished with the first file of Dr Donegan's references and moved to the second file. I notice that at the top of page 32 you rely, I think, on the *Pulse* article for your comment?

A I used the reference that Dr Donegan produced. I could have produced another one; I did not think it was necessary. As you said, one has to be selective to some extent.

Q Let us just look at this if we can. There is a number of pages or different pages from the magazine, as we can see. Shall we just work our way down? That might be the easiest way. "Meningitis 'not an epidemic'":

> "Although the number of meningitis cases reported over the last three years are the highest they have been for years, the problem cannot be termed an epidemic...
>
> Dr Mary Ramsay said the expected seasonal increase of meningitis reported during the last two to three years was higher than usual. 'We are not really experiencing an epidemic. The technical phrase is, we are going through a hyper-endemic period', she added."

I am not sure I understand it, but there we are.

> "'We are experiencing a higher rate than usual, but we don't expect it to keep on going up. This period usually lasts for three to four years and then the number of cases go down for another three or four years'."

Then, somewhat unhelpfully, there is a tag over the next bit, so I cannot read that.

> "Although the number of cases had increased, Dr Ramsay said surveillance had greatly improved over the last few years, perhaps accounting for part of the rise."

That is the point you make in your report?
A It is indeed, yes.

Q "Perhaps accounting for part of the rise", so there is no certainty of that, is there?
A No. No, there are other reasons. As I say, it exhibits a cyclical pattern like other diseases.

Q Just explain to a lay person: why is there a cyclical pattern? I am not sure I understand that.
A I can provide you with a graph of that, if it helps.

Q Personally, I would prefer an explanation rather than a graph?
A I do not have an explanation. That is one of the things that one does not understand about meningococcal disease. Some of the others it is fairly easy to understand in that you build up a proportion of susceptibles. That may well be part of it but it may not be just the whole story.

Q So there is no explanation for it at all?
A There is no explanation that explains all the variation in the numbers of cases, no.

Q If you are right, that vaccination – which is at a very high level?
A Yes.

Q Is both efficacious and safe---
A Yes.

Q ...then why is it – I am repeating the same question – that you had no information as to why it is that it does not always work?
A Sorry, we are talking about the meningococcal disease, against which we did not have a vaccine at the time, so the vaccine was irrelevant. Once we have introduced a vaccine the amount of disease has gone down enormously.

Q When was that introduced?
A 1999.

Q Are you saying there are now no cyclical epidemics?
A I would have to look at the figures, but they have certainly been blunted, if not gone away, for meningococcal C disease, yes.

Q You have that, do you, to hand?
A I do not think I have it actually in paper form. I might have it on my PC – but I could provide it for Monday if you want.

Q All right. Whilst we are on this page shall we look at the other papers on there? On the left – this is 1997:

> "Meningitis C is becoming more prevalent among teenagers ... experts said last night commenting on the deaths of three first year students at the University of Southampton".

A

Then further down:

> "There is increases of exposure to certain strains because of communal living conditions and the rate of social contact",

B this is at universities, obviously...
A Yes.

Q ..where the rate of social contact is as high as one can get?
A It is thought, I think, as Dr Donegan comments that if you are in residential halls the risk is even higher.

C Q

> "But the most commonly affected group is still children under four. 'Their immunity to the disease is lowest'. ... still many unanswered questions why certain clusters of the population are more susceptible to the illness".

D Then on the right dealing with recent outbreaks at university in the third paragraph down:

> "But it is understood that they were put off by the vaccine's limited efficacy and the scale of the task",

this is in relation to meningococcal C?
A No.

E

Q Sorry – could you help, please?
A For a number of years – decades – there has been a vaccine against meningococcal A and C. This is a vaccine that is a fairly crude vaccine that you just take a sugar capsule of the germ. It has only ever been used selectively. The vaccine that we now have is only against meningococcal C; it takes that sugar capsule, adds something on, which means it works in the young children whereas the A and C old one does not, so they are very

F different vaccines.

Q They maybe very different. So we are clear about it, because I thought you were saying that there have been no vaccinations against...
A No routine vaccines, no. It was used very selectively.

G

Q Let me finish. There has been no vaccination until 1999; that is what I thought you said?
A Sorry, I should have said; as part of the routine programme. So it would have been used in very isolated circumstances.

Q When you say "isolated" what do you mean?

H

A Usually when you were going abroad because the A component was important in travel and if you did have an outbreak of disease you may give the vaccine to prevent further cases; so it was never given, for example, to infants.

Q I think if you look in the right-hand column it says:

> "Studies have shown that university students are at increased risk of meningitis than other adolescents. The problem is that several hundred thousand students would have to be vaccinated when the incidence of the disease is actually very small"?

A In that age group.

Q In that age group, yes. Further down:

> "The National Meningitis Trust ... the department ruled out of a vaccination programme because of the limitations of a combined meningococcal A and C vaccine, that is only 80 per cent effective.
>
> The new ... conjugant vaccine that will be available in the next two years looks very promising".

That is it?

A Yes.

Q So that is the point. Can I look, please, with you at your reference, 26? I think this may deal with the point that you were making. I think we can see here that figures for what is called "group C", if we look at the third column – the first column is the date, yes?

A Yes.

Q Increased, as we can see, up to 1999, it went down a bit in 2000 and then fell after that?

A Yes.

Q One other point in relation to this, if I may, if you look please at Dr Donegan's report page 43 we can see that the graph – well it shows pretty much the same thing; it may not be worth repeating the same thing. Can we move on, please, to page 32 in your report, half-way down, and Dr Donegan's report at page 45? Dr Donegan's report, or the relevant parts in the second paragraph under, "Safety":

> "The control group in one of the three trials of this vaccine was of children who were vaccinated with Hepatitis B, which is problematic as it is not without its own side-effects such that it has been removed from the schoolgirl vaccination programme in France due to an association with multiple sclerosis"?

A Yes. That is what it says.

Q Lets us look at what you say. Half-way down the page, "Dr Donegan quotes no evidence for this", though in fact it is right?

A Yes. I mean it was actually not just schoolgirls, it was schoolboys as well and it

A was within school and not from those children, but, yes.

Q But obviously relevant to these two children who are both girls?
A No. It was withdrawn from boys and girls and it was not any longer given in school; it was still given by their general practitioners.

B Q But the fact that she has only put "Schoolgirls"...
A No. As I say that is not...

Q That is irrelevant...
A Not relevant to the fact that it was girls in this case.

Q Your criticism is that she does not include in that, that this was greeted with
C widespread concern by experts in WHO?
A Yes.

Q We had better look at the reference that you give, which is DE27. Again, this is a point that effectively you say that every time she makes the point she should put the other point of view?
A No, not necessarily. What I am saying is that when describing an "association" it
D is very easy to think that means there is a link and I think for a non-scientific medical audience "association" could be taken as saying "A is actually linked causally to B". I mean, as you say, I am not an expert in this and I do not know if someone is going to call an expert, but that is my common experience; if you say, "A is associated with B", people will think B is caused by A unless you are very careful. I am not complaining about the words, the words are correct, it is the impression that most lay people would go away with that is the issue. Therefore, one would have to explain it because my understanding of an
E expert witness is to explain the science to people, not just to quote it, so that they can understand it and draw a reasonable conclusion.

Q I do not know how many other expert reports you have seen but...
A Quite a lot. They should explain.

Q Maybe they should but there are not many that do, would you agree?
F A I am afraid so, but I will hope that is changing.

Q That maybe now, I do not know, but there is new rules in 2007 as you probably know?
A Yes.

G Q In any event, let us look at this press release:

> "On 1 October 1998, the French Ministry of Health announced the decision to suspend routine HB immunisation of adolescents in French schools while continuing the immunisation of infants and high risk adults. This followed concerns, despite lack of scientific evidence establishing a causal relationship, that Hepatitis B immunisation might be linked to the development or flare-up of demyelinating diseases such as multiple sclerosis".

H

It then goes on:

> "WHO, with the assistance of external experts", in a variety of fields, "carefully reviewed the scientific evidence on whether HB vaccine can cause demyelinating diseases such as MS. WHO believes that available scientific data does not demonstrate a causal association".

Is that what you mean by "widespread concern"?
A Yes. Well it was not just WO, but that was – being a world-wide organisation it seemed appropriate because it does represent the world.

Q I can only go on the references that you have given us and that is what you meant by it, was it?
A Yes.

Q There is series of documents in France – you probably are aware of this that there is a criminal case under way in France in relation to the vaccine?
A Yes.

Q I have got some documents, if you would like to have a look at them?
A No. I accept there maybe a criminal case that is in process.

Q Yes?
A Yes.

MR STERN: We will show the documents – the Panel have not seen it so even if you are familiar with it, it might be fairer if I at least give it to them. I cannot remember what number we are up to. (*Same handed*)

THE CHAIRMAN: D12.

MR KARK: I have not seen the document yet but can I ask what the relevance of this is? Whether there is a criminal case going on in 2007or not I wonder what the relevance it is to a report from 2002.

MR STERN: It relates to this particular vaccine. It relates to this particular vaccine and the issue, as I understand it, is safety of the vaccine and the points that are being made by Dr Donegan in this report. It may be thought by some that what she said in the report turned out to be partially accepted, we will have to see when you look at that. If Mr Kark wants to keep it from you it is not essential, but it is relevant on the point in France that we are talking about. Dr Elliman has already agreed that there was such a thing. (*To the witness*) Do you want to say something?

THE WITNESS: If I am going to be asked to comment on it I am sure you will understand that I would like some time to read it.

MR STERN: I am not going ask you to comment on it. I am merely using you, if you forgive me, as a tool through which to introduce the documents. I will do it in another

way, I can do it through Dr Donegan...

THE WITNESS: Can I make a comment? It might help if he introduces it from me and then we can read it before he asks Dr Donegan...

MR STERN: That is the point, you see. If I introduce it through Dr Donegan, Mr Kark will then say, "Oh but this was never put to Dr Elliman and he never had a chance to comment on it". I can leave it if Mr Kark prefers; whatever he prefers.

MR KARK: If there is material in here that relates to the position back in 2002 then I concede it could potentially be relevant. I have never seen the document before; this is one of the difficulties of being handed documents as they come to the Panel.

THE LEGAL ASSESSOR: Perhaps I can say that I have sympathy in one sense with both sides. I understand what Mr Stern is saying, but I am in the same position as Mr Kark as I have not seen it and so I cannot really comment or advise on the admissibility.

MR STERN: May I make a suggestion that I hope is helpful? Mr Grey is given a copy, Mr Kark is given a copy, Dr Elliman is given a copy; I will move on and then we can see what views they all come to in due course. Dr Elliman can look at it over the weekend.

THE WITNESS: This will come up, but this is an article from the web. It is from what is known as quite a radical anti-vaccination site and just reading one of the paragraphs gives that, so it is not an official document about the...

MR STERN: That is why the official document is behind it. If you look there is a paper behind it, that is why you have been given both.

THE WITNESS: Right. I need to read it. Thank you.

MR STERN: Do not comment on it for the moment. If the Panel want to see it and they agree it, Mr Kark can see it...

THE CHAIRMAN: Can we keep the numbering since we have given it a number?

MR STERN: We will see whether Dr Goodman wants to see it or...

(*To the witness*). If you are ready I am going to start again at page 33 of your report, which relates to page 45 of Dr Donegan's.

THE LEGAL ASSESSOR: The Chairman has been handed a note by one of the members of the Panel and followed it up with a second note. I think it maybe that the member of the Panel has misunderstood the situation, but the question is: "Is it appropriate and correct for Mr Stern to use cross-examination as a tool to introduce a paper and not to question the witness?" As I understood it, the answer to that is that you are introducing it with the intention of questioning the witness; that is perfectly proper. Equally it is perfectly proper, of course, that Mr Kark should intervene and say, "I have not seen this and I may wish to object to its admissibility". I add that because the Panel member also said, "Please could my question be answered by the Legal Adviser in open session?" So

I answer it by saying that it appears to be a misunderstanding because you were introducing this for the purpose of cross-examining the witness.

MR STERN: I am afraid I used legal-speak rather than clear, plain English. The learned Legal Assessor and, I am sure, Mr Kark understood what I said.

(*To the witness*) Page 33 of your report and Dr Donegan's report at page 45. It is the middle paragraph:

> "In 1997 the Department of Health was said to be resisting pressure to introduce blanket meningitis vaccinations for university students".

I think that is the point that you refer to in your second paragraph down.

> "The source of the information is *Pulse*, a GP newspaper. ... unattributed. Dr Donegan fails to mention this refers to reluctant to use then ... the new vaccine rather than the conjugate vaccine under development".

That is the point that you were making, that is what it says there?
A Yes. They were reluctant to use the current vaccine rather than the conjugate, yes.

Q I think the point in relation to this is, if you look at that whole paragraph, and she quotes the part; the problem is that several hundred thousand students would need to be vaccinated when the incidents of the disease is actually very small. If you follow that up with the next sentence, that there is an advice against routine vaccination of 8,000 new students because there is no clinical evidence to support it. I think the point she is making, if I may say so, is not in relation to either vaccine but that incidents of the disease is so low, in other words it is a point about the severity or incidents of the disease rather than the issues in relation to the particular vaccinations. Does that make sense to you?
A Yes, in part. It would be one of the reasons, yes.

Q I think we have looked at reference 73. I do not think we have actually looked at 74 of Dr Donegan's report which is the other Pulse article, if we can just look at this very quickly, if we can. So we can see where it has come from, in the left hand column there is a suggestion that all new students have Group C meningitis vaccination before they enrol.
A I am sorry, there are two articles.

Q I am sorry, I am at the top, I beg your pardon. If you go to the middle paragraph:

> "The question of payments is further complicated by the fact that students are being urged to seek vaccinations from their own GPs before they move to university towns"

and then at the foot of that column:

> "Southampton LMC chairman Dr Nigel Watson said they advised the health authority against routine vaccination of the 8,000 new students as there was no clinical evidence to support it".

I think if you look at the lower section, if you follow that particular paragraph right the way down you will see the third paragraph down:

> "A department spokeswoman confirmed that routine vaccination of students was not in line with national guidance".

A Yes, it says that.

Q Page 33 of your report referable to page 46 of Dr Donegan's report. Paragraph 2 of Dr Donegan's report is the relevant part:

> "By the summer of 2000 the CSM advised" ...

Can you just remind me what CSM is?
A Committee on Safety of Medicines, so it is where you send the yellow card reporting.

Q So what does the Committee on Safety of Medicines do?
A The Committee on Safety of Medicines oversees various aspects of safety and one of the things that they do is ask doctors and now nurses (in fact, it started about then for nurses) to report when they feel that something following a medication, so vaccine or drug, might be related to that drug.

Q Do they have the overriding decision, as it were, on the safety of medicines?
A I am not sure of the intricacies because there is another linked body.

Q

> "By the summer of 2000 the CSM advised that further side effects should be added tot he product information of the vaccine in relation to older children and teenagers"

and then there are various side effects. You have no criticism of that.
A No.

Q But it is this part that needs to be underlined:

> "Neck stiffness and photophobia have also been reported and convulsions a rate of one report per 100,00 doses"

and then it is pretty obvious it is a typo.
A It is a typo, yes.

Q Your complaint is not the typo. Your complaint in relation to it, although you mention it in your report, is that the article also contains a further paragraph which we had better look at. So can we look at Dr Donegan's references at divider 76, please. What I will do if it helps is to point out the paragraph that Dr Elliman has referred to, first of all, and then look at the article with you. If you look at the penultimate paragraph it begins "seizures have been reported" if you want to just bracket that paragraph. That is the

paragraph that he has cut and pasted, if you like, into his report.

Your complaint which is set out at the bottom of page 33 of your report:

> "Thus, while seizures have been reported after the vaccine, they have not been proved to be due to the vaccine",

although Dr Donegan has said no more than "have also been reported".

A Yes.

Q You say:

> "Selective quoting from this source could be misleading and she has again failed to distinguish between a temporal and a causal association".

That is your comment. So it could be misleading. Let us have a look at this report. "Current problems" is its heading. "Safety of meningococcal group C conjugate vaccines" and then it says at the top:

> "The balance of risks and benefits is overwhelmingly favourable".

A Yes.

Q So that is, as it were, the opinion of the writer.

A Yes.

Q

> "In November 1999, a mass national immunisation campaign to vaccinate all children under 18 years with the new meningococcal group C conjugate vaccine",

so this is the one you were telling us about before.

A Yes.

Q Then it says:

> "So far 2 vaccines have been used .... recently licensed and due to be used later in the year".

Can I just move to the third paragraph:

> "By 1 June 2000, the MCA/" (which is presumably another committee) "CSM" (the one you have already told us about, Safety of Medicines) "had received 4,764 reports of patients experiencing suspected adverse reactions to the meningococcal group C conjugate vaccines. This corresponds to a reporting rate of 1 per 2,875 doses distributed."

In the following paragraph:

> "After reviewing the data, CSM has recommended that the following adverse reactions are added the produce information of both vaccines in relation to older children and teenagers: nausea, vomiting, rash, malaise, lymphadenopathy"

I do not know what that is, what does that mean?
A It is enlargement of the lymph glands.

Q

> "Headache, myalgia and allergic reactions including anaphylactoid reactions"

which were reported rarely, as we can see. Then the next paragraph:

> "For infants and toddlers the safety profiles of the vaccines were well established at the time of licensing. The product information states that symptoms such as crying, irritability, somnolence, drowsiness, impaired sleeping, anorexia, diarrhoea and vomiting" (it sounds like an ordinary teenager!) "are common after vaccination but that there was no evidence to suggest that these are related to the meningococcal group C conjugate vaccines".

Then the paragraph that you refer to:

> "Seizures have been reported very rarely, with approximately 1 report per 100,000 doses distributed. Some of the reported seizures may have been faints, febrile convulsions, or co-incidental. A causal association between seizures and the meningococcal group C conjugate vaccines has not been established. The CSM has recommended that a statement to reflect this information should be added to the produce information".

So although there was no causal connection it was to be added to the product information.
A I must admit, I have not followed up what was to be added because if you add the whole paragraph it would start from seizures and then a causal association and I am assuming they added that paragraph in toto, but I have not actually looked to see what is currently on the patient information leaflet and the SPC which goes in the vaccine.

Q Then it says:

> "The vaccines appear to be safe and effective".

That is all it says, is it not?
A It is.

Q Next, please, page 34 of your report and this relates to page 46 also and is the last comment in meningococcal. The fourth paragraph of Dr Donegan's report and we can

start that paragraph halfway through if that is all right with you, Dr Elliman.
A Yes.

Q

> "When used on US forces the incidence of meningococcal C disease was reduced two to three times but the total meningococcal acquisition rate was essentially the same regardless of vaccine status."

Then this is the comment I think that you criticise:

> "Thus, the vaccinated recruits, although protected against group C organisms, acquired meningococci of other serogroups. In fact, the attach rate of group B meningococcal disease was higher among the vaccinated recruits".

A No, that was not the only point. I am not sure if I made it clearly.

Q I am coming to your points here because they are in the paragraph so we will deal with them. If I have misunderstood it, it will be clear when we look at the paragraph and you can explain to us where I have gone wrong. If you look at the paragraph there later on page 46 you deal with the account there and you say:

> "Her account is confusing and could be read as meaning that overall disease due to the meningococcus was unchanged as there was a reduction in disease due to C and an increase in B. This was not the case."

Then the reference, you say, is clear.

> "Acquisition of serogroup C fell and that of serogroup B rose"

And then you set out the figures there for that.

> "However the authors point out that 'the number of cases of Group B disease were too small to permit statistical analysis'."

Then I think your last sentence:

> "Therefore there was an overall reduction in disease due to meningococci. This is not the impression one may have gained from Dr Donegan's account".

Have I misunderstood what you have said?
A No.

Q Can we just deal with this because it is not an easy issue but the point that Dr Donegan is making I think in her report is correct, is it not, that you acquire or one has acquired meningococci of other serogruops?

A There are a number of points that Dr Donegan makes. One of them, if we start "when used on US forces" which is the fourth line "the incidence of meningococci C disease was reduced two to three times". In fact the incidence of disease was reduced by about ten times. There is a difference between disease which is you manifest the symptoms of something and the acquisition of the organism which means it is just sitting in your nose and throat and I think it is, as you say, a complex paper which talks about both those things.

Q We had better have a quick look at the paper if we could, please, at tab 77. Can I just ask you this? If from the sentence you have just referred one deletes the word "disease" and inserts the word "acquisition" does that make more sense?

A It does, because, as I say, the disease rate was even greater.

Q Then that is for Dr Donegan to explain and not for me to ask you, because obviously that is for her. We had better look at the paper anyway just so we can try and follow some of it.

> "Prevention of meningococcal disease by group C Polysaccharide Vaccine".

A So this is the old vaccine.

Q Right, thank you. Just looking at the abstract on the top left:

> "Group C meningococcal polysaccharide vaccine was administered to 13,763 Army recruit volunteers at five basic training centers ... no systemic reactions to the vaccine developed in these men. Thirty-eight bacteriologically proved cases of Group C meningococcal disease developed in the nonimmunized men; only one such case occurred in a vaccinated recruit".

A To be fair, if you look at that, that seems, what, a ratio of 38 to one, but there were different size groups so it is a lesser effect.

Q On the following page which has 418 at the top it says:

> "Finally, the experimental nature of the vaccine required that informed voluntary consent be obtained from the recruits"

And then at the foot of the next paragraph:

> "After receiving the meningococcal vaccine, the volunteers were given the mandatory vaccines (influenza and tetanus toxoid) along with the rest of their platoon".

A This is an era when certainly in the American forces consent was a novel idea. That is why they have written it there, I think.

Q Can I just turn to page 419 and just deal with this one paragraph and then leave

this paper, for my own sanity if not anybody else's. Just looking at the left hand side in the lower half and I apologise again that not all of it is clear:

> "It should be noted that whereas Group C acquisitions were reduced two to three times, the total meningococcal acquisition rate (per cent of recruits acquiring a meningococcus during the eight weeks observation) was essentially the same regardless of vaccine status. Thus, the vaccinated recruits, although protected against Group C organisms, acquired meningococci of other serogroups."

A Yes and it is important to remember we are talking about acquisition again.

Q Just on the right hand side above "Discussion" just to complete the picture it says:

> "On the other hand, there was no reduction in disease due to Group B meningococci among the vaccinated recruits. In fact, the attack rate was higher among them although the number of cases of Group B disease was too small to permit statistical analysis".

A Yes, it refers to the table above and it is very, very small numbers.

Q That is the point you make in the report that it is a small statistical analysis.
A Yes.

Q I think that ends meningococcus. I am going to move to measles. Page 35 of your report relates to page 49 of Dr Donegan's report. This is the egg allergy point. It is the second line down, a short point:

> "It is cultured on chick embryo so severe egg allergy is a contraindication".

A Yes. Would it help if I say that that is a point that I would not wish to pursue?

Q Let us move on, thank you.
A I think it would not be useful.

Q That saves at least one document. I should just ask you this, please, about page 35, not relevant to any particular point, but I notice in the middle paragraph your comment, and it may not matter very much what it is about, but you say:

> "Dr Donegan is correct in saying that 99% of the reduction in measles deaths occurred before the introduction of measles vaccination. Various 'social' changes have taken place to cause this, however examination of **appendix 7** will show that deaths seemed to have plateaued from the mid 1950s until the introduction of measles vaccine in 1968 when there was a further fall, suggesting an effect of the vaccine".

That is a temporal suggestion, is it not, that you are relying on there?

A It is one part of the evidence, yes.

Q So, as I understand it, you are relying on that as a temporal ----
A No, I am not relying. I say it is one part of a whole gamut of evidence that you would use. I will not use this as evidence. If I was producing a report about the effectiveness of measles vaccine I would not use this, I would go back to trials, as we have discussed earlier.

Q It is just the wording you use that says it suggests an effect.
A It does, yes.

Q Page 36 in your report, referable to page 49 also in Dr Donegan's report, second paragraph down. This again is not without its complexity.

> "Measles disease may depress cell mediated immunity".

Can I just pause there for a moment? Where it says "cell mediated immunity" is that as opposed to antibody immunity?
A Yes, the two do have cross linkages, if you like.

Q I will try and keep it as simple as possible:

> "Measles disease may depress cell mediated immunity for up to three years. The vaccine virus is attenuated"

(in other words weakened)

> "but has similar characteristics to the wild virus so it would be expected to have the same characteristics."

I do not think you would have a problem with any of that?
A No, the issue would be degree.

Q Yes.

> "Indeed a high titre measles vaccine used in populations in Africa caused higher death rates in girls from other infectious diseases compared to boys or unvaccinated girls. To give a vaccine that has such an effect on the immune system at the same time and in the same needle as two other live viruses is, in my opinion, risky."

That is what Dr Donegan says. Let us look at what you say so the Panel have it. You have no problem with anything that she has actually said, but in the last two lines or so of that first paragraph you say:

> "However she implies that the measles vaccine, using MMR, would be expected to also cause depression in immunity. In fact the conclusion of the paper quoted..."

A

And then you quote the conclusion, which says:

> "Reduced general cell mediated immunity may contribute to the higher long term mortality in children..."

You go on:

B

> "This shows that measles vaccine does not have the same characteristics as the disease, or at least not to the same degree, thus..."

This is a criticism not really of anything she has said but just her reasoning, I think is what you say there?

C

A My criticism is that the paragraph as a whole could be taken to refer to measles vaccine that we use. It does not. There are very major differences between the high titre vaccine and the vaccine we use.

Q Can we just deal with the point? She points out that the disease may depress immunity, and you agree with that?

A Yes.

D

Q She points out the vaccine has similar characteristics but is attenuated, and you agree with that?

A Yes.

Q And she makes it clear that what she says in the last line is in fact her opinion?

A Yes.

E

Q Shall we look at tab 85 of her references, please, which is the relevant one? I am in danger of being slightly away from home, with this being a Guinea-Bissau case?

A It is an enormously complicated topic anyway.

Q It is enormously complicated; I am already put off by it, but I will just try and have a quick look at it, if I may, please, with you. Do I understand that in relation to the 270 cases of people who had measles, 109 were vaccinated? Can you remember in relation to this paper?

F

A No, I cannot remember specifically in relation to this paper.

Q I think if we look at page 5 at the top in relation to results – I am not quite sure where I have got those figures from. Page 76, I think. Shall we look through and Dr Donegan will no doubt be able to tell us where it is in due course – my reference has gone askance there. Can we go back to the first page:

G

> "Objective: To investigate whether children who have had measles have reduced general cell mediated immunity three years later compared with vaccinated children who have not had measles.
>
> Subjects: 391 children, 3 to 13, who were living in Bissau during a measles epidemic in 1991 and still lived there. These included 131

H

A

primary cases and 139 secondary cases from the epidemic and 121 vaccinated controls with no history of measles.

Main outcome measures: General cell mediated immunity assessed by measurement of delayed type hypersensitivity skin responses to seven recall antigens."

B

The conclusion at the bottom of that page:

"reduced general cell mediated immunity may contribute to the higher long term mortality in children who have had measles compared with recipients of standard measles vaccine and to the higher child mortality in the rainy season in west Africa."

C

A That is implying there is a difference between the measles vaccine and measles disease.

Q That I think I have understood. Could we look at page 8 of the report, second line down:

D

"Overall, 109 of the 270 cases were clinical vaccine failures."

What does that mean?

A That means that they had the vaccine but they developed the disease.

Q At the foot of that page:

E

"After exclusion of vaccine failures the reduction"

- so once they were excluded –

"the reduction in the mean number of positive reactions was 16% in primary cases and 25% in secondary cases."

F

Yes, but I am reading that paragraph without knowing what the reactions were to and what the significance is.

Q Can we just look at page 11, because there are some explanations given there for it. The second paragraph says:

G

"There are therefore two possible explanations for our findings. Firstly, measles caused suppression of general cell mediated immunity---"

A Sorry, it does not say what findings they are referring to because we have talked about skin tests and all sorts of things. I think it illustrates it is very difficult when you just take a paragraph out of something to understand what it is about.

H

Q Which is why I have said to you on many, many occasions if there is a part you

A want to refer to---
A No, because this is a very complex thing and without actually going through the whole paper it would be quite difficult, and that is why I took the conclusion from the author's abstract.

Q I think the point you make is that this is an extremely complicated area?
B A Yes.

Q I will leave it. We can look at it in due course in any event. If you do not feel sufficiently prepared to talk about that, we will move on.
A If you want, I will read it up over the weekend and come back and talk about it on Monday.

C Q That would be helpful; if you look at it and then we can see whether or not we want to come back to it.
A Okay.

Q Thank you very much. At the foot of page 36 of your report, page 52, I think, of Dr Donegan's report, the short point in the middle paragraph, third line down:

D
> "After the campaign the incidence of measles was said to have been dramatically reduced but this would have been the case if only the new specific salivary test had been introduced as doctors are notoriously poor at diagnosing acute spotty rashes. In the recent Irish epidemic only 430 out of 1500 cases were actually confirmed as measles."

E That reference, I think, as the Chairman has already pointed out, should be 17 rather than 18. Then the words:

> "Despite the purposed success of this campaign a second dose (pre-school) of MMR was introduced in October 1996 to the UK schedule."

F Your complaint, I think, is in relation to the word "despite"?
A Yes, that is one of the issues I picked up.

Q I am looking at your report; obviously I can only respond to your report?
A I picked up the issue of notifications and salivary testing at the bottom of page 36
G of my report.

Q You said she is a bit confused about that---
A Shall I go into that?

Q I do not know. I can only work on what you have written in this report. If there is something more...?
H A No. As I have written in my report, notifications are based, as I have said before, on a doctor suspecting a disease. Salivary testing is a separate thing. They are not part of the numbers that are in the notifications in the sense that you do not do salivary testing

before you do a notification, so if a notification has changed it was not because of salivary testing.

Q I think your comment in your report is that it is the word "despite" is the one you say is not appropriate?
A Yes.

Q Because you say, at 37, I think it implies there is something not quite right with the vaccine?
A Yes. It suggests that even though we did that, we still had to go ahead.

Q You do not think that is a little bit quibbling?
A You could argue that, yes. Yes, is the answer to your question.

Q Shall we move on, please? Page 37, the next paragraph down on page 37, it is the middle paragraph there; it is a long paragraph but I think we can deal with the point that you deal with shortly. It is in Dr Donegan's report at page 52:

> "The Department of Health's Immunisation Handbook 1996 states that, 'Before 1988, more than half the acute measles deaths occurred in previously healthy children who had not been immunised.' This is very misleading"

says Dr Donegan, and she then refers to a paper by C Miller – not my solicitor, I am sure, but by a senior epidemiologist.

> "There were 270 deaths of which 126 were in people with severe pre-existing conditions"

- and then Dr Donegan sets those out – cerebral palsy, etcetera.

> "As in most outbreaks about half or more of those with measles have been vaccinated it is rather misleading to imply that all the cases of measles were unvaccinated, also, most people would agree that there is a gradient between such severe medical conditions and 'health'."

I have not actually asked the Panel to underline something because I am not entirely sure that I have understood your point on this, so perhaps you would like to help us. You set out what it is that Dr Donegan has said and then halfway down that large paragraph you say:

> "...she concedes that in UK between 1970 and 1983, when there were still significant numbers of deaths from measles, Christine Miller reported that in over half of these, the children had no underlying medical conditions."

That is the paper she refers to?
A That is true, yes.

A

Q And produced?
A Yes.

Q You say:

> "Dr Donegan argues that the children may have had more subtle problems affecting their immune system. This is pure supposition for which there is no evidence."

B

That, as I understood it, is your criticism about that?
A My criticism is partly that but it also could be said of the children in question, because I think what Dr Donegan was saying was that you are either healthy or not – there is a gradation, yes, between such severe medical conditions, which is the ones that would be reported, and healthy, and it may be that there are children with other conditions that were not picked up which could have affected their immune system. That is what I understand by her "gradation". It is not one or the other. That is what I understand by "gradient".

C

Q It is the "subtle problems" – that is the bit I am having difficulty with – that "Dr Donegan argues that the children may have had more subtle problems". Just help me with where that is?

D

A She has not used those words. The words used are "severe medical conditions and health". Gradation: there are children, as quoted, with cerebral palsy etcetera, but there are children with what would be considered with not severe problems. My understanding was that Dr Donegan is arguing that there may be children with minor problems whose immune system is affected, and those would not have been picked up in Christine Miller's paper. If I have got a wrong understanding that she was saying "No, those children aren't a problem", I do not understand the gradient.

E

Q It may be we will have to come back to that, because I was not clear what your comment was. I am obviously not entirely sure exactly that I can deal with it. Perhaps we can look at your reference at divider 30. This is the paper, is it not, of Christine Miller?
A It is the one that Dr Donegan refers to, yes.

F

Q Yes.

> "The annual number of deaths attributed to measles on death certificates fell from 39 in 1970 to 17 in 1983, but the ratio of deaths to measles notifications showed no declining trend over the period."

G

Then there is "Methods and results", and it is quite a narrow definition, is it not, in the right-hand side, second paragraph up, of the pre-existing conditions?
A It is difficult without a full description of the study. I think those are the conditions they found. They did not set out – I do not know because the methods are not here in detail – if they had a pre-set list and if you fell in to one that is okay, or if they just looked and saw what the children had.

H

Q Can we look at divider 84, please, of Dr Donegan's references? I recall now the point you were making. You in fact deal with it in your report. If you turn, please, to the

second page of that – you will have to turn it on its side – if we look at the top it says:

> "Before 1988, more than half the acute measles deaths occurred in previously healthy children who had not been immunised."

A It does say that, yes.

Q That is a quote that Dr Donegan has included in the paragraph that we have just looked at – it is right at the top?
A Yes.

Q What she is saying is that that is misleading when one looks at the paper by Miss or Dr Miller?
A Yes.

Q If we go, please, to what is page 72 in the bottom right-hand corner, I think you were making the point that it is not clear that they were relying on Dr Miller's paper?
A Yes.

Q If we look at page 72, we can see the fourth reference down, "Surveillance of symptoms following MMR vaccine in children" – Dr Miller's paper, I think?
A That is a different paper, I think.

Q I have been led astray – that is the wrong paper.
A Is it worth making a comment that the references are not the full background that they would have relied on and unfortunately they do not number the reference to fit the text either?

Q I am told it is the previous page, 71, second reference down.
A Yes.

Q I think that just deals with your point at page 37 of your report, the penultimate paragraph, where you say:

> "It is not clear that the Department of Health relied solely on this evidence for their statement."

A Yes.

Q But I think it is clear that they obviously relied to some extent on Dr Miller's research paper?
A Yes.

MR STERN: If we move on, please, to the foot of page 37 dealing with page 54 of Dr Donegan's report. In the larger paragraph just below half-way Dr Donegan says, "A report in the *BMJ* ... stated that after the 1994 measles rubella campaign".

THE LEGAL ASSESSOR: I am sorry, it may not matter in the least or I maybe being stupid, but you referred to the second reference down on page 71 as being – which is a

reference to the *BMJ* 1985...

MR STERN: I am told that is the reference of the paper.

THE WITNESS: The title is slightly different, but...

THE LEGAL ASSESSOR: Is that *this* paper?

THE WITNESS: No.

MR STERN: No. It is the paper of Christine Miller that was referred to by Dr Donegan in the paper.

THE WITNESS: In that, which is some pages from a book in the list of references, almost at the back there is one that refers to the paper by Christine Miller.

THE LEGAL ASSESSOR: Thank you.

MR STERN: Thank you for clarifying that. (*To the witness*) Going back to that paragraph:

> "A report in the *BMJ* ... stated after the 1994 measles rubella campaign there were 530 severe reactions reported",

that is the first point. You say in relation to that a number of points, basically. If we a look at the bottom of page 37:

> "Dr Donegan refers to the paper by Dr Cutts on 'revaccination against measles and rubella', however she is very selective in her reporting. Dr Cutts refers to 'suspected adverse reactions' but Dr Donegan omits 'suspected'",

but she has put there "reported". Is there a difference between "reported" and "suspected?" If one looks at the paper in fact they use both terms, if I may say so. We can look at it if you want...

A No. I think it is what we have talked about previously, really. If you leave out a word "suspected", to most people that adds a stronger basis to what you are talking about. If you put in "suspected" that makes the element of doubt stronger.

Q Are you evaluating this (because I think we need to be clear about it) in terms of what you as an expert, using your expertise, are giving us an opinion about, which is what you are entitled to do, or are you telling the Panel what ordinary people would believe by looking at it, which is not expert opinion at all?

A I am pointing out to the Panel where I think there are important omissions that the Panel should make that decision on because I think – as you will, well, perhaps not... I have had experience of being selectively quoted and you can change the meaning considerably not because it is inaccurate but because you leave out caveats, riders, *et cetera.*

Q Of course?
A That is my complaint, if you like.

Q I think the Panel needs to know (and as a matter of law we have to have this clear) whether you are telling us as an expert or whether you are just saying...
A I am pointing out a difference that if I was refereeing a medical journal I would certainly pick up on, if someone did not distinguish between something that was "suspected" and...

Q And something that was "reported"?
A Yes.

Q That is your comment on that; that the words "suspected" and "reported" are not the same. Let us look at the next point. If we look at the papers at Dr Donegan's reference 98, "Revaccination against measles and rubella". Your second comment is that Dr Cutts also points out that the rates of most serious neurological reactions are less than the background rates of these illnesses and the fact that they are omitted by Dr Donegan, yes?
A Yes.

Q Can we look at this paper then, please? It says at the top, "Side effects are outweighed by improved disease control", that is the headline, which is the opinion obviously of the writer rather than... Well, it is the conclusion of the writer, if you like?
A Yes.

Q The data itself we can see at the second paragraph (or the relevant part of it):

> "By the end of October 1995, Britain's Committee on Safety of Medicines had received 1202 reports describing 2735 suspected adverse reactions to the vaccines administered in the campaign among which 530 were serious, though none was fatal".

Then further down:

> "There were 91 reports of serious neurological reactions (including 61 reports of convulsions); but reported rates",

and then it sets out a number of diseases.

> "The one report of sub-acute sclerosing panencephalitis occurred one month after vaccination in a child with a history of wild measles infection some years earlier".

I think that finds its way into Dr Donegan's report, that particular part?
A Yes.

Q Again the opinion of the writer is that it is unlikely that the vaccine was responsible?
A Yes.

A

Q

> "The need to appraise risks as well as benefits is an obligation for vaccination programmes, but the difficulty in attributing causality to events that are temporally associated with vaccinations is well-known".

B

Then further down it says:

> "...case reports or observational studies. These either have no controls or have an opportunistically selected control group, which may lead to unmeasured confounding. Passive surveillance systems are subject to underreporting and information on long term outcome is often not available. The incidence of events in a specific period after vaccination can be compared with average background rates in the same period to derive an attributable risk related to the vaccination".

C

This is the point that I want to draw to your attention:

D

> "But clinical events are often ill defined and case definitions are rarely standardised in different data sources"?

A Yes. That is what she says.

Q When you say "she", you mean Dr Cutts?

E

A Dr Cutts, yes.

Q Presumably, if you were to include that the rates of the most serious neurological reactions were less than background rates of the illnesses, you would want to put in that the clinical events are often ill defined, would you not?

A No, because those are well defined. Those are severe events. Encephalitis, convulsions and Guillain-Barre; there would be no doubt that a child had it and they would be admitted to hospital. There would be actually a high accuracy in those particular things.

F

Q How many of those then?

A There were 91 reports of serious neurological reactions that were, in fact, lower than the expected background rate.

G

Q Yes, but 91 of those – you cannot just select the 91, can you?

A Well, I have referred specifically to the serious neurological reactions because those are the ones that are likely to be the serious end of the serious reactions and the ones that might cause a long-term problem.

H

Q Looking over the page so that I can clarify the point that I was making before, third line down:

A

> "Expert committees in the United States have reviewed the evidence on serious adverse events associated with measles and rubella vaccines. For measles, mumps and rubella vaccines they concluded a causal relationship was established for anaphylaxis",

it then gives the figures,

B

> "and death from infection of measles vaccine strain in immunocompromised children. They noted a theoretical risk of death .... The data were inadequate to accept or reject the causal relation with various other diseases".

The third point that you have made at the top of paragraph 38 is that, "She also suggests
C that the case of SSPE was unlikely to be due to the vaccine"; that is Dr Cutts, assume you mean by the "she"?
A I do, yes.

Q And not mentioned by Dr Donegan, we can see. Is it right that the report of the child with SSPE, the child had had measles, yes?
A Yes.

D

Q Therefore, it was obviously as a result of natural...
A Yes. Natural – well the child had natural wild measles and, therefore, developed SSPE and the immunisation was incidental.

Q Or it related to the immunisation; it must be one of the two, must it not?
A Well to say "or" suggests that there is a possibility of that happening. Now there
E is a very, very small possibility but what Dr Cutts was basing her opinion on was the fact that when people have analysed the brains of children who die of SSPE you find measles virus in them and in all cases it has been wild measles virus, not vaccine virus. As you remember, when we have went back to saying you could never, never prove a negative totally...

Q Yes, of course?
F A ..so that was why she came to that opinion.

Q Help me with where it says that in the papers?
A She does not give the rationale behind her opinion.

Q How is one supposed to know that?
G A One is not, as a non-expert, supposed to know that. She is an expert who has being interpreting the evidence; if you wanted to question her you would then go to the literature.

Q But it is not obvious on the face of this document?
A No, but she is very clear in her opinion even though she does not give the evidence
H for her opinion. She does specifically say...

Q "Side effects are outweighed by"...

A No, no. When we were talking about the SSPE, which is the second major paragraph.

Q Yes?
A The last sentence.

B Q Yes?
A She ends up saying, "Thus it is unlikely that the vaccine was responsible", so that is her opinion of the aetiology of the child having SSPE, but I grant you she has not put in...

Q So we are clear about this and have this in its context, going back to page 53 of Dr Donegan's report you will see two or three lines down it says, "Documented side
C effects of the MMR vaccine", so it is under that subheading that Dr Donegan has included all of this – well the next few pages really. Can you see that?
A I can see that, yes.

Q Looking at the foot of page 54, please, Dr Donegan has made it clear, has she not, that there is a noted theoretical risk of death from anaphylaxis or thrombocytopenia but no direct evidence; so she has made that clear. Do you have that?
D A I do have that. I am just trying to remember when that particular reference was published because thrombocytopenia is not a theoretical but a real risk and there is research to show that, as Dr Donegan herself has said.

Q Over the page she has also set out that:

> "The data were inadequate to accept or reject a causal relation with:"

E

A That is so, yes.

Q And she has underlined "causal"?
A Yes. And "reject".

Q Yes?
F A Not "accept".

Q Yes, but the point I am drawing to your attention is that she has actually used the word "causal" in the particular circumstances....
A In a later point, yes.

G

Q Obviously making the distinction. Page 38 of your report, please, the middle paragraph records Dr Donegan's page 55, penultimate paragraph, this is the study in France.

> "A study in France concluded there is sufficient evidence of a clear temporal relationship between MMR vaccination and the occurrence of ITP",

H

which is what it is, is that right?

A That is right.

Q I will not pronounce it. "...to make a causal relationship highly plausible". Your comment in relation to this is in the middle paragraph of page 38. You say:

> "(ITP) is a condition in which the number of platelets in the blood is reduced. This leads to a tendency to bruise easily and bleed. MMR vaccine is causally related to ITP",

so in fact she is more cautious than you in that regard?
A Possibly so.

Q Well...
A If you could just tell me exactly what her words were again I will...

Q Her words were "There was a clear temporal relationship" and "to make a causal relationship highly plausible", but you have actually gone one stage further and said that there is a causal relationship?
A Yes.

Q In relation to this particular point?
A Yes.

Q Can we look at Dr Donegan's divider 99? This is the 1996 paper and it deals with, "TP after vaccination with measles, mumps and rubella has occasionally been reported". Then over the page on the left-hand side, the conclusions:

> "According to the clinical course and biologic findings, vaccine-associated TP appears to be similar to that occurring after natural measles or rubella infections and is not distinguishable from acute childhood ITP not associated with vaccinations. Such observations, combined with a clear temporal relationship between measles ... make a causal relationship highly plausible",

and she has recorded that in her report?
A Yes.

Q I think you say that there is a later report?
A My comment here was not that I disagreed with the conclusion, but if I was producing a report I would go to the highest level of evidence because, as is said here, what they were basing things on was a temporal relationship and what is called a "biological plausibility"; we know it happens with the disease, therefore, it is reasonable to assume. Whereas there was research from this Country – actually I think it was published in the same year in 1996 – that was a much better standard of evidence and was a much higher standard of proof, if you like, and, therefore, it would be a better basis on which to advise somebody.

Q But she has not quoted it and not referred to it?
A No.

A

Q Again do you know if that is one that Dr Conway or Dr Kroll has referred to or not?
A I do not know, I am afraid.

Q Can we move on then please to the last point on page 38, which is referable to the
B last paragraph on page 55 of Dr Donegan's report. Dr Donegan says:

> "In the Avon longitudinal study, 27 children were hospitalised for febrile convulsions after MMR vaccination compared with an expected background rate of 16. Cases peaked at two weeks after vaccination with 14 admissions compared with an expected four".

C Your comment is that you accept what she says, but you say the reference is odd. Let us leave that aside for a moment because I think your criticism at the foot of page 38 is:

> "In the article Dr Donegan uses, there are two figures looking at the comparative risk after the vaccine – 27 cases in the first month after the vaccine as opposed to 16 expected and 14 in the first two weeks as opposed to four expected. Dr Donegan uses the latter figure. If
D presenting a balanced view she would have used either formal comparison or both"?

A Yes.

Q Can you tell me which figures are omitted?
A It is the bottom of page 55, "27 children were hospitalised compared with an
E expected background rate of 16". The 14 and the four. Now I have got it round the wrong way.

Q I am not quite sure – first of all, your criticism is that she is...
A The 14 and the four are the omitted ones. Dr Donegan quotes 27 and 16.

Q Look at the next...?
F A Sorry. I am in error, I did not realise that.

Q You presumably withdraw the suggestion that she has not presented a balanced view by putting the figures in there?
A I do withdraw the last bit of that statement. The source of things still stands.

G

Q Yes. Can we look, please, at page 39 of your report? The top of the page relating to the bottom of the page of page 56 of Dr Donegan's report. This is taken slightly out of order, I am afraid, in Dr Donegan's report. This is really, if one can summarise it, I hope fairly, a question of interpretation of studies.
A It goes back to the sort of standard of evidence.

H Q Exactly. You say it is not particularly great, putting it colloquially.
A Yes.

Q She has relied on it.
A Yes.

Q We will just look at it briefly, but that I think is the essence of your complaint. If I just draw the Panel's attention to the relevant part if they want to underline it so that they have it, it begins at the foot of page 56 dealing with the Steiner community. You might want to bracket it rather than underline it actually because I think it encompasses that whole paragraph and the next towards the end of the top of page 43, if that helps, and Dr Elliman's point on this begins at the top of page 39 "In talking further about the severity of measles disease" down to the end of "from this published evidence, it is clear that measles can be a very serious disease and has been downplayed by Dr Donegan". I think that covers that point basically.
A Yes.

Q I just want to give the Panel a bit of assistance obviously, because they are dealing with two very large reports and it is not easy. Can we just look at these then briefly. Dr Donegan's tab 102, please. This is published in Health 2001. I think this is a journal that you have actually written for or written to. Have I got the wrong reference? It is 102. It says at the top "Health 2001". Dr Elliman, you are looking confused.
A I have not as far as I am aware written anything for it.

Q Maybe I have got it wrong. I thought you said you had written something for Health. Is it "Health Which"?
A If it is, then, yes, I have.

Q Health Which.
A This is Health Which, is it?

Q No, I do not think it is. It does not say "Which".
A No.

Q

> "Attitudes of parents towards measles and immunisation after a measles outbreak in an anthroposophical community".

This is written by a GP, is it? Dr Duffell. Do you know who Dr Duffell is?
A No. He is probably not a GP because it is from the health authority, so he may be one of the local infectious disease people.

Q He is a doctor.
A He is a doctor, but I do not think he is a general practitioner.

Q The first paragraph:

> "The introduction of mass immunisation against measles in the United Kingdom" ----

A I am sorry, my puzzlement was at the title. The title of the journal is not Health. I think it is Journal of Epidemiology and Community Health. It has been chopped off.

Q

> "The introduction of mass immunisation against measles in the United Kingdom has seen the virtual disappearance of this disease. In some European countries with lower levels of vaccine coverage, however, deaths from measles are still common and the disease is associated with significant morbidity. In recent years adverse publicity surrounding the vaccine has depressed vaccine uptake in the United Kingdom. Parental attitude towards disease is known to be a powerful predictor of vaccine uptake. Indeed, reports from the Health Education Authority tracking studies of parental attitudes to vaccination suggest that confidence in the safety of MMR vaccine has fallen in parallel with vaccine uptake, and many parents now consider the vaccine to be a greater threat to their child's health than measles itself.
>
> An outbreak of measles among children from a predominantly un-immunised anthroposophical community in Gloucestershire provided an opportunity to explore parental views and study disease severity in this group."

This is the Rudolf Steiner group.

A Yes.

Q Towards the end of that paragraph it says:

> "Many adherents oppose the measles vaccine because they believe children gain physical and mental robustness from natural measles infection, when supported by appropriate nursing case".

So that is their state of mind, that is the stance they adopt.

A That is their philosophy, yes.

Q So let us look at the statistics, if we can. In the next paragraph, third line down it says:

> "A total of 126 questionnaires were returned, giving an overall response rate of 59%. Among the respondents the mean age of the cases was 7.9 years, the mean time off school was 14 days, 76 consulted their general practitioner, 61 received prescribed medication and one child was admitted to hospital. Some 62% of these respondents reported a change in their child's personal development subsequent to the measles infection, with many claiming a strengthening and maturing of their child both mentally and physically. Of the cases, 87% were reported to have been previously unimmunised with the measles vaccine."

Then "Discussion":

"The findings of low levels of morbidity associated with measles are similar to previous studies in the United Kingdom".

Is that right? There are previous studies that are similar?
A Yes, yes.

Q

"And support the notion that measles is not a severe illness in most children. These cases were, however, in fit, well nourished children from a community that advocates a healthy lifestyle and there were insufficient numbers of cases to observe many of the rarer sequelae."

Then a little further down:

"The observations from this survey suggest a more appropriate tack for vaccination campaigners may be to emphasise the safety issues of the vaccine and its effectiveness in a balanced argument. The results also suggest that, rather than simply repeating the scare tactics used in previous campaigns, it may be worthwhile exploring the views of vaccine refusers in more detail and considering alternative approaches to promoting vaccination in such groups."

There is a certain element, is there not, of truth in that, that although we are not dealing directly with the issue of whether to vaccinate or not to vaccinate, whether that is right or wrong, and you are obviously involved in this more than anyone else, but it seems as if there is almost no other subject that arouses the sort of polarisation of views in relation to vaccination?
A Vaccination certainly does arouse a lot of emotions in people, yes.

Q It is one of those few areas where debate is rather heated on both sides.
A Yes and there are lots of other areas but they are, shall we say, within the profession more.

Q Yes.
A Yes.

THE CHAIRMAN: Can I just point out that it is a female public health author, Dr Duffell.
A I am sure her science is just as good!

MR STERN: There are other papers, perhaps we ought to just look at those, in your references, as you are critical of these. Your reference is 32, 33 and 34. You set them out in your paragraph at page 39. I think there are a number of papers. It is perhaps not necessary to go through them. They are very short, just sort of headlines really.
A 32 is an account of Ireland epidemic.

Q Page 3 of 5 at the top we can just see:

"Measles outbreak in the Republic of Ireland: update".

A

I will just refer to one of these because they are not really full reports, are they?

> "Since the beginning of January 2000, there has been a large increase in the numbers of cases of measles notified in the ERHA area, as reported previously in Eurosurveillance Weekly.
>
> Altogether 844 suspected cases were notified between 1 January and 28 May 2000, compared with between 107 and 152 cases from 1995 to 1999. The last large outbreak was in 1993/4. The highest attack rate was in children aged 6-14 months ... So far, 101 children/patients have been admitted to hospital, six to intensive care units, and two have died".

B

C

I think the point you are making is that those show it is more serious.
A Yes and there are a number of them.

Q I have not gone through all them, but they all say the same thing.
A Yes and I think it is fair to say that in a study the size of the one that was referred to in the Rudolph Steiner population you would not expect to find any deaths because it is quite right, most people have measles and do not die.

D

Q Steiner was 126 people, was it not?
A That is right. You would not expect to find a death within that group from any of the statistics that have presented and there are sort of estimates of the order of one in 1000, one in 2000, so, as I say, statistically speaking you would not expect to find one in that group even if that rate was so.

E

Q The study that we just looked at, I think there were 844 suspected cases.
A Yes. That was part way through and what I have not put in would have been the detailed account because that was not published at the time Dr Donegan did her report.

Q I think you have made that clear in your report actually, that at the time of Dr Donegan's report the detailed analysis of it had not been published.

F

A That is right.

Q So obviously she would not know that. Can I just deal with the last point in relation to measles. At the foot of page 39 and the end of the first paragraph at page 56 Dr Donegan sets out at the top of the paragraph that she has not mentioned autism and in fact she does not go into it in any detail at all there, because she says there is much been said on it and at that time there was a large pending legal case.

G

> "Many of the arguments as to whether autism has increased since the introduction of the MMR vaccine rely on sophisticated statistical re-analysis of studies that were not set up to look specifically at whether there is a link or not. Autism, however, was not described as a disease until the 1950s"

H

and I think your point is, if we look at page 39, it was in fact described in 1943.

A That was the first description in the medical literature.

Q I think, to be fair, it was first described in 1943, but would you agree not widely described until the 50s?
A Yes, all right, yes.

B MR STERN: I think that ends measles and that may be a good moment to have a coffee break.

THE CHAIRMAN: Indeed. If we try and get back here at twenty past eleven.

MR STERN: We are definitely on track to finish the first report today.

C THE CHAIRMAN: Good.

MR STERN: So a counsel's estimate which might be accurate.

(The Panel adjourned for a short time)

(Discussion about timetable)

D MR STERN: Can we move on so far as mumps are concerned. Page 41 of your report. Page 58 of Dr Donegan is when mumps begins. At the foot of page 58 Dr Donegan is dealing with the swelling of various parts of the body and then in the last sentence:

> "In fact it is thought that having mumps with recognisable parotid swelling has a protective value against getting ovarian cancer in later years."

E You I think deal with that at page 41, as I say.
A Yes.

Q You deal with it and say halfway down:

F > "Dr Donegan suggests that mumps disease with parotid swelling has a protective effect against ovarian cancer. This is based on one paper from 1966 based on patients remembering whether or not they had mumps, and, as far as I am ware, there have been no studies to confirm this",

G But you say there is a study that comes to the opposite conclusion and you put the reference DE34. I think that is an error. It is DE36 actually. I am going to look at Dr Donegan's paper first which is Dr Donegan's tab 106. Just looking at this paper, we can see the abstract:

H > "A study of 97 cases of ovarian malignancies compared to 97 cases of benign ovarian tumours is analyzed. Between most of the variables there are no statistically significant differences. Three variables, however, are of special importance: (1) history of

A

> x-irradiation, (2) history of internalization of hormones and (3) history of mumps parotitis. In the first 2 variables no statistically significant differences were found....With the third variable a p value of 0.007 was encountered. The difference favoured having mumps."

B Then the final sentence:

> "A causal association with a possible protective value is suggested."

That is the point there, I think. So that is that. Can we just look at the second page of that report, which has 1002 in the top left-hand corner. The penultimate paragraph of that page, on the left-hand side:

C

> "Certain clinical facts concerning ovarian malignancies are striking. The signs and symptoms are few and, unfortunately, too late. The duration of symptoms has little effect on the prognosis."

Over the page again, at 1003, under the subheading "Materials and Methods", dealing with the study design, about four lines down:

D

> "The only exclusions were cases older than 75 years at the time of diagnosis, those cases having a co-existent malignancy of another organ that was not metastatic from the ovary and recurrent cases. Thus, all cases included had their origin within the ovary."

Then about four lines further down it says:

E

> "I interviewed each patient as soon as possible after the diagnosis was made."

Then "Definition of controls":

> "The controls were selected from female hospital patients matched
F for age, residence and date of surgery."

Then in the next paragraph – this deals, I think, with the point that you were making – you say it is based on one paper, which is this paper, and it is based on patients remembering whether or not they had mumps. That is your criticism of the paper rather than Dr Donegan, as it were?

G

A Yes.

Q Thank you.

> "Because the selection of controls is probably the most critical part of a case-history study, the cases and the controls were as comparable as possible in every respect except for the illness being
H investigated. A major assumption of this study is that the pt and the controls will remember or forget approximately to the same degree.

Thereby, no bias because of memory defect will occur."

So that is what the authors of the paper suggest?
A He says it is a major assumption, yes.

Q No, the assumption is that the forgetting will be the same as the remembering and therefore they balance each other out?
A Yes.

Q So although you have put it is based on patients remembering whether or not they have mumps, that is actually dealt with in the paper, is it not?
A This paper is one that is not blind, or at least it does not say it is blind, so the people who are involved in the study know what it is about. One of the reasons why you make a study blind is so that people are not in any way sensitised, shall we say? They do not know what you are asking, they do not know what it is all about. So in no way will they remember differentially. But if people know what a study is about, there is the danger that they will drag up things in a different way. That is my criticism; it is not a blind study and so you are relying on something that is fallible.

Q I was just dealing with the point that you had made in your report. You said, as I understood your criticism of this particular paper, that it was based on patients remembering and therefore the implication (I had taken to be) that because people forget, therefore they may have forgotten they had mumps and that would alter or unbalance the statistics. That, as I understood your complaint in your report at first---
A Sorry, I should have spelt out the two elements of the remembering that were a problem. One is the inaccuracy of remembering, certainly, and the other is the possibility of differential remembering if you know why you are being questioned and what people are seeking. That is why you would do a study normally blind so that the patients would not know what you are seeking. It may be that they did that, but they do not say they did it.

Q So the point you are making is a speculative one, as I understand it then?
A It is speculative on the basis that I do not know how it applies to this particular study.

Q In any event, dealing with the point you have put in the report, it seems as if the point you are making was taken into account by the person who did the study, the doctor who did the study, and he did allow for that?
A He thinks it is not a problem.

Q He thinks?
A Yes.

Q I can only deal with what he thinks. Whether it is objectively, one never knows
A Yes. If it was a study now, he would probably have used different methodology.

Q That may be. I am just dealing, as I say, with the comments you make in your report and whether they are dealt with in the report of the actual research – which they seem to be, on the face of it. Just so we can deal with the results section there:

> "One hundred, twenty-three eligible cases with malignancy were located from January 1, 1959 to March 31, 1960...The statistics of the malignant cases compare favourably with those with benign tumours with the exception that there were 7 deaths in the patient group and no deaths in the control group."

Can I just refer you to page 1007, which is the final page of that report? I think there is further mention of the point that you were just dealing with a moment ago – the top right-hand corner:

> "The third variable of particular interest is that of having had a clinically recognizable case of mumps parotitis. Here differences occur between patient group and benign controls and these are statistically significant. Can a patient recall if she has had a clinically evident case of mumps? This is speculative. But, as mentioned before, if patient and control pairs are chosen carefully, both groups should remember and forget in a random way and thus memory defect should not bias the outcome of this variable."

That is quite an important point in relation to the paper, would you agree?

A It is an important point that he makes but, as I said earlier, if someone was doing this study now or was critiquing this study, they would question his conclusion quite strongly.

Q That is that paper. Can we look at what I assume is DE36 rather than DE34? This is a paper that came to the opposite conclusion – yes?

A Yes. No, to be fair I think the point Dr Donegan was making was that if you had mumps and symptoms of mumps – so that is recognising the swelling of the gland – that protected you. I do not think she said that having mumps protected you, which is what this paper was looking at. You could have mumps without swelling of the gland but it would show up on the blood test. It is slightly different.

Q I was just quoting from your report, which is why I said that is what you were saying?

A Go on. Yes, okay. Then if you read my discussion.

Q You say that is not right; it is not the opposite conclusion it is something slightly---

A It is slightly different and I have tried to address this business of memory.

Q If you want to amend it, that is fine. Let us just look, please---

A Sorry. I do not want to amend my report. What I am saying is that I am trying to, as it says in this last paragraph, address the idea of memory and saying that a more objective way of getting at mumps would be to do this blood test. So this study is more likely to be reliable in terms of whether patients had mumps as it is based on blood test evidence rather than patients' memories.

Q As you have already said, the point is a slightly different one?

A

A Yes.

Q Let us just look at this report briefly, if we can. It is not terribly long. Just so we get, as it were, the headline in the abstract so we have it, it is in the second paragraph of the abstract, about five lines down halfway through:

B

> "No protective effect was associated with mumps virus infection. In contrast, risk increased significantly as serum mumps virus antibody titres increased."

I think that is the point of the paper?
A Yes.

C

Q If we look in the left-hand column about three lines down:

> "In China, the incidence of ovarian cancer is much lower than in most western countries, with the incident rate per 100,000 women being 5.0 in Shanghai and 5.8 in Hong Kong compared to 12.0 in Caucasian women in the San Francisco bay area."

D

Then on the right, "Material and Methods":

> "A total of 220 patients with newly diagnosed epithelial ovarian cancer occurring during the period 1984-1986 were identified through records at the Beijing Cancer Registry, a system designed to monitor all cancers in the Beijing metropolitan area."

E

About halfway down:

> "...116 cases were included in the study group, of whom 112 were interviewed and four refused to cooperate."

Three lines further down:

F

> "Because of the high nonresponse rate, we compared cases diagnosed during 1984 to the other cases and found no major differences with respect to the major identified menstrual, reproductive and medical risk factors."

G

So that is the background to it. Although I will not necessarily draw your attention to the particular passage, if you look at the next page there is a reference to excluding women with serious illnesses, so that is clear. If we turn now, please, to page 27 in the top right-hand corner, left-hand side, last paragraph:

> "Contrary to an earlier report, no protective effect of mumps virus infection was observed in this study, with 30 patients versus 69 controls reporting such a history. Furthermore, the mumps antibody titres of cases were significantly higher than those of controls."

H

A So there were none observed, I think is the way they put it there?
A Yes, and in fact I think you pointed out an error I made and that this study did actually look at the symptomatic mumps as well, so it was a direct comparison as well as the serology – so even stronger.

Q Look at the comments on the right:

B

> "The findings of this study must be interpreted in the light of three methodological limitations. Given the nature of cancer registration in China, some ovarian cancer patients may not have been ascertained for study, despite efforts to obtain a complete series by additionally reviewing hospital records."

C There are then a number of limitations in relation to the study?
A Yes.

Q Which are set out there. The third limitation is perhaps the most important one, about five lines up:

D

> "A third limitation was the exclusion of controls with current health problems. This exclusion should not have affected the results pertaining to childhood mumps or family cancer history, since it is unlikely that these conditions affected current health. However, it is possible that the exclusions could have affected the assessment of other medical conditions, e.g. thyroid problems.

E

> For these reasons, some caution must be exercised in the interpretation of certain results. However, since there is a paucity of data on ovarian cancer risk factors among women in low-risk countries, the results are of interest, particularly when compared with studies in other parts of the world."

So it seems as if there are other studies?
A I am not sure if they are based on history or serology.

F

Q Let us look, please, at the next page, page 28. Could you go to the right-hand side, about two paragraphs down:

G

> "Cramer *et al* suggested that mumps infection may cause oophoritis, leading to oocyte depletion and initiation of cancerous changes in ovarian epithelium. Although Menczer *et al* found that cases less frequently reported histories of mumps infection, we, similar to another study, observed no differences between cases and controls. In addition, we found exactly the opposite of Menczer, who reported lower serum antibody titres in cases than controls. Thus, our results provide little evidence for a protective effect of mumps virus infection."

H

So it seems as if there are other studies which tend to support the opposite view, or not?

A My reading of this is that the Cramer study was one that showed a link between mumps and cancer – not protection but a link between mumps causing cancer. The Menczer study suggests, as you say, that there was a lesser risk.

Q If was just that you have written in your report that you were not aware of any other studies?

B A That is true, yes.

Q Page 42 of your report, please, which is referable to Dr Donegan's page 59, and it is the last paragraph on page 59. I think we can deal with this rather shortly:

> "By 2000, cases of mumps were steadily rising... In some places such as Leeds and Bradford there were increases of nine times and
C 30 times the incidence between 2000 and 2001. One third of those affected were aged over 15, just the time when boys are likely to be made infertile."

If you just mark that particular part, that is the part we are concerned with. Your comment, at the top of page 42 – you deal with the comment first of all and then halfway down that first paragraph you say:

D

> "This is an age group who may not have received mumps vaccine at all, or only one dose. Nor will they have had the exposure to mumps as in previous generations. The rise in this age group is for these reasons and is not due to poor efficacy of the vaccine, although it is accepted that the mumps vaccine is the least effective of the three components of the MMR. The answer to the problem is to ensure
E that all susceptible people are immunised, not to withhold it."

That is your answer, I think?
A Yes.

Q How is it that you know that it is not as a result of the poor efficacy of the vaccine, which you accept it is?

F A Because people have looked at these groups by age, their immunisation history and have found what I have said.

Q But the vaccine does have a very low efficacy, does it not?
A It has lower than the others. It is probably about...it is debatable but shall we say
G 80 per cent would be a reasonable figure. Some people would say lower, some people would say it is higher at the beginning and then wears off, but of that order.

Q Lastly on page 42, this is referable to page 60 of Dr Donegan's report, the last sentence of the first paragraph:

> "There is a possibility that immunisation against mumps is causing a
H mutant strain to emerge with limited or no cross protection for the vaccine strain",

that is the part. Your comment in the middle. You quoted and then said, "There is no evidence to support this assumption". Yes?
A Yes, that is correct.

Q It comes from an article in *Pulse*?
A That is correct.

Q So it is the old *Pulse* point again?
A It is.

Q Can we look at 111 of Dr Donegan's references? If you can look, please, on the right-hand side about three-quarters of the way down you will see a sentence that begins:

> "The population among whom the current outbreak is occurring is mainly adolescents, the majority of whom, in Stockport at least, have received only one documented mumps vaccine; an MMR when it was first introduced in 1988. Many of the children also received an MR (measles and rubella) in the extended school programme of 1994".

If you can turn over two pages and goes to the middle block, I think it is already underlined to some extent there when Dr Donegan went through it?
A Yes.

Q You can see almost at the end of that block in the middle it says – well it is talking about G6 genotype:

> "Although this differs from the A genotype of Jeryl Lynn the advice from the Public Health Laboratory Service is that a cross-protection between strains should be sufficient. However, four of our confirmed cases have received two MMR vaccines and the remote possibility of a mutant strain (with limited or no cross-protection to the vaccine strain) selected out under pressure of immunisation should be looked into".

I think it also goes on to say that there should be two doses of the MMR?
A That is correct.

MR KARK: Can we identify the date for that?

THE WITNESS: 2000...

MR STERN: It is in the index. 2001.

THE WITNESS: I think it is 2001.

MR STERN: It is in the index. I have not given the dates to everyone because they are there for everyone to see.

(*To the witness*) It does quote some research there, does it not? I am not going to go back to it, but I am going to give you the research, please, if I can. Crowley and Afzal (*Same handed*); it is a paper referred to here.

THE CHAIRMAN: D13.

MR STERN: (*To the witness*) You can look at this over the weekend but it is a very short report. Let me draw your attention to the relevant parts and if you want to come back on anything on Monday that is no difficulty. Looking at the summary in the last few lines:

> "These findings raise the possibility of emergence of mutant strain under the selective pressure of immunisation, with limited or no cross protection induced by the vaccine strain".

Introduction, about five lines down:

> "In spite of good vaccination coverage in most developing countries, occurrences of mumps outbreaks is reported periodically. These outbreaks are usually attributed either to the presence of pockets of unvaccinated children or to primary vaccine failure in persons who do not seroconvert after vaccination or to waning vaccine-induced immunity. The possible role of different strains or genotypes of mumps virus in reinfection is not usually considered. Nevertheless, several genogroups of mumps virus have been described on the basis of nucleotide sequencing of the SH gene, which is the most variable part of the genome and the part that acts as a signature of the entire mumps genome sequence".

Then last line:

> "Recently we diagnosed mumps reinfection in adult female in whom there was an unusual antibody response with limited cross reactivity to other mumps virus strains belonging to different genotype groups".

If we turn over the page to the "results":

> "Mumps virus was isolated from urine selected from the 11-year old boy on his admission to hospital. However, serum collected on admission was positive for mumps-specific IgG though negative for mumps-specific IgM, suggesting previous infection or vaccination. In line with the National Immunisation Schedule the boy had previously received one dose of measles ... (MMR) vaccine and one dose of measles, rubella vaccine booster. Repeat serology four weeks after admission showed a significant rise in mumps neutralising antibody titre but the boy remained negative for mumps IgM confirming mumps reinfection".

A I am puzzled then by the date of the *Pulse* article because the *Pulse* article was

2001 and this is 2002 and David Baxter is using almost the same words. I know they work together...

Q I think – you may have heard Dr Donegan whisper that to me; that may be why and how it came about. Although it was not published until later, they had obviously done the research earlier?

A I presume so, yes.

Q Well, they would not have been able to write the *Pulse* article...

A Not unless there was something clairvoyant or something.

Q They maybe, but it looks as if they must have done the research and whatever it was in 2000?

A Presumably so, yes.

Q I am told...

A Do you want me to read this over the weekend?

Q If you would like to.

A Well, are you going take it further?

Q No. I am just making the point that there is research in relation to it, which I think you – although it was a *Pulse* article... I am just asked to draw attention to the last part, which I was going to but I got sidetracked by the dates. The last page on the right-hand side:

> "Reinfection with such mutants or their emergence under immune selective pressure in vaccines might account for some of the recent resurgence of mumps in the United Kingdom"?

A It is difficult, is it not, because there is an underlining just opposite that that says:

> "...both mother and son were infected with the same viral strain implying that host factors determine the immune response rather than viral genotype",

so it is difficult to know what to make of it.

Q Any way there certainly seems to be some basis for saying that there is a possibility that immunisation against mumps is causing a mutant strain to emerge?

A To be fair to the authors they say "remote possibility".

MR STERN: They do. Can we look, please, at the *BNF* for 1985-1989? (*Same handed*)

THE CHAIRMAN: That becomes D14.

MR STERN: Can we look, first of all, at the top of the first page, which I hope says, "Extract of British National Formulary 1985"?

A That is so.

Q Turning over page, please, to 14.4.7, "Mumps" and then it sets out the vaccine and it says at the top of the page:

> "Since mumps and its complications are very rarely serious there is little indication for the routine use of mumps vaccine"?

A That is so.

Q That was 19985. If we move on to 1986, fortunately the numbering of the paragraphs are the same so it is 14.4.7 and it has been circled, I think, for everyone?
A It has, yes.

Q It says exactly the same, yes?
A Yes.

Q Then 1987, it says, "Mumps vaccine is not at present recommended for routine use in the UK".

If we come to 1988; exactly the same.

In 1989 you will see it says:

"Mumps Vaccine

Mumps vaccine consists of a live attenuated strain of virus grown in chick-embryo tissue culture. See under MMR vaccine".

Although it was not necessary, according to the *BNF* at least, up until 1988, although it appeared not to be necessary prior to 1989, suddenly with the MMR vaccine it became automatic. Have I understood how it operated?
A You have understood the timescale of the introduction of the vaccine and where these comments fit with it, yes.

Q That deals with mumps. Can I move to rubella? Page 43 of your report is where it commences. Again I think this is rather short because you have one or two criticisms, I think, of this.

> "Rubella was once most frequent among children age five to nine but with the advent of immunisation programmes often directed primarily at this group as well as pre-schoolers, a greater proportion of cases is now being reported among older people (15-24) years".

Your comment we can see at 43 under the subheading "Comments on Dr Donegan's report". This is another one of our *Harrison* frame points?
A It is.

Q When you say that you look through and you cannot find it although the photocopy she provides is identical to the 15th edition and that would have been current.

A You then go on to say, "It is worth noting that the text Dr Donegan presumably used (11th edition)"; so presumably you found this, did you, by then?

A No. Sorry – yes. No, I said "presumably".

Q You said:

> "...presumably used (11th edition) relates to an era when only one dose of vaccine was used and it describes US rather than UK experience"?

B

A No. That was based upon the date of the 11th edition it obviously an edition published on that date would have to look back and I would need – at 1987 they only used one dose of MMR, that is why I put the "presumably". In 1987 was when the 11th edition was published, they did not introduce the second dose of MMR into the States until 1988 so that is why I said "presumably". I think it is a logical conclusion.

C

Q At the foot of page 43 over to page 44 is your second point and this relates to page 62 of Dr Donegan's report and it is the middle paragraph; this is the numbers point, is it not, I think?

A Yes.

D

Q

> "In the fivle years before the rubella vaccine was introduced in 1970 there were only 39 babies born with congenital rubella. In ten years after 1970 there were 454 cases. Even assuming the 14 year old vaccinated in 1970 did not start to have babies they were 24 (unlikely)".

E

Then this is the point:

> "In the ten years after 1980 there are still 333 affected babies. So the number of cases have gone up. It was only in the ten years after 1990 that the number of cases went down to 46".

F

Obviously when she says that the number of cases has gone up, it is pretty clear that 333 is less than 454?

A Yes.

G

Q So the number of...

A But it must have gone up from something.

Q Yes, they have gone up from 1970?

A Sorry.

Q If you look at 115, if you look at – you see what I mean?

H

A Yes.

Q You understand the point – I am sorry, do you have it?

A Yes, I have got it.

Q Whether you agree with it is another matter, but that is obviously what she meant because it could not have meant that it has gone up from – because it has clearly gone down; 454 to 333 is a reduction?
A Yes.

Q And that is pretty obvious?
A Yes.

Q But it has gone up from 1970, which is the first figure that she quotes. I know you make a criticism of that figure and we will look at that in a moment but it is obvious that from 1970 it has gone up?
A The number of cases reported to the NCRSP has gone up.

Q That is what I was saying...
A But it was not in existence before 1970.

Q No. As I say that is a second point, but it is obvious when she says that the number of cases have gone up she is obviously referring to the 1970s?
A Yes.

Q That is the first point. The second point you make is that there was no reporting before then and, therefore, that is a bad point she is making?
A Yes.

Q Let us look at the paper, it is divider 115. It says, "National surveillance of congenital rubella (CR) started in 1971 with passive reporting"?
A Yes.

Q So in fact there was reporting in 1970/71?
A From 71 onwards, yes.

Q Then it says:

> "With the success of the rubella vaccination programme the number of reported cases declined dramatically, from an average of about",

I am afraid I cannot see that figure there, something like 50 births and 740 terminations a year in 71-75 and an average of 23 births and 50 terminations a year in 86-90.

> "With so few cases occurring active surveillance was required, and CR first appeared on the orange card in January 1990".

So that is what is set out there. Then halfway down it says:

> "Active*(sic)*
>
> To monitor the effectiveness of the rubella immunisation programme

by determining the incidence of congenital rubella in Great Britain and investigating the circumstances surrounding any new cases".

A I am not sure if it is "active", the heading.

Q It may not be.
A It does not look as though it would be "active" from the bit I have got.

Q "Effective", is it?
A Yes.

Q Yes, it probably is, because it says "To monitor the effectiveness" so it may well be. The final paragraph on that side:

"Analysis

BPSU notifications: Since the beginning of active surveillance in 1990".

So passive surveillance in 1970, active surveillance in 1990, yes?
A Yes.

Q

"112 reports have been made through the BPSU. Of the 98 reports from England, Scotland and Wales, 39 are confirmed or compatible, previously unreported cases of congenital rubella, four are possible cases, and ten had already been reported from another source".

Then we have got the table in the middle of confirmed and compatible congenital rubella and we can see 39 cases between 1964 and 1969, 454 between 1970 and 1979, 333 between 1980 and 1989 and 46 between 1990 and 1999. That is what the table shows.
A That is what the table shows were reported, yes.

Q The vaccine was introduced, as I understand it, in 1970.
A Yes, to schoolgirls, so 12 or 13 year old girls.

Q On the face of it, there appear to be a number of increases.
A Can you point out the increases you are referring to and then I can answer specifically?

Q There is an increase, albeit from notification, 39, 454 to 333.
A Prior to 1970 nobody was systematically collecting this data, so there are figures in the literature which I did not bring with me because I did not think it was necessary, but there is no systematic collection of data before then, so there is no way you can compare people who have been told, "Please tell us all about your cases of rubella" with an era when that system just did not exist and another interpretation of this would in fact be that, as you say, the vaccine was introduced in 1970/72 and then in the next 10 years you get a fall which is exactly what you would expect, because those children would be having babies later on etc.

Q I think we have your point. Page 44 of your report referable to the foot of page 62. The point is:

> "Vaccinating 12 to 15 month olds with rubella (in the MMR vaccine) and again preschool almost guarantees that their antibodies to rubella will have worn off by the time they are likely to become pregnant".

That is the point that Dr Donegan makes and you say in your middle paragraph on page 44:

> "She provides no evidence for this."

Then you deal with Finland:

> "Where they have administered two doses of MMR to children since 1982, they have eliminated measles, mumps and rubella from the population"

and I think this is actually a study you referred to very early on in your evidence.
A I might well have done, yes.

Q

> "There have been no cases of congenital rubella since 1987 and, although cases of the three diseases have been imported, they have not spread within the indigenous population"

and you were making the point that that was because of the very high level of vaccination. I think it was when Mr Kark was asking you about immunity.
A That would be right, yes.

Q You say:

> "The authors do agree that they cannot be certain how long immunity lasts and it is important to monitor the situation."

You say:

> "Dr Donegan's statement 'almost guarantees' is not in keeping with the evidence".

I think your point, as I say, is "almost guarantees" is putting it too high.
A Much too high, yes.

Q Shall we look then at your referenced at tab 37. I do not know if we need to look at the initial bit, because, as I say, you have explained what the study is in your report and I think you have also mentioned it. Can we turn, please, to the penultimate page of that dealing with the comment part, second paragraph down:

"Despite the indisputable benefits, there is a concern that waning vaccine-induced immunity will put the population at risk for a resurgence of disease. A mathematical model of protection induced by an immunization program using a single rubella vaccine dose suggested that – assuming 80% of 2 year old children would be vaccinated, 90% of vaccinees would develop protective antibodies, and 1% per year would lose immunity – record low levels of congenital rubella syndrome would be reached within 20 to 25 years."

Then at the bottom of that page:

"First, no mathematical model truly depicts the actual situation since underlying assumptions are not necessarily fulfilled".

I think that comes back to the point that we were discussing some considerable time ago now.

A It is a predictive thing which may or may not be accurate.

Q It seems many weeks ago, but I think it was only a couple of days ago.

"Second, and more importantly, Finland relies on a 2-vaccine dose strategy. Our long-term follow-up studies" (this is the part that I want to ask you about) "indicate that antibodies decline over years, despite 2 vaccine doses, but we cannot interpret as yet the clinical relevance of this finding. We do not know at which point the danger – if there is a danger – of a substantial epidemic becomes real. We think that waning vaccine-induced immunity is a genuine phenomenon, especially in circumstances where natural boosters are totally lacking (as now in Finland). One dose of MMR vaccine, even when successful for all components, does not necessarily induce lifelong immunity unless reinforced by subclinical infection (natural boosters) or vaccination. The best we can do is to give 2 doses in the hope they will serve better than 1 dose."

That is not far off, is it, from "almost guarantees"?

A I think it is quite a long way off. They are saying two doses seem to be an appropriate idea and that we need to monitor the situation. "Almost guarantees" I think they would be saying "We are going to give two doses and then we are likely to give three doses". You are right, it is an emphasis on the certainty.

Q Can we move on to how vaccines work, just two points in relation to that, at page 45. It is page 45 of your report and pages 64 and 65 of Dr Donegan's. Again, this is a little bit complex, if I may say so, but if we look at the context of page 64 and the top of 65, this is to do with antibodies produced by the vaccination. That is what we are dealing with, is it not, in this paragraph?

A Yes, yes.

Q IgG. That is the antibody produced by the vaccination, yes?

A No. Vaccines produce more antibodies than IgG, as I said in my report, I think.

Q

> "The antibodies produced by vaccination (IgG) are only the final stage of a long series of protective measures by which a child deals with infections. When a child first meets an infectious agent they are protected by a skin barrier, unless it is breached. Organisms entering by the gut have to pass one molar hydrochloric acid in the stomach, those entering via the respiratory tract have to get past the mucus barrier. Having gone past these, the organism then has to contend with a secretory immunoglobulin"

and that is IgA, yes?

A Yes.

Q

> "Which is produced by the linings of the gut and airways (important in 'mucosal immunity')"

A Yes.

Q

> "Coated with IgA it then reaches the blood stream where it can stimulate an IgG response".

And an IgM response, yes.

Q

> "In the vaccination process, except in the case of oral polio vaccine, all these initial stages are missed and the attenuated organism or toxin is injected directly into the child, bypassing all the first stage defences and presenting itself 'naked' to the immune system, the very immature immune system."

Leaving aside "It is not surprising that problems occur, I think up until then you agree.

A No. It is more complicated than that, but I did not think it was relevant to the case because it would take an immunologist a week.

Q Your complaint, let us deal with that, is in the final sentence:

> "Only IgG antibodies are induced and mucosal immunity is not stimulated except in the case of oral polio vaccine".

A Yes.

Q That is the point and you say there are no references for that and complete discussion of this would take a long time beyond your expertise and then you draw out what you describe as a gross inaccuracy:

"She states on page 65(para 1) that IgG are the only antibodies produced."

It is a reference, I think, if one looks at the previous page to the fact that IgAs are produced which then lead to IgG.

A I would prefer not to go down that, because that is not my expertise. That is why I just commented on the one point.

Q It is a question of interpretation of the paragraph. I am not suggesting for a moment that it has been happily written and obviously Dr Donegan will have to explain that. I think the point is already dealt with here. With natural infection IgA is produced or is that something ---

A No, with most things that I can think of, though perhaps not tetanus, but most things, yes.

Q But it is not produced in vaccination.

A That I would not be prepared to answer without doing a lot of research. My point was about IgM.

Q I appreciate that, but if you can help on this it would be helpful, if you cannot you cannot.

A I cannot.

Q The second point is dealt with at page 66 of Dr Donegan's report. Can I just ask you, first of all, to look at the top where it says "Additives". This is additives to vaccines, yes?

A Yes.

Q

"Ethyl mercury in thiomersal has been used in vaccines for 60 years. The 1999 product information for the adult diphtheria vaccine states that it can cause kidney damage".

That is the one that we produced the other day that I think you said you did not realise was the product.

A That is right. I had not connected these two things, this one to what occurred about 50 pages earlier, because it does not have the full name, for example, in this one.

Q Then it says:

"In May 2002 pregnant women, babies and children under the age of 16 were advised to stop eating shark, marlin and swordfish as a precautionary measure because high levels of mercury that have been found in these fish. The risk was said to be highest in babies in utero as mercury can damage the developing nervous system."

This I think is the sentence that you are concerned with:

"In children possible effects on the developing nervous system might

A

> lead to impaired mental skills, such as attention and memory, and physical incoordination in childhood".

So she puts it as "possible" and "might" in there but your complaint is that Dr Donegan provided no evidence that they have caused damage to children as a result of vaccination. In that you are talking about thiomersal.

B A Yes.

Q I just want to go back, because you did deal with thiomersal when Mr Kark was asking you questions. This is Day 2, page 50, letter D:

> "The cumulative amount of mercury given to a child under six months would not have exceeded the dose which was recommended as the lowest safety level in any of the recommendations. The difference was that, in the States, they gave an extra vaccine which also had thiomersal in, and that pushed it over the boundary."

C

A That is true.

Q Can I just ask you, please, in relation to thiomersal, what level of thiomersal was there in ... we are talking about DTP, are we not?

D A That is the only vaccine that at the time was routinely given and had thiomersal in it.

Q That is right. What was the amount of thiomersal in a vaccine at that stage, can you remember?

A I think, but I am not absolutely certain, it is 25 micrograms. That is the sort of thing I would need to look up.

E

Q That is the information I have. What is the safety level?

A I cannot remember the different safety levels.

Q Can I just show you a document in relation to that and again if you need time to look at it, but I do not think you will. We have copied the whole document but there is only one paragraph of any relevance, just so there is no suggestion that we have, as it were, given you just a little bit of it. It is paragraph 45 in the conclusion. *(Same handed)*

F

THE CHAIRMAN: That will be D15. While that is being handed out, can I just point out what looks like a typing error on page 44 of Dr Elliman's report under section "Conclusion", in the second line the reference to "mumps" should presumably be to rubella.

G

MR STERN: What you have done I think is you have cut and pasted your conclusions, have you not, and put them for each one? That is what I have assumed you have done anyway.

A That is a reasonable assumption, yes.

H

Q It is from the Committee of Toxicity of Chemicals in Food, Consumer Products and the Environment. I presume you are familiar with that committee.

A I have heard of it. I would not say I was familiar with it, no.

Q If you look at the conclusions at paragraph 45:

"We consider that the JECFA".

B I am told, you may be able to agree or not, but obviously we can hear evidence about it in due course, it is the Joint Expert Committee on Food Additives. "PTWI"?

THE LEGAL ASSESSOR: Page 2.

MR STERN: The provisional tolerable weekly intake:

C "of 3.3 μg/kg bw/week is sufficiently protective for the general population. We recognise that the PTWI may not be sufficiently protective for women who are pregnant, or who may become pregnant within the following year, or for breast-feeding mothers. This is due to the potential risk to the developing fetus or neonate. We therefore consider that the EPA reference dose of 0.1 μ/kg bw/day (0.7 μg/kg bw/week) is more appropriate for these groups."

D I am sorry that is a lot of figures, but what it basically comes to, if you look at taking a...are you getting a calculator out?

A No, just a piece of paper.

Q If you take, for example, 3.3 μg a week, that comes to, I think, 0.47 a day, μg/kg?

A Yes.

E Q So if we take a 3 kg baby---

A Keep going, yes.

Q Or 5 kilo baby, that is obviously more than 0.47, is it not? What it works out is considerably less than the 25 μg, that is the point?

A I am sorry, I would need to have five minutes to do---

F Q You look at that and we can come back to it on Monday.

A Okay, thank you.

Q I should just make this clear to you, but you will notice this, I am sure, that the paper refers to methylmercury and vaccine contains ethylmercury, but I understand that the toxicity profile is similar?

G A I think that is a debatable subject and it is not so easy to say that.

MR STERN: We will give you another document that deals with that so you can have a look at that over the weekend as well.

H I think that concludes the first report.

THE CHAIRMAN: You want to pause there?

MR STERN: Yes, please.

THE CHAIRMAN: We will adjourn the case now and reconvene at 9.30 on Monday, 13 August. I note from your comments this morning that you did not include Dr Fletcher in the witnesses.

MR STERN: I do not think I mentioned particular witnesses but I said I hoped---

THE CHAIRMAN: You mentioned Dr Donegan but you did not mention---

MR STERN: I said I hoped the evidence would be finished by the end of the week.

THE CHAIRMAN: You did not mention him by name.

MR STERN: No.

THE CHAIRMAN: Have a good weekend.

(The Panel adjourned until 9.30 a.m. on Monday, 13 August 2007)