GENERAL MEDICAL COUNCIL

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

On:
Thursday, 9 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 Three)

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.

Transcript of the shorthand notes of Transcribe UK Ltd
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FITNESS TO PRACTISE

A THE CHAIRMAN: Good morning, Mr Stern. You were on point four on your list.

DAVID ELLIMAN, continued
Cross-examined by MR STERN (continued)

Q Could we look at some other parts of your report which do not deal specifically with points? We are on page 10 of your report. First of all, in the second paragraph in your report you deal with the point that we were dealing with about the temporal trend which may or may not be causative?
A Yes.

Q If I am summarising or paraphrasing that paragraph, you would say that would be a fair summary, would it?
A Yes, and that would apply to whether you are looking at the adverse effect of a vaccine or a change in instance of the disease and looking at how well the vaccine has worked, so both issues, yes.

Q Where the word "may" appears that is obviously an implication that something may be said or may not be said?
A It gives an element of doubt, as you say.

Q You put it better than me. Thank you. In the next paragraph you set out the best way to examine whether two circumstances are causally linked. This essentially comes back to the point we were dealing with with the level one randomised controlled trials?
A Yes.

Q You say in that final sentence there:

> "For most vaccines, such trials have been undertaken and the vaccines have been found to be effective."

As I understood your evidence yesterday, I think you initially could not think of any trial in that position?
A If I remember rightly the discussion we had, it was had a trial been done where you took a vaccine and you gave somebody nothing at all. The argument went, once you have got a vaccine available what you are usually doing is looking at what is the additional effect of adding something else in. So, when you have already got a vaccine, say against diphtheria and tetanus, you look at the additional effect of adding in a whooping cough vaccine. That is a randomised controlled trial, but there is not a placebo. I think we spent a lot of time about the placebo yesterday.

Q I think you would agree, or did agree, that you said it was unethical to deal with it in the way that I put to you, which is to have a group vaccinated and a group unvaccinated?
A Totally unvaccinated against anything it would be difficult to justify.

Q Looking at this paragraph, in the third line down you said:

A

> "To decide whether a vaccine protects against a disease, the most rigorous way would be to take a group of people…"

etc. etc. What you seem to be saying there is the most rigorous way, which is the way we have just talked about, vaccinated and unvaccinated?
A Against the particular condition you are talking about. It does not mean to say they are totally unvaccinated with anything.

B

Q That is really the issue, is it not?
A It is a very important distinction, yes.

Q It is an important issue. Do you accept that you have not made that particularly clear in that paragraph?
A I perhaps should have expanded upon it, but what I have said is give one group the vaccine and the other not. I did say "the vaccine". I perhaps should have said "the vaccine in question and allowing for them to be treated in a very formal way."

C

Q It is a critical distinction, as you have just accepted, and so therefore the comment:

> "For most vaccines, such trials as have been undertaken and the vaccines have been found to be effective."

D

does not relate to what I am going to call the gold standard, because you say the gold standard is unethical?
A No. Remember when we talked about the treatment of high blood pressure. If you are going to introduce a new drug you can do a randomised controlled double blind trial of the new drug against what is considered at the time normal treatment. For a vaccine, say we were introducing a vaccine against disease X now, a randomised controlled trial of that vaccine would not be giving some children that vaccine and other children no vaccines at all, it would be giving some children what we standardly give, plus X and the other group of children the standard without X.

E

Q I completely understand what you are saying?
A That is what a randomised double blind controlled trial of the vaccine would be.

F

Q It still comes back to the same point I was dealing with before, which is, subject to the one you say you found in relation to Finland or Sweden – forgive me I have forgotten?
A Finland.

Q That is the only trial where there is vaccinated and unvaccinated compared?
A Yes.

G

Q That does not feature in your report anyway, does it?
A No.

Q I am sorry if I have taken rather longer on that. We are going to come back to the order of things, but I want to deal with this point if I may: could you look at page 67 in Dr Donegan's report, keeping a finger in page 12 because we are going to come back to

H

it? It is a comment we ended up with yesterday. The Panel will have read this. I am going to summarise it, I hope fairly. Page 67 to 72 are what Dr Donegan describes as factors affecting immunity in general terms are infectious diseases or the treatment of childhood infectious diseases and the best interests of the child etc?
A Yes.

Q I think in your report you deal with those pages at page 45 of your report?
A I am afraid I have only got a line on that page.

THE CHAIRMAN: It is page 46.

THE WITNESS: Beginning "How vaccines work".

MR STERN: I want to refer to the last line of that paragraph:

> "I have not considered the matters covered on pages 67 to 72 as they have little relevance to the subject in hand."

That is your view?
A I think I said earlier on – I cannot remember if I have said it in my report – that social circumstances do make a difference to whether or not you get diseases, but what we were looking at was the difference that vaccines make.

Q Be that as it may, I want to confirm so that I can dispose of it and therefore not have to ask you any more questions. Are you saying that pages 67 to 72 have little relevance in your opinion?
A To the matter in hand, yes.

Q I am quite happy for any interruptions, because I know that obviously we are going to deal with a number of points. We are going to move on to a different vaccination very shortly, so if there is a point here that anybody wants to ask, I am quite content for that to happen. I know that keeping it all in one's head is not easy. (*To the witness*) Could you look at the bottom of page 10, going over to page 11 at the top? It was a matter raised by Dr Elliman yesterday at the end of the proceedings.

THE CHAIRMAN: Mr Stern, would you mind taking a point of clarification from one of the members?

MR STERN: Of course. I think it is probably easier for everyone on the Panel if we do this. If I cannot answer it now I may come back to you.

THE CHAIRMAN: It is only a point of clarification.

DR GOODMAN: I am on page 10 of Dr Elliman's report. I am not quite clear as to the meaning of the questioning of Dr Elliman and his reply, because it says in the second sentence of paragraph 3 – paragraph 3 starts:

> "The best way to examine whether two circumstances are causally linked…"

A

The second sentence states:

> "To decide whether a vaccine protects against a disease, the most rigorous way would be to take a group of people, randomly divide them into two groups and give one group the vaccine and the other not."

B

Now, Dr Elliman's report makes no mention of what you do about other vaccines that are normally given. I am in some doubt as to what the issue was that Mr Stern was questioning Dr Elliman about.

MR STERN: Do you wish to me to comment about that now? The issue is, when you give a vaccination - this is the point I am making - when you carry out a study, when you give certain people the vaccination and you do not give the others any vaccination, that is

C

the most rigorous way.

MR GOODMAN: With respect, Chairman, this is quite irrelevant, because this is not in Dr Elliman's report, and I thought we were discussing Dr Elliman's report.

THE CHAIRMAN: My understanding is that is an observation.

MR STERN: It is an observation. If I have misunderstood it, then obviously I am open

D

to comment by Dr Goodman.

THE WITNESS: Am I allowed to ---

MR STERN: Well, everyone else is, so why not?

THE WITNESS: This will seem perverse, but I can see what you are doing.

E

MR STERN: You understand what I am saying?
A Yes.

Q Thank you.
A I think one of the concerns you have ---

Q Sorry, just wait. While you are agreeing with me, I would like everyone to hear it.

F

A You may sit down, if you want.

Q If I do not sit down, I may fall over.
A The concern, and I apologise if I am putting the wrong words in your mouth ---

Q No, I am sure they are the right words.

G

A If you give a vaccine to people who are already having other vaccines, you may not, I think it is being argued, be able to tease out the effect of that vaccine. I will argue very strongly that that is not correct, but I think that is the gist.

Q That is precisely my point. Again, you have put it better than me. I hope Dr Elliman has explained what I meant.

MR GOODMAN: I am quite clear now, Chairman. Thank you very much.

H

MR STERN: As I say, I am grateful for the intervention. There is nothing worse than sitting there thinking about something and then moving on to another vaccination. Thank you very much.

Q Bottom of page 10, moving on to page 11, this is what I think is called mathematical modelling.
A Well, no, it is not modelling, because what people refer to as modelling is usually taking data and trying to predict what might happen.

Q Right.
A This is actually measuring something that has happened. It is not in any way a predictive thing. It is describing the situation.

Q Is it a fair point to say that in relation to that mathematical equation, it is obviously not established as reflecting reality or may not reflect the reality?
A No, it is not true.

Q It does not say that?
A No.

Q You have given a reference of D5. We better look at it. It is Dr Elliman's references, and still on file one, divider 5. This is the paper you produced which shows that model that we have there, a mathematical formula, I am going to call it. The summary sets out:

> "During a measles outbreak in Northern Ireland, (between October 1988 and March 1989) it was noted that a proportion of cases occurred in children who had previously been vaccinated against measles."

Then it sets out a cohort study had been done of those; 94 per cent of children had received the vaccination. In the introduction about four lines down it says:

> "Several primary health care workers expressed disappointment at the number of cases occurring in previously vaccinated children. The Department of Public Health Medicine therefore decided to investigate the efficacy of vaccination against measles."

The method is set out there. Then over the page, please, the discussion part:

> "Our finding of a level of 94% efficacy is consistent with other estimates which range from 80% to 95%. The doubts expressed...therefore, unfounded by may have been fuelled by the observation that the proportion of cases in vaccinated children had increased."

I read that merely because that is relevant to the study, but it is not relevant to the point we are dealing with, which is the mathematical equation. The second paragraph deals with this and puts it in this way:

A

> "The object of our study was to provide a rapid estimate of vaccine efficacy. However, this approach does contain possible sources of error. Firstly, no attempt was made to validate the vaccination status through parents or general practitioners. Secondly, measles notification rates were accepted as a proxy for the incidence of measles...Many cases of measles are not notified and we made the assumption that under-notification would occur at similar rates in the vaccinated and unvaccinated groups. It is possible that [GPs] might be less likely to diagnose and notify measles in vaccinated compared with unvaccinated children leading to an overestimate of vaccine efficacy."

B

The point, really, I think is made essentially that there are a number of variables that may or may not lead to a possible error.

A There are a potential number of things. As with any - almost anything will have an estimate and what people describe as confidence.

C

Q Lean a little forward, if you will, please.

A Sorry. Anything that one describes is rarely described with 100 per cent certainty. So, yes, it is an estimate, but it fits in with what people have found previously. In fact, they answer some of the potential errors further on in the discussion.

D

Q I may have put it a bit high as to say it was not based on reality, but there are possible sources of error, I think, is probably a better way of putting it?

A Yes, there are possible sources of error.

Q Can we now deal with page 11 of your report at the bottom. For this, we will need to look at page 11 of Dr Donegan's report, paragraph 5. It is the last paragraph on page 11, which is the point:

E

> "The fact that there are so few cases of diphtheria reported in this country is more likely to be due to a trend towards decreased virulence of the organism and better resistance of the host - humans - because other diseases that have been vaccinated against have not disappeared in such a satisfactory fashion despite very high vaccination rates eg whooping cough, measles and mumps."

F

That is the point. Your criticism at page 11:

> "Dr Donegan provides no evidence, or even a reasoned argument to support this assertion."

Yes?

G

A That is correct. Yes.

Q First of all, just looking at her opinion again, please, she says it is more likely to be due to a trend, so there is an area of possibility about her comment?

A Yes, but the implication is the balance of probabilities.

Q Diphtheria, am I right in saying, is not routinely tested in the UK?

A How do you mean it is not routinely tested?

H

Q Well, one does not routinely test individuals as to whether they have diphtheria?
A No. In fact, unless it has changed very recently, when people have throat swabs taken for a sore throat, in fact the way it is tested often tests for diphtheria as well. When you look at the notifications of diphtheria germ isolation, it is more than people who have the disease.

Q That may be in hospital, but ---
A I am not sure it is just in hospital, either.

Q Do GPs ---
A If a GP tested by sticking a swab down your throat and sent it off to laboratory, certainly up until recently ---

Q If they sent it to laboratory, yes.
A Oh, yes.

Q That is what I meant. If it goes to Colin ---
A No, no, no, any local laboratory.

Q Local laboratory.
A As I say, that may have changed recently, but it was certainly extent up until the late 90s and possibly even early 2000, which is how you get these reports.

Q Can we look, please, at your reference ---
A Can I...

Q I am sorry.
A ...just clarify something.

Q Yes.
A Notifications are not notifications of finding a germ. They are notifications of finding a disease.

Q Yes.
A Which is a different thing, because you can have the germ without the disease. You could notify a disease and, in fact, the notification was wrong because it had been made on a clinical diagnosis which subsequently turned out to be something else. So they are not inextricably linked.

Q Can we look at your reference, please, DE6.

THE CHAIRMAN: Behind tab 6?

MR STERN: Yes, please.

Q Looking, please, at page 98 and 99. First of all, you would agree, would you not, with Dr Donegan's assertion that there are few cases of diphtheria reported in this country?
A Yes.

Q It is the question of whether it is more likely to be due to a trend towards decreased virulence and better resistance of the host?

A Yes.

Q The passage that we have already referred to in this textbook, I think, is of at least a similar view, is it not? We have already looked at this. Should we read it again?
A Yes. I think you need to point out, because there are two slightly separate things. He develops an argument and an impression early on may give one impression and later on another.

B Q In the second paragraph it says:

> "It is tempting to attribute the decline of diphtheria deaths between 1895 and 1922 to treatment by antitoxin, and the rapid fall since 1940 to immunization. Nothing in the evidence is seriously inconsistent with this interpretation, and if mortality from the other common infections had increased or remained constant in the same period it could possibly be accepted unreservedly."

C Then this is the point is it not:

> "But the fact that, without prophylaxis or treatment, diseases such as whooping cough and measles" - which is I think the examples that Dr Donegan gives in her report - "also caused far fewer deaths, suggests that other influences may also have been at work in diphtheria. With due regard for this reservation, it seems probable."

D We have looked at this point.
A I think it is quite important, because it is the development of an argument in taking the sort of background without taking a conclusion as giving a wrong impression. I think the fact that he ends up saying "the evidence is," is quite important, the last sentence.

E Q The last sentence?
A Yes, because it implies - he is saying ---

Q

> "Evidence for England and Wales in 1961-3 indicated that the risk of an attack of diphtheria was about six times greater, and the risk of a fatal attack ten times greater, in those not immunized than in those" ---

F It says, "...immunized than in those immunized."
A Than in those not immunized and in those ---

Q Those not immunised.
G A My interpretation is he is saying the vaccine works.

Q That is his interpretation of it? That is his conclusion?
A Yes.

Q One is entitled, as we have already been through, to have one own's interpretation of the material.
H A Most definitely, but one would expect that if quoting from an author who says

A vaccination works, you come to the conclusion, a different conclusion, and specially if you are quoting from the paper, then you would need to say, "In spite of what Dr Blog said," and using a quote, "I think otherwise."

Q Well, that is ---
A If you take out the first bit of the development of his argument, you are giving the impression that he thinks there is doubt about whether diphtheria vaccine worked.

B Q He does not say that at all. It is just a question of what has been the greater - had the greater effect, that is all, whether it is vaccination or whether it is a trend towards decreased virulence of the organism, possibly as a result of vaccination?
A I do not understand how that could be so; how the organism would be less virulent because of a vaccination.

Q Well, once the vaccination is given, am I not right in saying that the disease becomes less virulent for those who catch it?
C A Sorry, I think I am being pedantic. The organism itself does not change with vaccination except in very, very rare instances. What happens is that the person is now immune so they are less susceptible to the effects of the organism. It is not that the organism itself has changed, which is what would be meant by a decrease in virulence of the organism. Sorry, I am not explaining. It is not a change in the germ, it is that you have immunised people or they have had the disease previously.

D Q In any event, I do not think that actually is a quote from any paper, is it? It is not set out as a quote?
A No.

Q Can we move on to page 12 in your report? I think there is an error in your report in relation to that, because it is page 12 rather than page 11 that your point comes about this. I think your report says it is page 11 but it is actually page 12?
E A I think that is correct, yes.

Q It is the paragraph just above "vaccination recommendation" – that is the point that you are dealing with?
A Sorry, you have lost me. Which page of whom are we on?

Q We are on page 12 of Dr Donegan's report and, coincidentally, we are on page 12
F of your report?
A Okay.

Q The paragraph that you complain about is the final paragraph before it says "Vaccination Recommendation", all right? What Dr Donegan has written is:

G

> "Listed side effects for the single, low dose, adult diphtheria vaccine *(Adsorbed Diphtheria Vaccine for Adults, Secretary of State for Health, Department of Health rev 1999…*"

Sorry, do you have the passage?
A I am there, yes.

H

THE CHAIRMAN: Mr Stern, your working sheet should read 12/4, not 11/4.

THE WITNESS: It was my fault.

MR STERN: I took the reference from Dr Elliman's reference---

THE WITNESS: It is a page wrong.

THE CHAIRMAN: It should be 12/4.

MR STERN: Thank you. So we are on the last paragraph, just before "Vaccination Recommendation":

> "Listed side effects for the single, low dose, adult diphtheria vaccine *(Adsorbed Diphtheria Vaccine for Adults, Secretary of State for Health, Department of Health rev 1999)* are local pain at the injection site, redness and swelling. It also mentions that the thiomersal in the vaccine can cause kidney damage. Adults who are given the high dose children's vaccine can suffer severe systemic reactions. Long term effects are not known."

The part that you are critical of is the first four lines, essentially. What you say is this:

> "Unfortunately, I and members of the Immunisation Division of the Department of Health, have been unable to trace the document mentioned."

Then you say:

> "Dr Donegan says that it *'mentions that the thiomersal vaccine can cause kidney damage*'…"

And you say:

> "I am unaware of any document produced by the Department of Health or its predecessors, that has ever indicated that a vaccine may have caused kidney damage because of the thiomersal it contains. As it is not qualified, Dr Donegan's statement is likely to be read as suggesting the vaccine may cause kidney damage. Dr Donegan's statement is therefore misleading."

Yes?

A Yes. I have thought again quite hard about that statement and I would stick to it.

Q Sorry, stick to which bit of it?

A The lot.

Q Why have you thought long and hard about it?

A Because it was something raised by your expert, so I am agreeing that that is what

A

I wrote and that is what I think is the case.

Q First of all you could not find the document?
A No.

Q I take it you have not seen the document?
A I have not seen the document and it was not provided for us.

B

Q Would you like to have a look at it, please?
A I would.

THE CHAIRMAN: Mark it "D6", please.

MR STERN: Just looking through this document again, the first page, you will see it is an application by Mr Miller, my instructing solicitor, to MHRA Information Centre on 5 December 2006 – yes?

C

A Yes.

Q Over the page you will see there is a letter dated 2 January 2007 in response, saying:

D

> "Re Package insert
>
> Thank you for your recent enquiry to the Medicines and Healthcare products Regulatory Agency.
>
> I have enclosed a copy of the patient information leaflet for Adsorbed Diphtheria Vaccine for Adults (Department of Health) that was amended in 1999.

E

> N.B. Information is not released on Marketing Authorisations that are currently under assessment."

The copy they sent is not easy to read, so it has been enlarged for your benefit on the next page. Let me take you to halfway down the page – I think it has already been underlined:

F

> "Precautions before Use
> Do you have any type of infection?
> Do you think you may be allergic or sensitive to any of the ingredients in the vaccine which are listed above, in particular to thiomersal, which can cause kidney damage?"

G

A Yes, I can see that.

Q Let me ask you first of all how it is that you are not aware of that document?
A I do not know why I was not aware of that document, because I made enquiries of the Department of Health. What I am slightly puzzled by – and you will understand that although you have had it for nine months we have not had it, so this is my first sight of it – this is, I think, a patient information leaflet. This is a leaflet that is put in a vaccine

H

A pack, not by the Department of Health, it is put in the pack by the manufacturers. I am slightly puzzled by the titled "Adsorbed Diphtheria Vaccine for Adults (Department of Health)". If I had known it was a patient information leaflet, I would have gone to the manufacturers.

Q Leaving that aside for the moment, are you saying then that you were aware that there was patient information which was given which showed that thiomersal in the vaccine may cause kidney damage?

B A I was not aware of that because I did not search for that because I had been referred to another source to get the document. What this says –

> "Do you think you may be allergic or sensitive to any of the ingredients in the vaccine which are listed above, in particular to thiomersal, which can cause kidney damage?"

C My understanding is that the patient is being asked "Are you allergic to thiomersal, which we know causes kidney damage?"

Q Just pause for a moment because I have just been handed a document that may help on this particular point. I will just mark it, if I may, so that you can see it. I understand that this is the other side of the same piece of paper. I have not got a copy but

D perhaps you can look at it and we can get it copied. *(Same handed)* I have asterisked the part which is relevant.

A Thank you.

Q I hope that helps.

A I have got it, yes.

E Q Just read it, because obviously nobody has got a copy?

A This is a whole list of points. The heading is "Administrative Data" and this is point 7:

> "Marketing Authorisation Holder
> Secretary of State for Health, Department of Health…"

F and it gives an address.

Q So on the face of it that seems to be suggestive of it being the Department of Health. Whether it is the Department of Health or not the Department of Health---

A Can I finish? It says "Revised 1998". The reference given in the report is 1999.

G Q We can see 1999 on the page that I have just shown you?

A Sorry, it is written on here "Revised 1998" in handwriting at the bottom.

Q I am not sure any of this is particularly---

A I was asked to read it.

Q I think that is the advice to the doctors, is it not? That particular sheet that you

H have, the second sheet, is the advice to doctors; the one to the patient is revised in 1999.

All right?
A Okay.

Q Because we can see it at the bottom. Whether it is 1998 or 1999 the point that I think you will agree is significant is this, that if Dr Donegan has written here that thiomersal in the vaccine can cause kidney damage – and she set out a document that actually said that – there are a number of points that I need to deal with you in relation to this. First of all, are you saying that you were never aware that that was a consideration in relation to thiomersal, that it may cause kidney damage?
A Two separate issues. The answer to your question as asked, yes, I am aware that thiomersal causes kidney damage.

Q And you were aware when you wrote this report?
A Yes.

Q Forgive me for saying, why did you not put that in there?
A Pardon me while I do read my report.

Q Your report says:

> "I am unaware of any document produced by the Department of Health or its predecessors, that has ever indicated that a vaccine may have caused kidney damage because of the thiomersal it contains. As it is not qualified, Dr Donegan's statement is likely to be read as suggesting the vaccine may cause kidney damage."

That is precisely the point that you apparently did know?
A No. With respect, what I am saying is that I am aware of no evidence, no document, that says that thiomersal in a vaccine has caused kidney damage. That is what I meant and that is what I thought I had written.

Q You have not written that at all?
A I have. Sorry, I should not argue.

Q No, no. You have written you are not aware of anything that says "may have caused kidney damage" and that is precisely the point?
A I am still not aware of any document that has said that thiomersal in a vaccine has caused kidney damage. This document does not say that. It says "If you are hypersensitive to thiomersal you should not be given the vaccine" and it says that thiomersal has caused kidney damage. It does not say that the thiomersal in the vaccine has caused kidney damage. The whole issue is that you are talking about quantities of substances---

Q Let me just interrupt you for a moment, if I may---

DR GOODMAN: May we hear the witness without interrupting?

THE WITNESS: There is no debate that thiomersal causes kidney damage. There are no articles at all that I am aware of that have made any good evidence of a link between the

amount of thiomersal in a vaccine and kidney damage. I cannot think of an analogy except one that is going to sound very facetious. Water is potentially a poisonous substance. If you have too much of it you die, but obviously a small quantity is okay. So it depends upon the quantity that is involved. The quantity that is in a vaccine is a small quantity and even the people who have been jumping up and down in the States about thiomersal in vaccines, it has not been predominantly about kidney damage. My concern is that as phrased the implication is that the thiomersal as it is in the vaccine has caused kidney damage, and that is not so.

MR STERN: Why is it on the package insert then?
A This is someone who has had a hypersensitivity reaction. This is different from… It is like if someone was allergic to some vaccines you would not give them. It is not because it is a poisonous substance, and I am not aware that this is still in things, but that is another matter.

Q It is another matter, but do you accept that your report – this is the point I was going to interrupt on, because we are dealing with you report – that your report says that Dr Donegan's statement is therefore misleading and you have written in your report that it is therefore misleading on the basis that you could not find the document and you are not aware of any document. That is the way your report reads, is it not?
A I still think it is misleading, even though I have now found the document.

Q That may be. The point I am asking you about is this: you have put in your report, have you not, that the document is missing, it is not there and you are not aware of it?
A Yes.

Q No-one in your department is aware of it and therefore, essentially, Dr Donegan's statement is therefore misleading. Why did you not include in that particular part, "I am well aware that thiomersal can cause kidney damage and to that extent Dr Donegan's statement is accurate?
A Perhaps in retrospect to save the questioning I should have done.

Q It gives, to coin a phrase, does it not, a totally misleading impression?
A No, I do not.

Q You do not agree?
A No, because I phrased it very carefully. I have said:

> "I am unaware of any document produced by the Department of Health or its predecessors that has ever indicated that a vaccine may have caused kidney damage because of the thiomersal that it contains. As it is not qualified, Dr Donegan's statement is likely to be read as suggesting that the vaccine may cause kidney damage."

Q Not qualified in which way?
A It does not say that thiomersal causes kidney damage and there is thiomersal in vaccines. It says the thiomersal in the vaccine causes kidney damage. I am sorry. I am not explaining myself very well.

Q No, if I may say so, with respect, because this passage does tend to suggest, I suggest to you, a completely misleading impression of what Dr Donegan has produced and is referring to.

MR KARK: That is presumably meant to be a question.

MR STERN: It is a suggestion. I said, "I am suggesting."

THE WITNESS: Could you repeat it?

MR STERN: What I am suggesting to you is that your report gives a completely misleading impression. If one did not have the document, but just had that passage in your report it would create a completely misleading impression I am suggesting to you?
A No, I do not agree.

Q On the face of it your report there seems to suggest, does it not, that Dr Donegan had no basis for the suggestion that she had?
A That thiomersal as in the vaccine causes kidney damage?

Q Can cause kidney damage?
A Yes.

Q Whereas you may disagree with its weight, but it does in fact say in that patient leaflet:

> "Do you think you may be allergic or sensitive…"

I have read it already once,

> "…to any of the ingredients in the vaccines which are listed above, in particular to thiomersal which can cause kidney damage?"

A That is a statement that is there.

Q Do you not think that it might have been fairer to have indicated that particular point or not?
A The point that in general thiomersal in large doses can cause kidney damage?

Q Or to say there is some suggestion in patient information leaflets in relation to diphtheria that sensitive patients or allergic patients may – may cause kidney damage as a result of the thiomersal contained within it, something along those lines? Do you not think that that would have been fair?
A You have me at a slight disadvantage, because I have only just got this. Before answering that I would like to re-read it carefully. No, I do not think it is fair that I should have known that, because I was provided with what subsequently turns out to be an inaccurate reference and not the material, so I could not address the point directly.

DR GOODMAN: Chairman, may I suggest an adjournment?

THE CHAIRMAN: There are two ways to proceed. You could move on to another point and allow Dr Elliman to read this during our coffee break and come back to it, or you could give him time now.

MR STERN: As you wish. If Dr Goodman wishes to have an adjournment I am not against that.

DR GOODMAN: No, Chairman. I absolutely agree with your line.

THE CHAIRMAN: Carry on and come back to it? Why do we not allow Dr Elliman to have another read and carry on until our natural break.

MR STERN: I have got the second page as well. It is copied so you can have that now. (*Same handed*)

THE CHAIRMAN: We will try and break about quarter to eleven or eleven.

MR STERN: I am coming to the end of diphtheria so it may be a convenient moment to have a break.

THE CHAIRMAN: May I suggest that you complete the diphtheria questioning.

MR STERN: I am coming to an end, but if it would be helpful for Dr Elliman to read this, then, of course, he should.

THE CHAIRMAN: Why do we not break now then?

THE WITNESS: I only need two minutes.

THE CHAIRMAN: We need to have a little discussion as well. We will stay here, if you could retire, come back at quarter to and have your coffee break at the same time.

(*The Panel adjourned for a short time*)

THE CHAIRMAN: Thank you for that time. I think it was helpful. I hope you found it helpful, Dr Elliman, to have refreshed your memory.

THE WITNESS: Thank you very much. It did require more than two minutes.

THE CHAIRMAN: As a point of clarification, was there any reason why this was not in the reference bundle produced earlier on?

MR STERN: I do not know, but I can get back to you. It is referred to and set out there, but I do not know why it was not in the reference bundle.

THE CHAIRMAN: It was asked for in December 2006.

MR STERN: Asked for?

THE CHAIRMAN: A covering letter.

MR STERN: Obviously Dr Donegan included it in her original report. Nobody raised any questions about it until Dr Elliman's report, which we got in September 2006. Obviously as a result of that work then had to be done on dealing with the points made by Dr Elliman. It may be it was not included as part of Dr Donegan's references. I do not know why it was not given at court, but I can certainly find out.

THE CHAIRMAN: Are there many other such documents?

MR STERN: Not many others, but there are some additional documents.

THE CHAIRMAN: Would it be helpful to the other parties if they were disclosed earlier rather than later. I am just anticipating any such hitches.

MR STERN: We have not had any hitches as yet. I am entitled, without going technically into it, to deploy information in the way I consider appropriate. I hope that I am not in any way seeking to ambush people. The document is there and it was only when we got Dr Elliman's report and he said he could not find this document that inquiries at some stage were made.

THE CHAIRMAN: I am not suggesting in any way how you should run your case, Mr Stern. I am just saying that in the documents of references is glaringly not there and should have been in this volume, perhaps it would be sensible to produce it now. Carry on.

MR STERN: (*To the witness*) Dr Elliman, you have had a few minutes to look at this now and collect your thoughts on the subject. Is there anything that you want to say about this?

A It may be helpful to explain what it is.

Q Yes, certainly?

A So one knows it provenance.

Q Yes, of course?

A The EU passed a regulation some while ago – I am not sure when it became mandatory – that in every medication, not just vaccines, there should be some instructions for the person administering it and for the patient. The instructions for the person administering are called the "Summary of product characteristics".

Q It is the second page, the one that we produced during the course of your evidence?

A Yes.

Q That is the second page, for those who are not familiar. Those who are will obviously know that. The first page is the one for the patient?

A That is right. They are supposed to be the same, but one is, if you like, in English rather than medicalese.

A

Q One is in doctor speak?
A Yes.

Q Looking through the one for the patients, which I now understand is what which Dr Donegan used for her reference, it does indeed talk about thiomersal. I think I would have to concede that one could put an interpretation on it that thiomersal in vaccine may cause kidney damage. I am puzzled, though, because when I read further down to almost the bottom there is a heading:

B

"Does Absorbed Diphtheria Vaccine for Adults have Side Effects?"

when I would expect it to list side effects. Nowhere does it mention kidney damage due to thiomersal. I have written, as have others, on the inadequacy of these documents. What I would have said in my report, if I had it, is that this is not an appropriate source to justify an expert report. It may be part of what you would submit the patient information leaflet says, but I would expect it to be backed up by some scientific literature, for example, the paper that Dr Fletcher produced, because it is not a science…

C

Q Your criticism now is not that it is misleading, but that it is not as reliable as other papers might be?
A There are two criticism. One is that I think it is misleading. The other is that most places people go to is:

D

"Does the Absorbed Diphtheria Vaccine for Adults have Side Effects?"

It does not mention that. The assumption would be therefore that is not a side effect.

E

Q The point is, because we are dealing with your report rather than the actual document itself, if I may say so… Your report – I do not want to go through it again – is essentially saying that it is missing and does not deal with the facts that you have now accepted?
A I am sorry. What is missing from what?

F

Q That you accept that an interpretation could be that this vaccination can or may cause kidney damage?
A I am accepting that if you take one paragraph, yes.

Q What I am saying to you is that that does not feature in your report, that particular point?

G

A It cannot, because I did not have the document. It is difficult to reply to a document I do not have. What I have done, as is said in my report, is relied on what I know the Department of Health would have put out in CMO letters.

Q You are saying you did not know – forget about the document – the point that lies behind the document before this was drawn to your attention this morning?
A I did not know that in a patient information leaflet in 1999 it stated what it says in this…

H

Q That is not the question I am asking, with respect, is it?
A Please elaborate.

Q The question I am asking is: did you know prior to today the point that I put to you that is contained in that leaflet?
A I am not being difficult. If the question is: did I know that someone had suggested that thiomersal in the vaccine caused kidney damage, the answer is no.

Q That is what I am saying. You did not know?
A I was unaware of any scientific evidence to back up that assertion.

Q Before about ten o'clock this morning?
A Yes. I know people have said it, but people have said lots of things. It is whether there was a scientific report, evidence or whatever to back that up.

Q We have your answer on that. Can I deal with page 13 of your report, which is the conclusion? Again, I do not want to do this every time we come to your conclusions. I will do it just once if I may, but you can take it that my point is the same to you, if that helps you. You have set out there what essentially you say is the impression given by Dr Donegan's report?
A Yes.

Q I think you would accept that you are not an expert – you said yesterday you are not an expert in impressions, but you are, I believe, an expert in relation to vaccinations?
A I am not an expert in impressions, but I have read the literature on how vaccines are described and covered, which there is a lot of research, and the misapprehensions that will be given, depending upon the quote balance put in a report.

Q Yes. I understand that. Ultimately, that is a matter for the Panel. You accept that?
A Oh, yes, definitely.

Q Not a matter for expert evidence?
A No. I can offer an opinion, but I am not an expert on that.

Q Yes. There is a danger, do you agree, that you have crossed over the boundary between being an expert and an advocate, or do you not agree?
A I do not - I am not quite sure where the boundary would be, to say I had crossed it.

Q Well, let me give you a further example. In your report, and I do not want to spend a lot of time going back, as it were, but in your report, at page 3, when you talk about your association with Professor Kroll and Dr Conway you have described there, "Both Professor Kroll and Dr Conway, have also, at various times, sat on" - then you set out that committee - "My time on the committee has overlapped with theirs." Now, you told us yesterday that, in fact, you had been on the committee with Professor Kroll since 2004.
A I think that is so.

Q That is what you told us.
A Yes. I would have to look up the membership to make sure exactly, but I think it

A

is of that order.

Q You said over the last three years and are still on the committee with him?
A Yes.

Q You told us you were on the committee with Dr Conway for about a year?
A Yes.

B

Q About three years, ago, I think you said?
A I think it was, yes.

Q About. You were not too sure exactly when. That is not, strictly speaking, made clear, is it, when you say, "My time on the committee has overlapped with theirs." You are presently still on the committee with Professor Kroll?
A Yes.

C

Q So you are associated on a fairly regular basis with Professor Kroll and Dr Conway, or were at one stage. I know not whether you see Dr Conway.
A The committee meets twice a year. In between that, I would have had no contact with Dr Conway.

Q Dr Conway or Kroll?
A Conway, and occasional contact with Professor Kroll, but perhaps another twice a year.

D

Q You have told us that you also associated with Dr Donegan in the sense that you knew her before you were asked to write a report?
A Yes.

Q You had appeared on radio with her, and - yes, I think that is all I wanted to put to you. In fact, you are associated with almost everyone in the case?
A Yes, I suppose so.

E

Q Did you not consider that the criteria of being an independent expert was that you were independent of everyone?
A Independent, I had assumed, meant that one's views were independent, not necessarily as a person was one independent. The reality is that, and this is something that crops up again and again, that the people who are involved in the vaccines who know - and I am sorry if this sounds arrogant...

F

Q No, I know what you mean. You know the most about it?
A ...the most about it, they are going to mix with each other. They sit on the same committees, they often do research for drug companies. It is unavoidable.

Q I entirely understand that, which is why it is even more important to make it absolutely clear what your associations are at page 3, is it not?

G

A That is what I did. Yesterday I thought I was being criticised for writing down that I was involved in research with vaccine manufacturers. I was trying ---

Q I specifically said I was not criticising you, if you recall.
A Oh, right. Well, there was some surprise that I had written it down. I was trying to give the full picture. I am sorry if I should have given the number of meetings and the number of years that this happened, but I did not think that was necessary. I thought I

H

had given enough information.

Q Overlapped was sufficient information? You thought that was sufficient information?
A I did, yes.

Q Can we turn to pertussis, please? Page 14 in your report it is the reference under the sub-heading "Dr Donegan's report," and it is page 15, paragraph 4 of her report. Let us look at what Dr Donegan says. I will start off with the beginning of the paragraph, just to put it in context, so there can be no suggestion I am not:

> "It is undoubtedly the case that whooping cough became a milder disease in this country over the course of the first half of the twentieth century. The death rate had fallen by over 99% before vaccination against pertussis was introduced in the 1950s."

You make no criticism of that. I am assuming you agree with it?
A Yes.

Q Again, you have to answer, sorry, rather than a nod.
A Sorry. It is a given that I believe that vaccines are not the only thing that has affected disease mortalities, certainly.

Q Let us look at what Dr Donegan says:

> "The introduction of the vaccine reduced the number of notified cases of whooping cough but peaks continued to occur every three to four years as they always had."

She is, as it were, recognising the efficacy of the vaccine in that sentence?
A It would seem to be, yes.

Q "Deaths continued their steady decline."
A Yes.

Q Do you include that in your report, in looking at her overall impression?
A I would have to refresh my memory. No, perhaps I do not include that.

Q Perhaps you do not.

> "This was most clearly seen in the 1970s and 80s when the vaccine coverage fell less to 40% in 1976 because of health scares."

This is the part, if anyone wants to underline it:

> "In 1978 and 1982 there were over 65000 notified cases of whooping cough but no..."

- and then this is the word -

> "...concomitant rise in the number of deaths."

A Your criticism at page 14 of your report, in the part that I have already referred the Panel to:

> "The scale on Fig 2 is such that it is impossible to see the numbers of deaths at the times referred to."

I think that is a reflection of most of the graphs in relation ---
A Yes. It is not a criticism. It is a statement of fact.

B Q I was just checking that. I did not think it was.

> "Data readily available from the Health Protection Agency showed there had been an increase in deaths in those two years, but perhaps not as much as might have been expected from the rise in number of cases."

C Then you set out, "From 1975 to 1984," and then you have helpfully underlined the 12 and the 14, being the relevant number of deaths for the year of 1978 and 1982. Is that correct?
A Yes.

Q In fact, Dr Donegan provides this data herself, you say. Now, the point she is making, I think, is a simple one, really, that there was an increase in notified cases?
D Again, sorry, you have to answer.
A Yes.

Q So it went up to 65,000?
A Yes.

Q But there was no concomitant; that is to say, no accompanying increase in deaths. That is the point she is making?
E A Yes.

Q Do you agree that is right?
A Well, there was an increase in deaths in the two years that it was said there was not an increase in deaths.

Q Right.
F A You can see the pattern in the ones I have underlined are increases in death.

Q We will look at it then, if that is what you suggest. You say that is a concomitant increase?
A Well, that is an increase at the same time, which I thought was concomitant.

G Q Let us look at her reference 26. It is Donegan reference tab 26, please. You will be pleased to know, at least the Panel will be pleased to know, I am only going to be referring to the last page in that divider. Obviously if there is anything I have missed, no doubt you will tell me. First of all this is, as we can see at the top, "Whooping cough: Notifications and Deaths in England and Wales." Notifications, we can see 1970 through to 1998. Yes?
A That is correct.

H Q Obviously you will appreciate I am going through this because the Panel will not

A

have seen this or may not have seen this document before. 1974, there were 16,225 notifications. I think that was an epidemic, was it not?
A Yes. It follows a four-yearly pattern or thereabout.

Q If we look to the right of that, we can see the number of deaths was 13.
A Yes.

Q The fatality ratio per 100 notifications was 0.08?
B A Yes.

Q The vaccination coverage at two years of age was 77 per cent?
A Yes.

Q We see that, in 1975, 8,900-odd and 12 deaths, with a fatality ratio of 0.14, vaccination rate said to be 59 per cent. '76, it goes down to 3,900, three deaths. I think everyone has probably got the point now. Three deaths, 0.08, 38 per cent. '77, we can
C see just under 17,500, seven deaths, 0.04, and 39 per cent. 1978, which is one of the years, it goes up to almost 66,000?
A Yes.

Q With 12 deaths?
A Yes.

D Q Well, on the face of it, although there is a massive increase, and I think you would agree, a massive increase in notification? Do you agree?
A Yes.

Q There is not, is there, a significant increase at all, if an increase there be, in relation to deaths?
A There is an increase in the two years '74, '75, but, as I have said in my report, it is not an increase as much as you would have expected.

E

Q It is not a concomitant increase, is it? Look, the point is - let us just take this: 16,225 in 1974 when there is epidemic, 13 people died. Yes?
A Yes.

Q 66,000 people notified in '78, but there is not the multiple, if you like, of deaths that one would expect ---
F A There are not as many deaths as you would expect, no.

Q That is really the point, is it not?
A That is what I have written in my report. There was a rise in deaths, but not as many as you might have expected, at the bottom of page 14.

Q Well, what is wrong with Dr Donegan's ---
G

MR STERN: Yes, thank you. The ratio is in fact - I am grateful. I was going to come to that.

Q The ratio is 0.02, is it not?
A Yes. It is not as many deaths as you would have expected.

Q No, no. The ratio is 0.02, which is even lower?
H

A Yes.

Q Likewise for 1982, when the notification was 60 - just under 66,000?
A Yes.

Q Deaths, 14, 0.02, same fatality ratio?
A Yes.

B Q I should add, for the sake of completeness, vaccination rate 31 per cent in relation to '78; vaccination rate for 1982, 53 per cent?
A Yes.

Q Just so we have the complete picture, in fairness. I am sorry to come back to this, but what is unfair in any way about what Dr Donegan is saying?
A Sorry, I obviously misread the word "concomitant." I thought it meant an increase at the same time of deaths as there were of cases, and there were undoubtedly an
C increase in number of deaths. As I have said in my report, it was not as many as you would have expected.

THE CHAIRMAN: Would you prefer to have a dictionary definition of "concomitant," for our benefit?

MR STERN: All right. I will look it up. Anyway, whether or not one has got a
D dictionary definition, what I am putting to - maybe Dr Goodman wants to look it up.

THE CHAIRMAN: Would you like to do it?

MR STERN: No. I am quite happy.

THE CHAIRMAN: We can actually continue.

E MR STERN: It is very difficult to carry on when a particular point is obviously festering in the mind of someone.

THE LEGAL ASSESSOR: Do you want us to read it out?

MR STERN: Yes.

F THE LEGAL ASSESSOR: It says, "Concomitant. Adjective. Existing or occurring together; associative." The Latin origin.

MR STERN: I do not know if that helps Dr Goodman, if that suffices? Yes. Thank you.

Q Can we move on? Page 15, still in your report.

G MR STERN: If I may say so, I do not know what one takes from a dictionary definition, but ultimately you will be looking at the state of mind of Dr Donegan and what she meant and what she interpreted.

THE LEGAL ASSESSOR: Perhaps I could interpose there. Of course, from a judicial point of view, concomitant means what the writer of the word intends it to mean.

H MR STERN: Can we look, please, as I say, at page 15 of your report, and the second

point in relation to it is in that second paragraph down. You are referring - I think the point in Dr Donegan's report is at page 18, first paragraph at the top. Let us see what Dr Donegan is saying. It begins in the sentence, "During natural infection." This is the part to underline, I think. "During natural infection with pertussis IgG, IgM" - I am sorry, Dr Elliman. Do you have it?

A I have it, yes.

Q

> "IgG, IgM and IgA antibodies are produced. These IgA secretory antibodies are very important as they specifically stop the bacterium from sticking to the heads and multiplying. Vaccination against pertussis does not produce this IgA antibody which is important in protecting against further infection."

Your comment, again, I think this is one of those Harrison's 15th edition points, is it not?

A It is, yes.

Q You have checked through the copy of the reference provided by Dr Donegan and, "I cannot find the quote she gives, nor can I find any statement along similar lines."

A Yes.

Q Now, again, you will have seen, I have no doubt, Dr Donegan's reference, being the 11th edition?

A Yes.

Q You will have seen it both in her report and also in her list of references?

A Yes.

Q And also, I think, if you look at the front of *this* bundle at page 4 of the references, which are at the front of Dr Donegan's bundle C2?

A Yes.

Q Typed up by the solicitors for the Council. It is C2 right at the beginning, the index of the references helpfully set out by those instructing my learned friend. I am going to come to the paper in a minute but right at the beginning you should have these references and if you turn to page 4 in the bottom right-hand corner number 20 as it is set out there is *Harrison's Principles of Internal Medicine, 11th Ed*?

A That is so, yes.

Q First of all, did you see all of those references to the 11th edition?

A I did, and I was provided with a copy that came from the solicitors of a reference that was Harrison.

Q Sorry…?

A Yes, I did see those listed things but I was also provided with a copy of a reference from Harrison.

Q The 15th edition?

A Yes.

Q It is the same point and I do not want to make it again. You, presumably, could not find the 11th edition?
A That is correct, and I have said in my report that I accepted that it might have been in the 11th edition but I commented, as we have gone through before---

Q Where do you say that? Just draw my attention to that?
A This is sort of – we are talking about the second paragraph on page 15---

Q Yes, I have got the paragraph, I just cannot see the bit where it says "11th edition"?
A It says:

> "I cannot find the quote she gives, nor can I find any statement along similar lines. The photocopy she provides is identical to the pages from 15th edition. This would have been current at the time Dr Donegan wrote her report. If this is correct, it is interesting that the current edition, the one Dr Donegan should have used, no longer has this statement."

The way I meant to write that, and I am sorry if it did not give that message, is "If I am right and it was the 15th edition then it is not there". If it was not the 15th edition – so that is why the "if this is correct", meaning it was the 11th edition that was being used, "then it is interesting that the current edition does not have it in".

Q I have made the points and I am not going to make them again and again. You do not accept that it would have been fairer to have said "The references relate to the 11th edition. I have not been able to find a copy but if" – if – "it is there, it is interesting to note that it is not in the 15th edition" or whatever---
A I perhaps should have spelt out that it was the 11th edition that there was a contest about but I thought I had spelt it out that it was unclear which edition we were talking about.

Q It was not unclear at all. All the references show it is the 11th edition. I know the document that you were given is the 15th edition but all the references show the 11th, and I would have thought… It is not for me to think – there we are. We have the 11th edition and you have got a copy of that now, do you?
A I have, yes.

Q Perhaps we can hand that out now? *(Same handed)*
A Did we not have this yesterday?

THE CHAIRMAN: Did we not have this yesterday as D5?

MR STERN: No, it was diphtheria yesterday. It is a massive document and this is a different extract.

THE CHAIRMAN: I beg your pardon. This will be D7.

MR KARK: I am so sorry – it is just on numbering. The two documents that we were

given earlier, we called the first one D6. Are we calling the second one D6B or something?

THE CHAIRMAN: It is the other side of the leaflet so it is all part of the same exhibit.

MR KARK: Thank you.

MR STERN: Perhaps you could put it, if you wish to, in Dr Donegan's bundle at 26 because then you could put it on top of the 15th edition – if that helps.

THE CHAIRMAN: Thank you.

MR STERN: At least you have got them together and it is easier to find them then afterwards.

THE CHAIRMAN: Behind 26?

MR STERN: Sorry, it is tab 20 – I apologise. Let me just deal with this swiftly, if I may. It has got 122 at the bottom, the third line down on the right-hand side:

> "Antipertussis secretory IgA is protective and specifically inhibits bacterial adherence to cilia."

Then if I can draw your attention to the last paragraph on the right-hand side:

> "An enzyme-linked immunosorbent assay (ELISA) can be used to detect IgM, IgA, and IgG antibodies in serum and may be useful in patients with negative cultures. The ELISA technique also can be used to detect IgA against B. pertussis in nasopharyngeal secretions beginning in the second or third week of illness up to at least 3 months."

Then this, I think, is the relevant point:

> "This antibody is induced by infection but not by vaccination."

A It is there, yes.

Q Do we need to spend any more on that point or not?
A No.

DR GOODMAN: Chairman, may we know who the author is of this new one? I cannot see the name of the author of what is D7.

MR STERN: May we find that for you and let you know?

DR GOODMAN: Thank you.

MR STERN: I will move on, if I may. Page 15 of your report still, your third point on

this page, the second half of the page refers to Dr Donegan's report at page 18, second paragraph?
A Yes.

Q You made three points in relation to this paragraph and I am going to have to deal with them separately, though not necessarily in the order in which they feature in this paragraph. The point that you are dealing with here is in the middle of that paragraph, beginning "Because of continuing increases"?
A That is correct.

Q So if anybody wishes to underline that bit, that is the bit I am going to deal with:

> "Because of continuing increases in pertussis notifications in the UK, especially in young babies, an 'accelerated' schedule"

- which I think came in in 1990 –

> "of vaccination was introduced (vaccination at 2 months, 3 months, 4 months instead of the previous 3 months, five months, 10 months, to try to reduce the incidence of disease."

A That is correct.

Q Your complaint, if we look at the point here, you quote it first of all and then you say:

> "The new 'accelerated' schedule was introduced in 1990"

– we dealt with that.

> "Dr Donegan does not give a source for this, but her own data (Figure 1, page 16) shows that there was a continuing fall in disease between 1980 and 1990, i.e. directly contrary to what she stated."

A That is a wrong reference. It should be to figure 2, page 17.

Q That is correct. That is an error by you, I think?
A Yes.

Q If you turn to page 17 of Dr Donegan's report, because obviously page 16 only goes up to 1972 so it could not be right?
A Yes.

Q Could we look, please, at Dr Donegan's reference, tab 25? I should just say that tab 25, I think you will find, is in fact reference 21, which is the number which features at the end of that paragraph of Dr Donegan's report at page 18. Let me just check that, because I do not want to make a bad point about this if I can avoid it?
A It might help if you say what it is as well as the number, because I have got lost, I am afraid.

MR KARK: Actually tab 23 is the reference for that.

MR STERN: Thank you.

THE CHAIRMAN: Is it the HMSO?

MR STERN: It is the HMSO 96 document?
A That is 25 then, I think. This is one that is on its side and has got two pages on each.

MR STERN: May I just explain, I hope, if you have not already gathered. The references at the bottom here, for reasons that are nothing to do with Dr Donegan, but they have been given different numbers for the preparation of this case by the General Medical Council. I see Mr Kark shaking his head but they are obviously different numbers. They are different numbers from the report as set out in Dr Donegan's reference.

THE WITNESS: The reference numbers in her report were in sections, so it went 1 to whatever and then it went back again to 1.

THE CHAIRMAN: Let us just get this right. Reference on page 18 at the end of paragraph, which starts "Despite vaccination", it says "(21)". That 21, if you look at the 21 on page 24 of her report, is a study by a number of authors---

THE WITNESS: That is 23 in our bundle.

MR STERN: It is 23 in the reference. It may not even be worth making this point, but let me just clarify it if I can. The number 21 at the bottom of page 18 at the end of that paragraph in fact relates to number 23 in the reference – I see Dr Goodman has got there ahead of me – but in fact is tab 25 which is why this case, I am afraid, is even more difficult than it might otherwise be because we have, I think, at least three different references to the same paper, but not duplications of the paper.

(To the witness) I am sorry to divert you. What I actually want to look at is Dr Donegan's references, bundle 1, divider 25. If you turn to the second page you will see, if you turn it on its side, you will come to the heading "Pertussis". The first paragraph:

> "Until the mid 1970s, mortality from pertussis was about one per 1000 notified cases with a higher rate for infants under one year. In 1978 however when there were over 65,000 notifications (in E and W), only 12 deaths were notified."

I note the emphasis on "only"?
A Yes, and then read the next sentence.

Q I am just about to read the next sentence; I am just about to read it.

> "The actual number of deaths due to pertussis is undoubtedly higher

A

> since not all cases in infants are recognised. In 1990, there were six deaths from pertussis, all in infants under four months of age. The timing of routine pertussis immunisation was accelerated in 1990; from 1991 to 1995 only five deaths attributed to pertussis were reported (in England and Wales), all in infants too young to be immunised."

B

I draw that to your attention for the sake of completeness. Could we look, please, at tab 23? This is the 1999 paper which deals with 1995 to 1997 – yes?
A Yes.

Q In the middle of the summary it says:

> "There is a continuing significant and under-reported mortality associated with pertussis in the very young age group."

C

You will appreciate, as I said to you yesterday – let me repeat the point that I am making; I will not be making it every time – I am selecting various points. If there is something you want to add to, I know you are not shy in pointing that out. You will appreciate I am trying to make the points in the way that I can. A few lines further down:

D

> "While overall levels of pertussis notifications have declined in recent times, vaccination efficacy wanes with increasing age, and pertussis remains a significant cause of mortality and severe morbidity in the very young."

Then, "Introduction". It says:

E

> "A number of recent international reports have focused on a resurgence of whooping cough notifications despite high vaccination rates, often associated with significant mortality in very young children."

Then on the right it just talks about, in the top of the paragraph there,

F

> "…a possible lower duration of efficacy associated with the accelerated vaccination schedule used."

Over the page, just looking under the section "Data analysis" which is on the left-hand side:

G

> "This model also enabled estimation of linear trends over the 3 years where the trend parameter is defined as the annual proportional drop in vaccine efficacy from 100%. This is equivalent to the proportional increase in the relative risk of disease in vaccinated compared to unvaccinated. An estimate of the linear trend for the decline in vaccine efficacy with increasing age was also calculated."

H

Then on the right, about five lines down, it says:

A

> "The proportion of notifications occurring in patients over 15 years of age since 1991, has increased from 4.4 to 9.3% and there has been a marked increase in the proportion occurring in children under 6 months of age…"

Then it sets out the figures there. Yes?

B

A Yes.

Q From 6.3 to 19.1 per cent. Is that not what Dr Donegan is saying there?

A Can you redirect me… No, I have got it. It is all right…. I think there are two slightly different but important statements. The paper by Buynder is talking about proportions of cases and Dr Donegan's statement was because of continuing increases in pertussis notifications especially in young babies. That is an absolute number.

C

Q I am sorry to interrupt you, but if you look at the rest of the sentence it says:

> "…to try to reduce the incidence of the disease."

A Yes. Even if you have got low levels of the disease you could still try and reduce the incidence until you get to nothing. The paper that is presented here is based upon, as I think it says in the summary, an enhanced surveillance, so during that period 1991 to 1997 they were using lots of data sources, so you cannot compare what they collected in this paper with what was happening in 1980, because they were trying to get hold of every case, not just notifications, which is what we have been talking about up to now. Their conclusions in terms of trends can only be during the period that they did this enhanced surveillance. Perhaps if we look at the first line:

D

E

> "…including notifications, hospital admissions, deaths and an enhanced laboratory-based surveillance…"

Q The first line of the summary?

A Yes. It describes what they are doing, so they are not just using the notifications, which is what we have been talking about up to now, when a doctor is saying something has happened. They are trying to get every possible case they can, hence enhanced, so in terms of time trends, if you compared what they were finding in this period with another period you would expect it to be higher, even if there was no genuine change, because they are getting a higher proportion of them. It is all right to look at what they are talking about within, in terms of absolute numbers, but to try and extrapolate and say they found more in 1991 than there were in, say, 1989 one would have to be careful with that proviso.

F

G

Q I have read the part of the summary where it says:

> "There is a continuing significant and under-reported mortality associated with pertussis in the very young age group."

A Continuing. It does not say increased.

H

Q No, but the fact is that they did change it, did they not?
A The schedule was changed, yes, not because there was an increase…

Q What?
A What we used to have was a schedule, as Dr Donegan said, where we gave infants pertussis vaccine at three months, five months and nine months. What we found was, as the graphs have shown and other research, that that did reduce the number of case. Of course, any baby born before nine months has not had the course of immunisation.

Q Most babies are born before nine months?
A I am sorry. Any baby up to nine months will not have had the full course of immunisation. Thank you. Even if it is a perfect vaccine it would be difficult to protect those, so by moving the age down one has a better effect. It is not to say the previous one was wearing off or had changed or there was an increase. There certainly was an increased proportion, but there had been a total number that had reduced. Therefore, even if you had the same number in young babies the proportion would be going up. My concern was the difference between proportion and number.

Q An absolute?
A Yes. My reading of Dr Donegan's report was there was an absolute increase. I do not think that is the case.

Q You do not think that is a little nit picking, if I may say so?
A No, not at all. I think talking about the numbers who die, as opposed to the proportion, is extremely important. If I said a hundred people die of measles and then I said the number had gone down or I said it had gone down, but actually it had gone up because the number of cases of measles had gone up, that is a totally different message.

Q She has not talked about people dying?
A Or cases, for that matter.

Q She is talking about the increase in the number of cases and, in order to try and reduce the incidence of the disease, there was an earlier vaccination?
A What I am saying is there was not an increase in number of cases. There was an increase in the proportion of cases that were in younger children because the absolute number of cases had gone down and therefore the proportion, if the absolute number in those young children stays the same…

Q I have understood your point unless you want to repeat it again?
A No.

Q I have understood it, unless anybody would like you to repeat it. Can we look at the right hand side of page 136 in the bottom right hand corner. I am still on the same paper at tab 23. HES data, halfway down:

> "The age specific admission rate for whooping cough decreased with increasing age and in children less than 6 months of age, was higher than the officially notified rate of illness. These figures are shown in Table 2 and suggest that both laboratory reports and notification data

A

substantially under-estimate the true burden of pertussis-attributable morbidity in young infants."

A That is so, yes.

Q Then we deal with the enhanced surveillance system:

B

"… identified 1368 pertussis isolations over the 3-year period 1995-7, of which 250 were detected solely by the reconciliation…"

You will have to help us with what that is:

"…of CDSC and PRL…"

C

A I think you have got a Panel member who might do better than me. Communicable Diseases Surveillance Centre is the centre in Colindale where, if you take a sample, it goes for specialist examination. PRL will be a reference laboratory.

Q In that last two and a half lines:

D

"During the 3 years studied 729 cases (53%) were less than 6 months of age, compared to 16% of notified cases."

Over the page we have got pertussis notifications, which, on the face of it, for six months appears to be increasing. Do you agree?

A In that period of time using that system, yes.

Q Looking at "Mortality" on the left:

E

"A total of 12 deaths…"

A Again, we are talking about percentages, not numbers on that graph. If you look at the axis on the left hand side…

Q I am not looking at the graph. I am looking at the table?

F

A Okay. Yes.

Q The table is numbers, is it not?

A The table is numbers. It is difficult to say there is an increase, because if you look at the ones under six months it starts off at 939 and goes down to 325, 214, then it goes up again, which is what we talked about with they cyclical pattern. It then goes down again. I think to say that there is even a changeover there would be more than I would interpret. I would not make…

G

Q Looking at "Mortality":

H

"A total of 12 deaths were identified from the enhanced surveillance system during the 3 years. Nine of these were male and 10 were less than 2 months of age."

A

A little further down:

> "Mortality data from ONS identified only 5 pertussis deaths during the same period. Of these 2 had been identified in the enhanced surveillance database and all 5 cases were less than 3 months of age."

B

Then there is something called anecdotal information in the last paragraph on the left?
A Robert Booy is a paediatric infectious diseases person who will see children who are severely ill with pertussis and other infections, so presumably he just told the authors, "I happened to see a case."

Q I have assumed that is what it meant by "anecdotal".

C

> "Anecdotal information (R. Booy, personal communication) identified a pertussis related death in another child of less than 2 months not recorded in any of the above systems; thus, there were at least 18 pertussis related deaths in the 1995-7 period and this is likely to be an underestimate of the true number."

D

At the top of the next paragraph, or the last sentence:

> "We estimate the total number of pertussis deaths during the 3 years to be 28 (95% CI 19-58)."

A That means they think there are 28, but they cannot be certain. It is somewhere between 19 and 58.

E

Q If we look at page 139 in the bottom right hand corner:

> "This increased severity of serotype 1,2 was not related to differences in proportions fully vaccinated, partially vaccinated or to differences in the age distribution of cases with differing serotypes."

F

Then "Vaccine efficacy" in the third line down:

> "There was a significant downward trend in efficacy with increasing age from 95.8% in the 6-11 month age group to 75.8% in the 5-14 year age group."

G

Then there are various figures given on the right hand side. We are going to look at those, because I think you give a figure for the vaccine efficacy and criticise Dr Donegan about it, but, if I may say so, your figure, on the face of it, appears to be inaccurate, but we will have to come back to that. There is quite a lot in this paper. Perhaps we can deal with it now while we are looking at the paper and then if people want to come back to it that might save a bit of time. I am still on page 140. The table at the top headed "Table 6. Vaccine efficacy according to age, using screening method". If you look at the penultimate column you will see "Vaccine efficacy (95% confidence intervals)"?

H

A Yes.

Q I think the efficacy is 95.8 for one to four year olds in 1995. Let me explain how this works. The age group is on the left. We have got 6-11 months and then 1-4 year olds?
A Yes.

B Q Then 1995 on the right, fully vaccinated, partially vaccinated, unvaccinated, national vaccine coverage and the vaccine efficacy, 95.8, taking the highest figure?
A Yes.

Q For 1-4 year olds. For 1-4 years olds in 1996 the efficacy is down to 92.7?
A Yes.

C Q For 1997 it is down to 88.9?
A Yes.

Q I may not be a mathematician, but it looks like the vaccine efficacy is reducing?
A That is part of the point of the last table, to say whether these are significant trends.

D Q The comment on it is a different matter. Let us deal with the facts of it, first of all?
A I think it is quite important. As you say, there are two bits to the figure. There is the first figure and then there is the bit in brackets. It is, "I think it is round about this, but it could be anywhere between the two figures."

Q I appreciate that. It goes back to the point before. I think everybody can take it
E that every statistic is…
A An estimate.

Q …an estimate. Nobody here is sufficiently green enough to say that a statistic is cast in stone?
A But it is quite an important point, because with that degree of uncertainty, if you are going to say something is different, you need to know how uncertain you are. If you
F are very uncertain and something changes a little bit you cannot say it is a genuine change. It could be by chance.

Q I appreciate that, but the general trend… It is not PhD on this particular point. The general trend, as we can see from that, is that the vaccine efficacy is reducing?
A No, I do not accept that, because of the reasons I have said.

G Q Let us look at what the authors say:

> "There was a significant downward trend in efficacy with increasing age from 95.8% in the 6-11 month age group to 75.8% in the 5-14 year age group."

H A That is right. That is a trend with the age of the children, not over the period 1995

A to 1997.

Q Let us look at the next column, three lines down:

> "…whereas for the 104 year olds there was a significant downward trend in efficacy…"

B A That is right. That is for the 1-4s, which is, I grant you, the ones you pick out, but you have got, as you were saying yourself, this upturn in 91.8% at 1-4 years old.

Q Let us read the rest of it so that I am not leaving it as a bald assertion.

> "The reason for this is not clear as all these children were exposed to the accelerated vaccination schedule at 2, 3 and 4 months of age (introduced mid-1990) with the exception of some of those aged 4 years in 1995."

C It is a perfectly reasonable point on this paper, is it not, that Dr Donegan is making?
A Do you want to refer me to the comment I have made? I think that is what you are querying.

D Q You said that there is a continuing fall in the disease between 1980 and 1990?
A That is right.

Q Directly contrary to what she stated. That is your comment?
A That is not addressed by efficacy. That is a different matter. That is numbers of cases.

E Q But she is making the point – if I can be permitted to call her she – that because of the continuing increase in pertussis notification in the UK, especially in young babies, accelerated schedules of vaccination were introduced to try to reduce the incidence in the disease?
A That is right. What I said – and that was the previous point – was that there was not an increase in disease. What we have just been talking about is how well the vaccine works.

F Q I think Dr Donegan is making a fair point. You are referring to 91.8% as not going up. If you look back at the table, as far as this matters, the 91.8% is for all years, 1995 to 1997. It is the second figure up in the vaccine efficacy, 91.8%?
A Yes.

G Q I thought you had said that it had not gone up because of 91.8%. You said there was an upturn in the 91.8%?
A If you are going to use the just looking at the figure bit, there is an upturn in 91.8%. It is bigger than it was the previous year, which was 88.9.

Q If you look on the left you will see it is for all years, 1995 to 1997. That is the point Dr Donegan was making. If you look on the left and not the right you will see it

H says:

A

"All years 95-97".

You are looking at the right of the paper?
A What I am looking at is the 91.8%.

Q I know you are. I can see where you are pointing to, but if you look on the left I am trying to help you?
B
A Also what I was looking at was the 88.9 at 1-4 in 1997, which is a small increase. I am not going to make anything of that because of the statistics…

THE CHAIRMAN: I think what happened is that the figures were concertinaed for those three years – two years, 1995 to 1997?
A I take your point.

C

MR STERN: Sometimes what I say does make sense. You should listen sometimes?
A I listen all the time.

Q If you look on the left you will see it accumulates those figures, so your point in relation to 91.8 is a global figure?
A I take your point, yes.

D

Q Can we just look then at the discussion at page 140:

"Some models of vaccine coverage, immunity…"

I want to deal with the third line down. I do not want to keep repeating it, but if there is anything I miss out you will let me know.

E

"…England and Wales, an expected constancy of incidence rates and an increase in proportion of cases in older children and adults…"

is the point being made there. Over the page in the third line down:

F

"There was an increase in the numbers of notifications in 1996 and 1997. However, early 1998 data … suggests the increase although modest by historical proportions is already at a peak. This contrasts with some other countries with similar vaccination rates, the United States and Netherlands, where recent substantial increases in pertussis have been described. In Scotland there were also increases in notifications in 1996/7 which were predicted to continue to 1998 and have since declined."

G

In the next paragraph, if I could draw your attention to the fourth line down:

"The trend to increasing notifications in both those too young for vaccination and in older persons many years post vaccination and without the benefit of natural boosting."

H

A

Then can we go to the right please, three lines up from the second paragraph? It is discussing this particular research and it says:

> "…it may also be an early indication of a more rapid decline in efficacy with lack of boosting from reduced exposure to circulating …*pertussis* in recent years."

B

A I have got lost on that.

Q If you look to the right you will see the second paragraph down begins:

> "The limitations…"

C

A Yes.

Q If you go to the foot of that paragraph, the last three lines, it says:

> "…it may also be an early indication of more rapid decline in efficacy…"

D

A Yes.

Q That was a possible. Then it says:

> "As with a number of recent international reports from the United States and Australia our data show a significant recent mortality in very young children affected by pertussis and an increasing proportion of cases in very young children.
> In the presence of continued high vaccination levels, and early signs of more rapid waning of the efficacy of whole cell vaccine under an accelerated program, high levels of morbidity and mortality death in young children can only be addressed by providing booster vaccination in older groups and increased recognition of disease in milder forms so that those at risk of severe disease can be given antibiotics at an early stage."

E

F

A Yes.

Q Just to complete this paper so I do not have to come back to it, looking at the next page, page 142, on the left-hand side, about ten lines down, two words in from the right, it begins, "In the Netherlands." Do you have ---

G

A Yes.

Q Thank you.

> "In the Netherlands the recent 10-fold increase in pertussis incidence, which has occurred despite continuing high coverage with whole cell vaccine, has been associated with an increase in serotype 1, 2."

H

A

Then about four lines further on from that, "...it has been postulated that changes in" - I do not know how you pronounce that.
A Pertactin.

Q Pertactin. Thank you. "...subtype may be associated with the recent re-emergence of pertussis in the Netherlands."

B With a degree of joy, I leave that paper. Can I just ask, please, that you be given another document, chief medical officer's document. You will, I know, have seen this.

THE CHAIRMAN: This will be D8. *(Same handed to the Panel)*

MR STERN: I am sure you are familiar with this document.
A Yes. *(Same handed)*

C Q I thought you would be. It was issued in October 2001 from the chief medical officer. It is to the usual culprits, if I can put it that way, generally.

> "This letter is to update you on several important immunisation issues, [namely]: 1. The introduction of a pre-school acellular pertussis booster immunisation; 2. Thiomersal in vaccines; 3. MMR vaccine update."

D Then just dealing with "Pre-school acellular pertussis booster":

> "...is to be modified by the introduction of a pre-school booster vaccination against whooping cough as part of a combined...(DTaP) vaccine."

E So the vaccines altogether, a one in three, if you like?
A Yes.

Q

> "Why this change is being made. The current immunisation programme against pertussis consists of a series of primary immunisations at 2, 3 and 4 months of age. Despite high vaccine uptake (about 95%) pertussis continues to be the cause of significant morbidity and mortality in children too young to be fully protected. There is evidence that these babies may be catching pertussis from older siblings or possibly parents. In addition there is a growing awareness that pertussis in adults [and older children] is a significant public health burden."

F

G Over the page, "1.3 The Joint Committee on Vaccination and Immunisation." Is that a committee you have actually sat on while I am on that point?
A No.

Q It is difficult to keep up with all these committees.
A No, it is not.

H Q It is difficult be for me to keep up with them. It may not be for you.

A It is sometimes difficult.

Q What is that committee, the joint committee?
A That is the committee that advises the Department of Health on vaccine policy, not just children, but across the board, so flu as well.

Q I see.
A It is composed of - well, it may be relevant, because Professor Kroll either does or has sat on it.

Q Yes. He has put it in his report. I think the committee will have already seen that. The JCVI, if I can shorten them, "has considered whether the introduction of a booster dose of pertussis vaccine would help reduce these levels of morbidity and mortality. Up until now a booster dose has not been part of the UK programme. The existing wholecell pertussis vaccine, as used in the current DTP immunisation programme at 2, 3 and 4 months, has been considered unsuitable for use as a routine booster due to the increased rate of reactions in older children."

Then a little further down, about three lines down:

> "Mathematical modelling by the Public Health Laboratory Service has demonstrated that a booster will reduce illness in older age groups and reduce the transmission of pertussis to babies too young to be fully protected. This is expected to reduce morbidity and mortality..."

Obviously acting on this evidence, the JCVI has therefore recommended a booster, preschool booster, that is. It then goes on to say:

> "Many countries across Europe as well as the USA already have acellular pertussis boosters in their routine programmes. There has not been cause for concern over either over efficacy or safety."

Then thiomersal, over the page, we may have to come back to. We can leave that for the moment, if you do not mind. Can we move, please, to page 16 in your report? Just give me a moment. *(Pause)* I will move on. I may have to come back to something, so forgive me, doctor, if I do go backwards at one point. At the top of page 16, referable to Dr Donegan's report, page 18, paragraph 2. The point that you are dealing with in relation to Dr Donegan's report is the last three lines of that paragraph:

> "As with a number of recent reports from the UK, USA and Australia, there seems to be a trend towards increasing numbers of deaths in very young children and a 'waning' of vaccine effectiveness in 1-4 year olds."

That is the point.
A Yes.

Q Let us look at what you say about it, if we may. You quoted at the top of page 16, then you say, "The reference, (tab 23)", which is the one we have just been through. Yes?
A Yes.

Q "...does not give a real indication of any trends in mortality, as it only covers 1995-7. However, it does support her suggestion of waning immunity in 1-4 year olds." So there is no criticism there.
A I have got the figures wrong.

Q This is the point I wanted to make. Rather than going back to the paper, I thought it would be more helpful to deal with the paper in one go.
A Yes.

Q

> "What Dr Donegan does not point out is that this is a fall from 95.8% protection to 91.8%. This latter is still a very high degree of protection."

You accept, obviously, having looked at that, you were wrong about that?
A I would change the figure of 91.8 to 80 - whatever it was.

THE LEGAL ASSESSOR: 88.9.

THE WITNESS: Thank you.

MR STERN: Thank you very much. 88.9
A I would have still had the next sentence in, though.

Q You think that is still a high degree of protection?
A It is very good, yes.

Q Not quite as good as 91, obviously?
A No, no.

Q Even though it is an estimate?
A Yes.

Q Then, as regards deaths, I do not think you make any other point, really, in relation to this particular paragraph. Therefore, I can leave that. I better just deal, if I may, with two papers that you refer to there. Your reference 7 and 8. When I say "your reference," I mean divider 7 and 8. That is Dr Elliman's references, divider 7, first of all. This is from Down Under, the vaccinations in Australia.
A Yes.

Q "National Centre For Immunisation Research and Surveillance of Vaccine Preventable Diseases June 2000," dealing with a position in Australia from '93 to '98. Can we just turn - the page numbers I am looking at are in the top left-hand corner. If you turn to page 22, under "Secular Trends." 34,848 notifications of pertussis; dates of onset between '93 and '98; median, 396 cases notified each month; lowest rate was 23.5 in '95, highest was 58.9 in '97.

> "Pertussis notifications peaked in 1997 when 10,907 cases were notified, approximately doubled the number in previous and subsequent years."

Over the page, please, page 23 at the top right. There is a figure 7 there. There are, as

you have already referred, the cyclical peaks? You have to say yes, rather than just nod.
A Sorry. Yes.

Q Cyclical peaks and, on the face of it, the cyclical peaks appear to be getting higher, on the face of that?
A Sorry. I do not know that that is true, because when you are looking at this thing, you have to look at it a bit more - crudely is the wrong word, but if you get into too much detail, it is confusing, because things do go up and down within the cyclical peaks. I think I would agree with you that the peak for '98 is bigger than the peak for '94 of notifications, but seeing as that is only two peaks, it is a bit difficult to talk about a trend.

Q Right. I was not mentioning a trend. I was just saying, on the face of it, the peaks look like they are getting higher. I see, you interpret that as a trend.
A Sorry.

Q No, that is a perfectly fair point. In any event, the notifications, on the face of it, are 1600, or thereabouts, in 1998, which is double from '97, roughly? I am only doing roughly; 800 to 1600. Then, if we look at table 6 below, "Pertussis notifications, hospitalisations and deaths by age group Australia 1993-1998," the age group 0 to 4, there were nine deaths in that age range. Yes?
A Yes.

Q Then over the page:

> "Between 1993 and 1997 there were nine deaths attributed to pertussis: all were less than 12 months of age; six occurred in 1997."

It follows that half the deaths were in the final year, '97?
A It does.

Q Therefore, that could be interpreted as an upward trend, would you agree?
A No.

Q You do not agree?
A Not one set of figures.

Q I see.
A That is my criticism.

Q That is your point?
A The fact is right, but an interpretation is a trend.

Q There obviously must have been fewer deaths in the previous years? That follows?
A In that study, yes. Reading my report, I said, "This is not enough to indicate a trend." In fact, in the next three years, there was only one death.

Q We are going to look at the next year because it is the next reference that you have, is it not?
A Yes.

Q

A

> "Age and sex distribution. The highest notification rate was overall in infants aged less than one year."

Then two lines below that:

> "Children aged less than five years accounted for 71% of hospitalisations."

B

Yes?
A Yes.

Q Over the page, there is a comment:

> "Pertussis caused the greatest morbidity of any vaccine preventable disease, both over the entire review period and in the most recent year reviewed. The highest numbers of pertussis notifications and hospitalisations were seen in 1997, with most jurisdictions experiencing an epidemic in that year. This epidemic affected all age groups with more deaths recorded than in any year since 1960."

C

That you do not say is a trend?
A No.

D

Q An epidemic is not the same as a trend?
A No. What they are saying is that if you look at all the figures from 1960 onwards, this was the highest one.

Q Yes.
A A trend to me would indicate that over a period it had been rising, but it is one isolated example, which is quite a different thing when you come to interpret what it means.

E

Q All right. Then we can see in the next paragraph:

> "The high proportion of hospitalised infants less than one year demonstrated the increased morbidity of pertussis in this age group. Notification rates are known to underestimate incidence."

F

Then that was demonstrated by various things and I need not trouble you. Over the page, can I just draw your attention to one particular aspect in the middle paragraph, second line down:

> "However, in the [United States] adults are less likely to be notified than in Australia, as the [United States] does not include serological diagnosis in its case definition. In the Netherlands, serological diagnosis is included, but the serological case definition is much stricter than in Australia."

G

Does that mean, essentially, blood and saliva analysis?
A Predominantly it would be blood. Some people may be experimenting on saliva.

H

A

Q Basically a blood diagnosis?
A Yes.

Q Can we turn to the next reference, which is 8, which is, as you have already indicated, the following period for the same particular aspect.
A Can I comment on these two papers?

B

Q Yes. Should we look at them first? Obviously the committee have not looked at this one yet.
A well, I think it is relevant.

Q Yes.
A It is to say that these two I found on the Internet. If you note, the second one was made --

C

Q You have dropped your voice.
A These I found both on the Internet when I looked in 2006.

Q I see.
A The last one is dated May 2002. I think I have said in my report it may not have been so readily available at the time.

D

Q You are absolutely right. You have put that in your report.
A Can I just look at the second page of that, which has a 42 in the top left-hand corner. Under the sub-heading, "Secular trends," it says 10,339 notifications of pertussis were received, with dates of onset in 1999 to 2000; average at median. "The notification rate in 2000 was the highest since 1997." On the face of it, it does seem to be going up, does it not?
A The amount of disease, yes, but we are talking about deaths, disease, et cetera, and it needs to be very clear which we are talking about on each occasion.

E

Q Also looking at the next page we can see, page 43, there is the extension of the same graph that we looked at before.
A Yes.

Q So there is a couple - the peak - the epidemic, if you like, has reduced, but the peaks, on the face of it, seem to still be going up?
A Yes, they could be interpreted as that.

F

Q Could we just look at the comment in the final page, page 46. In the middle paragraph, "Notification rates are known to underestimate incidence..." and then three lines further down:

G

> "It is noteworthy that the hospitalisation rates for infants was lower in the 1999 to 2000 inter-epidemic period than in the previous inter-epidemic period 1993 to 1995. This may be an early indication of an impact from higher coverage with acellular vaccines, which were introduced in 1999 in infants, but confirmation of this will have to await [data] from the next epidemic period.
>
> The temporal pattern seen in the reduction in notification rates in Australian children aged 5-9 years coincide with an increase in rates

H

A

> in 10-14 year olds strongly suggests an effect from the introduction in 1994 of the fifth dose of pertussis vaccine for preschoolers, who are now in the 5-9 year-old age group."

Have I understood this correctly? Despite five doses, we are still getting the cycles of disease?
A There is still a cyclical pattern to whooping cough disease, yes.

B Q Despite the five doses - have I understood - five doses for one individual? I have understood that correctly?
A I am not sure if the five doses apply for these ten to 14-year-olds. The third paragraph says:

> "1994 of the fifth dose of pertussis vaccine for preschoolers, who are now in the 5-9 year-old age group."

C Q I was not sure, which is why I was asking – I thought you might know the answer?
A I think the ten to 14 year olds would not have been affected by that.

Q It may not matter; we have got enough to get on with.
A I am slightly lost where this relates to my report, because I was talking about
D deaths specifically.

Q I appreciate that; I appreciate that you are talking about deaths specifically, but I am dealing with the second point, which is the waning of vaccination effectiveness as well.
A Ah, right.

E Q I am afraid I think we do have to go back to your references at 9 and 10, which is the same sort of report, but we can deal with it rather briefly, for the United States. Just turning it on its side, we can see half-way down is "Pertussis (whooping cough)" and this is "deaths from selected diseases, United States, 1984-1993". We can see the dates at the top – 1984 through to 1993. 1998 and 1990 were twelve; 1991 none; 1992 five; 1993 seven. Then if we just go to divider 10 we have exactly the same table for the next period – just one more year or two. That finishes at 1993, so just looking from 1994, if we can.
F Again, halfway down: 1994, eight, six, four, six and five deaths. Yes?
A Yes.

Q That is from the US. You have said at the foot of that paragraph at page 16 that the addition of a booster dose of pertussis vaccine in October 2001 is a very logical response to a situation where it is known that immunity wanes over time. When you say
G it is a very logical response, is that a logical response to the increase in the disease or the decrease in effectiveness of the vaccine?
A I have said that I do not think the disease was increasing in this country in the age group. The problem is, as has been outlined, is the pertussis in babies is the big killer but there is a lot of pertussis in adults. We know that the vaccine wanes, therefore to protect the babies we need to protect the adults so they do not get the disease and cannot pass it on to the babies. So it is a logical response to a known decline in the efficacy of the
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vaccine with age.

Q Can we look at the next point, unless there is anything more you want to say about that?
A No.

Q Again, page 16, penultimate paragraph – page 16 of your report I am talking about – and it is referable to page 18, paragraph 2 of Dr Donegan's report. It is the first sentence at paragraph 2:

> "The incidence of pertussis death and disease was falling well before the vaccine was introduced in the 1950s."

That is the part to underline, I think, because that is the point that you deal with in your report. Your complaint:

> "On the previous page of her report there is a graph showing that indeed, the deaths were falling, but there seems to be a temporal relationship between introduction of the vaccine, its uptake and the incidence of disease. This suggests the vaccine may have had an effect, yet Dr Donegan does not mention this."

A Yes.

Q Do I take it you are happy to rely on the temporal association when it is to the advantage of a vaccination but not when it is against?
A No. The reason I used that is because it was information that was provided and I felt that I should start by commenting on the information that was provided. I could have produced trial data, which has been mentioned elsewhere, that showed that whooping cough vaccine does not work.

Q But you have included in that particular paragraph, you say "This suggests the vaccine may have had an effect"?
A It does. I do not say it proves, I say it suggests.

Q I take it that you have no difficulty when Dr Donegan writes in the opposite fashion "this suggests/may have been" or something along that line?
A Not if there is a reasonable basis for that to be said.

Q You have used as a reasonable basis that there is a temporal relationship?
A It is a starter.

Q Can we just have a quick look at the graph if we can, please, because looking at page 16 of Dr Donegan's report, if we turn it on its side it is a graph. It goes, as we have already noted, 1867 to 1972 on the bottom axis?
A The one related to deaths.

Q Pertussis death rates, England and Wales, yes – thank you. We can see the death rate on the left, the date on the bottom axis, "Pertussis vaccination introduced" at the

beginning of the arrow I think you would agree, or thereabouts?
A Yes. As we have said, it drifted in.

Q It is obvious from that graph, is it not, that there was a decline in deaths from pertussis way before the vaccination?
A I would agree entirely.

Q It speaks for itself, does it not, that graph, fairly obviously?
A Yes.

Q So it follows, does it not, from that – maybe it does not, I do not know; you tell me whether you agree – does it not follow from that that there are other factors other than vaccination that reduce the disease?
A Sorry, I am not being pedantic for the sake of it but there is incidence of disease and death. This is a graph of death.

Q There must be other factors that reduce the number of deaths from pertussis then?
A Undoubtedly, and that would apply across most of the infections we could think of.

Q If you will give me a moment, I will see whether I do need to refer to this or not. *(Pause)* For the sake of completeness, could you look at your reference, please, divider 6? Internal page 103 on the top right, subheading "Whooping Cough":

> "The death-rate from whooping cough in England and Wales has declined since the seventh decade of the nineteenth century. The effectiveness of treatment is still in doubt, and the more important issue is the contribution of immunization."

We can see the graph just below it. Over the page:

> "As mortality had fallen to a low level before immunization was introduced, its value must be judged in relation to morbidity, of which the evidence is the trend of notifications. This source is notoriously unsatisfactory because frequently cases are not notified."

Then in the final paragraph on that page:

> "Opinion, including medical opinion, is still divided over the relative advantages and disadvantages of immunization against whooping cough. A decision is important in practice; but it is not essential for this analysis."

Then it deals with intellectual honesty of the author by the number of phenomena he or she leaved unexplained. Page 16 of your report at the foot of the page, going over to page 17:

> "It is true that vaccinated adults do develop pertussis, due to the waning of the effects of the immunization and that there is some

A

> evidence that the proportion of the various serotypes causing disease has changed."

That relates to Dr Donovan's page 18, paragraph 3. I need not trouble you with it because it is a paragraph for which you have no comment – or I think you agree, essentially?
A Yes.

B

Q Page 17 of your report, page 19 of Dr Donegan's report – I can deal with this quite swiftly as I think I have already made the position clear so that you knew what it was yesterday or the day before (I have lost track of the days) – it is under the subheading "Does the vaccine cause brain damage" – yes?
A Yes.

C

Q Dr Donegan is dealing with a study there and in relation to the part that says that:

> "…only the numbers who had been vaccinated against pertussis in the seven days before the neurological event",

that was an error, all right? It follows that the following point is a bad point that she is making:

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> "This means that a child could have had a serious neurological reaction two or three weeks after pertussis vaccination and this would not have been included in the 'pertussis vaccine' figures."

Obviously, it follows from the mistake that she made. Having said that, I do not need to ask you about it. However, the conclusion, you agree with, is accurate?
A That is within the time frame of 0 to 7 there was a 2.5 times increased risk. I do agree with that, yes.

E

Q As you say in your report:

> "Dr Donegan's reporting of the IoM's conclusions on pertussis vaccine are correct?

F

A Yes.

Q So the conclusions are accurately recorded, although there is obviously a point there which is not right?
A Yes.

G

Q Moving to the second paragraph down on page 17, this relates to page 20 of Dr Donegan's report---
A I am sorry to go back but the wording is quite important because what Dr Donegan has stated on page 19---

Q Which page are you on?
H A Her page 19, "severe neurological damage". There were two groups of children

A that they were talking about, and I would have to go back to the figures to be exactly certain. There was a group of children who had an acute neurological illness, so they had something which was very severe but ended – they got better – and then there were children that they would have referred to with a permanent problem when they followed them up. Off the top of my head, I cannot remember whether the 2.5 referred to the larger group who had an acute problem or the smaller group that had the long-term problem, which I would call "damage". I agree with the essence of that.

B Q Dr Donegan can look it up and if we need to come back to it, we will. I think a similar point occurs on the next page that I am about to deal with, so let us deal with it in that way and we can come back to it if we need to. Page 20 of Dr Donegan's report, page 17 of your report, and the point in the third paragraph down:

> "A similar case-control study in the United Stated found an association between pertussis vaccination and neurological damage."

C Going over to your report you say, having set that out:

> "The reference is to an abstract of a conference presentation. I have been unable to access this, but I have found the study published in a peer review journal. The study refers to acute neurological illness and not neurological damage."

D That is your complaint, as I understand it?
A And that is what I was referring to previously.

Q That is a separate study. I just want to point out, if I may, the paragraph just below the one that we have looked at in Dr Donegan's report, which says:

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> "All these studies and reviews of them say that the risks of the vaccine are small and where the evidence is not regarded as sufficient to either accept or reject a causal association this is taken to mean that the vaccine is safe and that parents should be encouraged to carry on vaccinating their children."

F So that is a significant balancing point, do you agree? I am going not come on to the damage and deal with that; I am not talking about damage.
A What I am hesitating about is I do not think it would be fair to say that because you do not have evidence of a problem you should assume there is no problem – which I think is "where the evidence is not regarded as sufficient to accept or reject". So it is saying "We don't really know" and my reading of this is if we do not really know that is
G interpreted as "It's okay". Is that right?

Q It is obviously a matter for the Panel as to how they interpret it, but you have made no comment about this. It seems, on the face of it – obviously, one can read anything in two ways but on the face of it it seems as if she is saying that the risks of the vaccine are small and where the evidence is not regarded as sufficient to either accept or reject the causal association, which is pretty obvious---
H A That means we cannot make a decision.

Q There are some instances where you cannot, is that right?
A That is right, but I do not think that would necessarily mean that people would say it is safe. What they would be inclined to say is "We know that it cannot be a very common problem" and would use that when they come up to weigh their risks and balances.

Q It might be phrased slightly differently but in essence she is saying that that is taken to mean that the vaccine is safe and parents should be encouraged to carry on vaccinating their children?
A The Institute of Medicine's terminology, which is this "accept or reject a causal association" does not go on to say "Therefore, it is safe".

Q I am not going to quibble about individual words and the tenor of it – obviously, one can make what they want. As I say, your point is that damage is not mentioned in the paper – yes?
A Yes, or that damage and acute illness are different.

Q If you look, the paper was actually missing from the list of references, being the one that was before the Court; that is the reference at the back of the report. You might need to go back to the bundle. Can I just give you a reference so that if you want to go back to the bundle in due course, the list of references that is headed "In the High Court of Justice, Family Division" and it says "References from Dr Donegan". It obviously deals with the pertussis point and it is number 9, which says "Library Copy Only. Inquire ongoing regarding reproduction". I think that is the one?
A Is this the HMSO one? I have an abstract of it.

Q The easiest way for me to show that point is if you go to bundle 1 of Dr Donegan's references and go to divider 11 – in mine it is empty?
A It is empty. It is a 200 page document.

Q You have kindly put that in your bundle at divider 12?
A It is 11. Which are we referring to, the Alderslade?

Q It is 12. It is Dr Elliman's references, divider 12.

MR KARK: Can I assist, because we picked this up prior to these proceedings beginning? I think Dr Elliman was going to obtain a full copy.

THE WITNESS: It is not the full copy, but there are 70 odd pages of it.

MR KARK: What we have in divider 12 of Dr Elliman is an abstract from the American Journal.

MR STERN: I think that is clear because it says JAMA. You have already told us about that and that it is a journal. We have not got the full paper here, have we?

MR KARK: I think Dr Elliman has got the abstract.

A MR STERN: We can get it later if we need to because we are coming up to the lunch adjournment and I do not want to waste more time as we have got a lot to get through. We are not moving at a great pace. (*To the witness*) This is a long paper. It is 70 odd pages or something like that. We are talking about the one you have got at divider 12?
A The one you have got at divider 12 is a paper in an academic journal headed "Risk of Serious Acute Neurological Illness" by Gale.

B Q Yes?
A That is not a long thing. You have got it. We were referring to the previous one, number 11, which was the NCES study, which we have just talked about.

Q Let us deal with this one, because I am on a different point and I am in danger of confusing myself. Looking at this, this is January 1994:

C > "Objective: To evaluate the association between serious acute neurological illness and receipt of whole-cell pertussis vaccine."

I notice you have omitted the word "serious"?
A I have, because I mistakenly encompassed all neurological illness, yes.

Q Looking at the "Subject":

D > "A total of 424 confirmed cases of neurological illness were identified prospectively during a 12-month period…"

This was to determine whether illness occurred within 7 days of immunisation in case children?
A Yes.

E Q Then "Results":

> "The estimated odds ratio (OR) for onset of serious acute neurological illness within 7 days for young children exposed to DTP vaccine as 1.1."

F That is what it says?
A It does. I am looking at the article. It flips between serious and just neurological illness. The subject that you read out described it as neurological illness and then later it talks about serious acute neurological illness. I possibly should have put in "serious", yes.

G Q On page 2 in the first paragraph, two-thirds of the way down:

> "The NCES found that children hospitalised with serious acute neurological conditions or with seizures or encephalitis were more likely to have received DTP in the previous 7 days than were control children."

H A Yes.

A

Q The next paragraph in the third line down says:

> "…this study was not intended to answer definitively the question as to whether pertussis vaccine given as DTP causes neurological illness."

B That was not the purpose of the study, was it?
A No.

Q If we go to "Case Definitions" at page 3 we can see four lines down:

C

> "Acute encephalopathy was defined as a diffuse disorder of the brain lasting at least 24 hours and characterised by two or more of the following: (1) a change in mental status as shown in either behaviour or personality; (2) a decreased level of consciousness independent of a seizure; or (3) a seizure. Encephalopathies with evidence of inflammation, indicated by a white blood cell count in the cerebrospinal fluid of more than …"

a certain number,

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> "…were included as long as cultures were not positive. Static (residual, nonrevolving) encephalopathy alone did not qualify. Infantile spasms were defined as seizures with a characteristic manifestation and other clinically consistent data, even in the absence of a classic hypsarrhythmic electroencephalographic pattern. Complex febrile seizures were those that were accompanied by a temperature of at least 38 degrees C and lasted approximately 15 minutes or more or with focal manifestations during or immediately afterward. Total seizure time was cumulated if several seizures occurred during a 48-hour period."

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In the next paragraph:

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> "To be eligible for study participation, case children had to have an episode of one of these illnesses during the study period while they were between the ages of 1 and 24 months and living in either Oregon or Washington."

That is the nature of the study. On page 5 under the sub-heading "Results", the last four lines:

G

> "Of the 424 case-control sets available for analysis, 100 met the more restrictive NCES-like case criteria. Ninety of these case children had been admitted to hospitals, six were seen in emergency departments, and four were seen in hospital-based outpatient clinics."

H

A

On page 8 under "Risk Estimate by Diagnosis":

> "Of the 358 incident case children, 22 had acute encephalopathy, 182 afebrile seizures, 144 complex febrile seizures, and 10 infantile spasms."

Under "Comment" on page 9:

B

> "Our study was designed to assess the feasibility of conducting a definitive study of the association between DTP and serious neurological illness in the United States. We demonstrated that a study that avoided several of the alleged shortcomings of the NCES could be mounted in the United States; specifically, that population-based surveillance of serious neurological illness … could be implemented…"

C

A little further down:

> "…and that exposure to DTP could be confirmed from medical records for 91% of subjects. However, to have adequate statistical power to rule out any possibility of an association between previous vaccinations and neurological events such a study would need to be several times larger than our effort and would be extremely expensive. Given the rarity of the neurological events and the inherent limitations of an observational study of this controversial issue, it is not clear whether a single such study would have a reasonable chance of settling this controversy."

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On page 10 in the second paragraph down:

> "Our findings are consistent with several other relatively large controlled studies that found no evidence of an association between DTP vaccine administration and onset of serious acute neurological illness."

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In the next paragraph:

> "However, when our analyses were restricted to the 100 cases that met the eligibility criteria compatible with those in NCES, the adjusted OR increased to 3.6. The NCES investigators observed an OR of serious acute neurological illness resulting in hospitalisation of 3.3 (95%) within 7 days of receipt of DTP vaccine and estimated an absolute risk of one case per 140 000 DTP immunisations in that study with a population estimated to have received over 2 240 000 doses of DTP vaccine."

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In the last few lines of that paragraph:

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> "However, recent in-depth reviews of NCES have suggested that the

> various biases were probably not sufficient to have accounted for all of the observed increase in the relative risk for acute neurological illness."

It says at the foot of the page:

> "It is reassuring that, if there was any risk associated with the vaccine, its absolute magnitude is so low that it cannot be detected in a study of this size."

Of course, that is not necessarily that reassuring for the parents of the individual child who suffers, but I understand what that means?
A I think there is a general thing that it would be very, very difficult to prove that something never happens. What you are talking about is the size of a risk. That is the best you can do.

Q Likewise, it is extremely difficult to prove that something does happen?
A It is easier to prove that something does happen, because if it is moderately common you can do research. If something happens, which is what is being argued here, perhaps it happens once every 200,000 times you do something, you are going to need a million or more people to know that it does not happen, so it is actually easier to prove that something does than that something does not.

Q It may be relatively easier, but still to prove a causation is virtually impossible, is it not?
A No. We are getting into an…

Q Academic argument which may not be that helpful. Let us move on to the rest of that page:

> "All major advisory bodies in the United States, Canada and the United Kingdom have concluded that the benefits associated with protection against pertussis clearly outweigh the potential risks from vaccine administered in accordance with current guidelines. However, they have also concluded that a relationship between serious acute neurological illness and DTP vaccine cannot be dismissed with absolute certainty."

I think that may be a convenient moment.

THE CHAIRMAN: We will break for lunch and return at two o'clock. Dr Elliman, you remain under oath unless you need to contact your team.

MR KARK: There is one matter I need to talk to him about. I have only mentioned it to Mr Stern.

MR STERN: Yes. As with yesterday and you can take it throughout, I have no objection to Mr Kark speaking to Dr Elliman at Mr Kark's discretion.

THE WITNESS: I wanted to speak to Mr Stern as well to ask him if he wanted some materials that have been mentioned.

MR STERN: I think Mr Kark is going to deal with that.

THE CHAIRMAN: You are free to leave.

MR KARK: While I am on my feet and just before we break, there is one piece of legal advice you received earlier in relation to the word "concomitant". The Legal Assessor said, "I think the words mean whatever the writer intends them to mean." I am not sure he intended that.

THE LEGAL ASSESSOR: I meant it in a judicial context. What I meant was, effectively, in this case.

MR KARK: In terms of what the Panel have to decide about Dr Donegan's statement, that is absolutely right.

THE LEGAL ASSESSOR: That is what I meant by a very bad phrase when I said, "In the judicial context." I was going to say, "In the forensic context", but people always think that has to do with something else. Anyway, we agree.

THE CHAIRMAN: Two o'clock.

(*The Panel adjourned for lunch*)

THE CHAIRMAN: Please continue.

MR STERN: Dr Elliman, we were about to look at the next point, which is to be found at page 17 and 18 of your report. That is the last paragraph on page 17, going over the page to page 18.

A Yes.

Q That corresponds, as we can see, with pages 20 and 21. That is the foot of page 20, going over to the top of page 21, and that top paragraph there.

A Yes.

Q Just to refresh your memory, bottom of page 20, Dr Donegan's report, this is the Michel Odent report, a 1997 retrospective study and then:

> "A larger prospective (looking forward) study of 9444 children in Avon which failed to show an association."

A I was just going to say yes.

Q Essentially, although you may say it is a short report, which I think is the point you make about it, that you describe it as being dismissed in one line, the Avon report, it, nevertheless, is set out there by Dr Donegan?

A It is there, yes.

Q All the other reports are dealt with in similar short form?
A Well, adding up the evidence, if you like, there are six and a half lines suggesting there might be a link, which are using very dubious methodology, and one line suggesting there might not be a link, using much better methodology. My point was that I did not really think that was giving the same weight to things as should have been.

Q She does say it is a larger prospective study?
A Yes.

Q And set out the number of children involved in it?
A Yes.

Q Your other point in relation to that is that you say, over the page, there is an omission of a paper by a man called Nilsson. I assume it is a man. I really should not assume that.
A I think he is, yes. I think.

Q Somebody called Nilsson, and you say, at the end of the paragraph at page 18:

> "This is the most powerful evidence on the subject and to omit it is inappropriate."

A Yes.

Q Did you check whether or not Dr Conway or Professor Kroll produced that paper?
A I did not. Well, no, it would be unfair. I cannot remember.

Q If they did not point to that paper, presumably it would be equally inappropriate for them not to have done?
A I think if they were producing a sort of overall picture, it would depend upon what they produced in it, but it would be one of the things that I would consider, producing in a report I would produce. Certainly.

Q Well, if I tell you that they did not produce it or refer to it - I should not say produce it, did not refer to it, that puts the matter in a little bit of perspective. Do you agree?
A I cannot remember if they specifically addressed the issue of asthma and pertussis vaccination. If they did, then I would expect this paper to be in it because it is one of the better ones.

Q Can we look, please, at Dr Donegan's reference, divider 16. This is the reference to the larger prospective studies, is it not?
A It is.

Q The paper is here for all to see.
A Yes.

Q If we look, please, at the first page of it, we can see the abstract, which is:

A

> "To examine the relation between pertussis vaccination and the prevalence of wheezing illnesses in young children."

It is a prospective cohort study. Halfway down we can see:

B

> "Results. Unadjusted comparisons of the defined wheezing illnesses in vaccinated and non-vaccinated children showed no significant association pertussis vaccination and any of the wheezing outcomes regardless of stratification for parental asthma or allergy."

C

> "Conclusions. No evidence found that pertussis vaccination increases the risk of wheezing illnesses...Further follow up of this population with objective measurement of allergy and bronchial responsiveness is planned to confirm these observations."

So that is essentially what the report says. There is not much more to it, is there?
A No, I would agree with that.

Q Can we look at your reference?

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MR STERN: Can we look at divider 13, please, in your references. Now, this is where I thought you said perhaps you did not phrase it as happily. I am paraphrasing what you said. I think that is essentially what you were saying. If we look at your report at page 18, in summarising the Nilsson study you have put:

E

> "There were over 2,000 in each group (ten times as many as in Dr Odent's study). There was no difference between the groups and symptoms of asthma. This is the most powerful evidence..."

Presumably the most powerful point about it is the fact there were 2,000 in it?
A No, it was the methodology as well. These were children who were initially recruited into a study looking at how well whooping cough vaccines, in the plural, work, and side effects. So these were randomly selected children, which is unique to all the four studies we now have before us. They were randomly assigned. So it was as much the methodology as the numbers that was the crucial difference.

F

Q Did you just read the letter or did you actually read the study which follows on at divider 14?
A The reason why I say it is perhaps a little misleading, is because this is one study looking at two aspects. Same cohort of children. The letter refers to the whole cohort where they were looking for symptoms of asthma, eczema and hayfever. The second part of it is where they take a small sample, still large, but proportionately small, and did further tests on them. So they were not asking for a clinical diagnosis of these conditions. They were doing skin tests, for example. So, where I am saying I might have misled people is leading them to the second study implying there were 10,000 in total there --

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Q Two thousand.
A Sorry, the second part of the study, implying there was a total of 10,000 there

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A where, in fact, the total of 10,000, which is four groups of just over 2,000.

Q You said 2,000, not 10,000.
A It is 2,000 in each arm of the study.

Q I appreciate that, but I am looking at your report. You say there were over 2,000 in each group.
A All right.

B

Q Then you made the conclusion that there was no difference between the groups in symptoms of asthma.
A That is right, yes.

Q Is that right?
A Yes, it is right.

C

Q Let us look at D14. Just looking at this paper, we can see on the first page:

> "Background: Pertussis vaccination in infancy has been suggested to increase the risk for development of asthma and allergy. Patients and methods: A total of 669 children were randomized to 1 of 4 vaccine groups..."

D

The children were evaluated by means of questionnaires. To the right, the results. The last three lines:

> "Among 47 children with proven pertussis, atopic disease appeared in 19 (40%). [Of these] 47 children, 9 developed asthma, as compared with 58 (9%) noninfected children. Conclusion: We found no support for a drastic increase in allergic manifestations after pertussis vaccination. There was a positive association between whooping cough and asthma by 2½ years of age."

E

Is that quite the same as saying there is no difference?
A The larger study, the 2,000 in each group, because it is larger, you can be more confident of your conclusions. So when they were looking at the large group of children, and I would emphasise, when you read out the methodology for this small group, it was not just questionnaires, it was questionnaires and skin tests.

F

Q Yes.
A This was a subset that they had done particular tests on.

G

Q Yes.
A So when looking at this subset, there is a smaller number. So if they look at this subset, they would have to be more cautious about giving a conclusion than when they look at the whole group, which is an enormous number, and you can be much more certain if you do not find an effect, that not finding the effect is a genuine finding. If you remember back our discussion about being certain about --

H

A

Q Let us just look at the rest of the paper so everyone can follow it, first of all. Let us go to page 737. The numbers are in the middle at the bottom. At the foot of the page, the last penultimate paragraph.

> "We intended to study whether pertussis vaccination of infants would increase the risk of atopic disease and were fortunate to obtain data in randomized and controlled experiment. Even though 669 children completed the trial, the estimated risk levels had large margins of error. Aiming at an 80% power to detect 10% increase in risk rate, a treatment group and a control group with nearly 4000 infants in each would have been needed. As each group in our study consisted of about 175 infants, any true differences would have to be nearly 50% to obtain an 80% power of detecting the differences. This is acceptable as the main purpose of the investigation was to detect a largely increased risk similar to that reported by Odent for a WC vaccine. A similar vaccine was included in the present study."

B

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It is commenting on the Odent study, is it not?
A Yes.

Q Over the page, four lines down:

D

> "The results indicate that it is unlikely that WC pertussis vaccination increases the risk of atopic disease up to 2½ years by more than 4% (single-sided upper 70% confidence limit). It may be argued that the observation period was too short to detect allergic respiratory disease."

E

The last few lines in that paragraph:

> "It seems presently reasonable to conclude that WC pertussis vaccination is not associated with a major increase in the risk of atopic disease."

Then in the next paragraph, two lines down:

F

> "The estimated risks of atopy following pertussis vaccination were about 10% larger than the estimated control group risk levels. Our results indicate a possible small increase in the risk of atopic disease after acellular pertussis vaccinations. The upper 95% confidence limit for an increased risk was considerable, however. In the large Swedish pertussis vaccine trial, the parents answered questions concerning symptoms of itching and wheezing in 9617 children."

G

About five lines below that, will you see the words:

> "These results suggest that any negative effects of acellular vaccines are not much larger than 10%. Whooping cough is a debilitating disease and, in infancy, there may be complications. The reasonable

H

A

> conclusion seems to be that acellular vaccines would at most be associated with small to moderate increase [in atopy]."

Now, does that find its way in your report, small to moderate increase?
A That there is a possibility of it, no.

Q You have written, "There was no difference between groups and symptoms in asthma."
B
A Statistically speaking, there was no difference, no. It goes back to the discussion about whether things could be by chance or not.

Q If you look at the next paragraph, it says, "We also observed an association between pertussis and asthma." It specifically says that, does it not?
A That is pertussis disease in asthma, not vaccine.

C

Q I see.

> "This could, for instance, be due to a causal relationship in that pertussis might increase the risk of later becoming asthmatic...It might also be due to transient bronchial hyperactivity after whooping cough.
>
> At present, we recommend pertussis vaccination during early infancy, independent on any family history of atopic disease."

D

You have selected, as it were, the 2,000 group and put the result there, have you?
A I selected the 2,000 group, because that was the one that was most readily available, and I would have expected it to have been available to someone who perhaps did not have advance searching facilities. It is the one that would come up. You might see the journal sitting in your library. Yes, very readily available.
E

Q Yes, but it is not the availability. That is a separate point, is it not?
A I was trying to be reasonable to what one could expect someone to have at the time.

F

Q Sorry. Forgive me for interrupting again. The point is whether you have reported it inaccurately. It is not a question of its availability.
A Reading the last paragraph of the large study, that is reference 13:

> "We found no significant differences between the DTP vaccination groups in the proportions of children with reported wheezing, itchy rash, or sneezing."

G

This is what they say in their letter.

Q Yes. I think if you look at the end of that letter, right at the end of the letter, you will see it says:

H

A

> "In-depth assessment of 720 of the children of 7 years of age will further clarify the associations."

A Yes.

Q I will comment about that later on. There we are. That is what you say about it. Thank you. Page 18 of your report, please. Referable to pages 21 and 22 of Dr Donegan's report. Her comment in relation to this is in the middle of page 21, which is:

B

> "Questions have also been asked about the incidence of invasive bacterial infection in children who have recently been vaccinated against pertussis. A 'natural experiment' took place in this country when the acceptance the vaccine fell dramatically in the mid 1970s to the mid 1980s and there was an accompanying fall in number of deaths of children aged four years and less from invasive meningococcal disease. The numbers began to rise again as vaccine uptake increased."

C

That is from the mid 80s. Coupled with that is the graph at page 22. You say:

D

> "This is a very poor standard of evidence and, in any case looking at her data, the prevalence of meningococcal disease does not mirror vaccination uptake. If anything, it is evidence against any link. There are studies that have looked at this and would have been available to Dr Donegan. A study in USA found no increase in hospital admissions for invasive bacterial infections in the 28 days after [DTP] immunization. An almost identical study but looking up to 30 days post immunization came to the same conclusion."

E

Those are your points, yes?
A That is true.

Q All Dr Donegan is pointing out in her report is that questions had also been asked. That is her comment?
A Yes. That is what she starts off with saying.

F

Q That is what she starts off with.
A Yes.

Q The studies that are referred to by you, can we just look at those, please? They are your references 15 and 16.

G

A Yes.

Q First of all, at divider 15, the abstract:

> "During the acellular pertussis vaccine trial in Sweden, 4 children who were randomly assigned to receive the vaccine died of

H

A

> suspected or confirmed bacterial infections compared to 1 expected. There were no deaths in the placebo arm."

Then at the bottom of the abstract:

> "These data provide reassurance that the use of DTP vaccine is not followed by a large increased risk of serious bacterial infections."

B

Yes?
A Yes.

Q Your report says, "A study in the USA found no increase in hospital admissions." Is there some distinction?
A Can you read out the bit again that contradicts that?

C

Q Well, it says:

> "These data provide reassurance that the use of DTP vaccine is not followed by a large increased risk of serious" ---

A Yes. That means - back to the discussion, again, you can never be certain of a
D negative, but if you were talking about something that you were to pick up crudely on notifications, like comparing two charts, you would expect to see it in this sort of study. If there was a very small thing that you would not see on notification data, then it is true, you might need a larger study than this.

Q You will have to forgive me – I am a lay person, as you understand. Can I just ask this simple question? How is it that "no increase" can equate "no significant
E increase"? That is really the question I am asking?
A Perhaps then as a general point go back to what I said before. You can never prove a negative, so all you can say from a study is that "We saw no significant increase". You cannot say "There is not a small increase".

Q Why did you not say that then?
A Because that is a given through everything. You can never be absolutely certain
F of something never being there. I suppose I ought to have started off my report with a discussion of research to say that research can never prove that something never happened.

Q I appreciate that, but where you are writing for a lay Panel as here – essentially a lay Panel, if Dr Goodman will forgive me – "a study in the USA found no increase".
G That, in plain English, to most people, I would have thought, is different from "no significant increase". Do you not follow that?
A What I am saying is no, I do not think it is. Sorry, it is but the interpretation is different.

Q Do I understand this? Although the paper says "No significant increase" your interpretation – your interpretation – of that, for various reasons (that I need not trouble
H you with) is that that equals no increase?

A That paper did not pick up an increase that could not be ascribed to chance.

Q Let us just look at the rest of the paper for convenience. Page 641 in the bottom right-hand corner is the page number. Right-hand column, about four lines down:

> "There was no significant increase in infections in the early immunization period following the first, second or subsequent DTP immunizations."

B

Then in the discussion part, three lines down:

> "There is not an apparently biologically plausible explanation to support a causal connection, and there are few other data that have addressed this issue. There are no experimental data on the risk of serious bacterial infections following DTP vaccinations in humans. However, the effects of pertussis vaccine on the susceptibility of experimental animals to infection includes evidence for both an increased and decreased susceptibility to infection depending on the animal model used.

C

> Our study was limited to the investigation of seriously culture-proven infections. Since all study children received at least one DTP immunization, we were unable to compare risk of infection between immunized and unimmunized children."

D

That was the point that you helpfully explained the other day for the Panel that I was trying to make. Then the last three lines:

> "These data thus provide reassurance that use of DTP vaccine is not followed by an early large increased risk of serious bacterial infections. The applicability of these results to acellular vaccines is unknown."

E

Again that seems to be, on the face of it, talking about no significant increase but we have your explanation. Can we go to divider 16, please? Just the left-hand side:

F

> "The purpose of this study was to determine whether children hospitalized with a primary diagnosis of infection were more likely than matched controls to have had a diphtheria-tetanus toxoids-pertussis immunization in the 30 days before hospitalization of the case."

G

Do I understand that all of the individuals in this study had the DTP vaccination at some point?

A I would need to read through it carefully, but that is not what I understand from the beginning, because it says "match controls".

Q If necessary, we can come back to it. Looking on the right-hand side, "Introduction", about eight lines down:

H

A

> "Vaccination with pertussis toxin has been shown to increase the susceptibility of mice to illness with the influenza virus."

Then in the last paragraph:

B

> "In a double blind placebo-controlled efficacy trial of two acellular pertussis vaccines conducted in Sweden, involving 3801 children, 3 children died from bacterial infections 2 to 10 weeks after receiving a DTP vaccine. All 3 children were in the group who received the acellular pertussis vaccine. No deaths occurred in the placebo group."

Is that significant or not?

C

A If we read further down---

Q I am going to.

A Sorry.

Q Sorry – no, no. I should not have interrupted – sorry. If we read further down, what?

D

A It says:

> "These researchers evaluated the relative risk for hospitalization due to systemic and respiratory infection in two acellular pertussis vaccine groups compared with the placebo group (relative risk, 1.07, 0.83, and not significant, respectively)."

E

I was going to summarise that. If you look a few further lines down, it says:

> "The results provided no evidence for a causal relationship between the studied acellular pertussis vaccines and decreased immunologic functions. However, these subset groups consisted of small numbers of children and the sample size may not have been large enough to demonstrate statistical significance."

F

A They are referring here to a previous study.

Q Then it is talking about:

G

> "In a study done in Israel 82 children were prospectively studied for infectious episodes after immunization with DTP. The incidence of illnesses before and after vaccination was compared and the investigators found a statistically significant increase in the number of cases of fever, diarrhoea and cough postvaccination."

Which are, of course, infection illnesses – invasive bacterial infection?

A No, they are not. Cough, diarrhoea – and I cannot remember what you said.

H

A

Q Cough?
A Cough is not invasive.

Q Fever?
A Fever is not necessarily invasive. Invasive would be if you got organisms in your blood, in the brain, somewhere inside your body, but a fever most commonly would be due to an ear infection or a sore throat and that would not be included as invasive.

B

Q Thank you very much for helping me on that. Can I turn to page 733, just looking at the discussion:

> "There has been considerable concern regarding potential adverse effects of DTP vaccine. In the Swedish efficacy trial of two acellular pertussis vaccines, three children died from bacterial infections 2 to 10 weeks after receiving an acellular DTP vaccine. The investigators in this initial study were concerned that the vaccine increased children's risk of serious infection."

C

Then it is the subsequent retrospective cohort study:

> "…hospital charts on children in the Swedish vaccine trial who were hospitalized were reviewed for discharge diagnoses of severe bacterial infections."

D

Then the last three lines, please, of that paragraph:

> "The authors caution that the small number of cases made it difficult to exclude a possible connection between vaccination and an increased risk of serious bacterial infections."

E

So if they came to a conclusion it is a tentative conclusion to say the least?
A In the discussion, what you have just read out is referring to the previous studies that have prompted these people to do the bigger study.

Q Because it goes on:

F

> "In our study, controls were 1.96 times more likely to have had a DTP immunization in the 30 days before hospitalization of the case. Controls were also significantly more likely to have had any type of immunization."

G

A Yes. So that is the people who are well.

Q Yes. Over the page it says, in the second paragraph, three lines down:

> "Controls were 10 times more likely to have been vaccinated in the 30 days before hospitalization than were cases. Controls were also 6.2 times more likely to have received any type of vaccine."

H

A Yes.

Q Then, halfway down:

> "In our study controls were significantly more likely to have been breast-fed in the 30 days before hospitalization of the case."

Then a few lines further down:

> "However, breast-feeding might be a marker for other social factors, including parental education, better maternal care and more appropriate use of the medical system."

Then at the bottom of this page:

> "The objective of this study was to determine whether DTP immunization was a risk factor for hospitalization with an infectious illness. It would have been reasonable to assume that no difference would have been found between cases and controls. It was surprising to find that controls were significantly more likely to have received DTP immunization than cases."

A Yes, but they do go on to produce possible reasons for it.

Q It says "there are several possible explanations for this finding"?
A Yes.

Q Obviously, they can be seen. They are lack of maternal transfer of antibody etcetera, etcetera – various reasons. The final paragraph:

> "Many syndromes that have been temporally associated with DTP vaccination have been shown to have no association when further investigations have been done. In this study no association was found between DTP immunization and increased risk of hospitalization with an infectious illness. We conclude that there is no association between DTP immunization and an increased risk of hospitalization because of infectious illnesses."

So that is their conclusion which, on the face of earlier comments and discussion and results, is, do you agree, a rather brave conclusion?
A They perhaps ought to have put a caveat round it; the usual "more research is needed", which probably had not been completed at that time but has now.

Q Can we move to the next point, please, page 18 at the bottom of your report, moving over to page 19. This is dealing with page 21, paragraph 3, of Dr Donegan's report. This is the Japanese study, which may or may not be of any relevance but at any rate we will deal with it swiftly, if we can. It reads, in the first sentence or so:

> "The Japanese raised the vaccination age to two years in 1975 after a

number of reports of severe reactions and deaths. This reduced the total number of deaths in infants younger than one year."

There is no doubt, is there, that there were a number of reports of severe reactions and deaths in Japan?
A I think it is true to say that what precipitated the withdrawal of the vaccine was two children who died cot deaths soon after receiving a vaccine. I phrased what I said very carefully – I did not imply a causative link. That was the circumstances as I understand it.

Q Because whatever the rights and wrongs of it, the Japanese government decided to cease DTP vaccination?
A Yes, temporarily. I think it was just a few months.

Q If we look at appendix 5 of your report, it is my page 68 – it probably is not?
A It is.

Q This is 1982 to 1996 graph, "Reported cases of and deaths"---

MR KARK: It is page 69, for those who are still trying to find it.

THE WITNESS: I think, with respect, are you looking at infant mortality or whooping cough?

MR STERN: No, Mr Kark is right, 69. Thank you. That is why I said Appendix 5 because my page numbers have become dislodged for some reason. It says "Figure 1. Reported case of and deaths" – I assume if means notifications of some sort. They have left out a word, have they not?
A I am not quite sure how they do it in Japan – it is a different methodology. Deaths will be a central register just as we have in this country.

Q It is a mystery as to what else they mean but there should be something there, probably notifications. The top part of the graph…I see "Reported cases of and deaths from" – I am grateful to Mr Grey. "Reported cases of and deaths from pertussis in Japan" and the top part is the cases and the lower the deaths. I think we can see that there was an increase in the deaths prior to the cessation of the vaccine?
A Yes.

Q It is right to say that there is an increase then of deaths after the cessation of the vaccine?
A There is an increase of deaths due to whooping cough.

Q That is what the heading says, "pertussis"?
A On this graph, yes.

Q This is not general deaths, this is only pertussis?
A That is right.

Q That is why I read the top first. Then I think we can see that there is a reduction

in the death rate prior to the reintroduction of the vaccination?
A Yes, about four years after the vaccine was ceased there is then a fall, which was prior, as you say, to the reintroduction of the vaccine. For the record, it is not reintroduction because it is a different vaccine.

Q It is DTAP rather than DTP?
A Yes.

Q I think the notifications in that intervening period went from 10,000, if we follow across, down to about 3,000, because that is a very big span, is it not, that 1,000 to 10,000 span there, so actually the notifications went down from 10,000 to about 3,000 in the intervening period between the peak from the cessation of the vaccine to the introduction of the new vaccine, very approximately the figures?
A The reason I hesitate is because I do not think I have got the reference with me, but it was not as simple as that. What happened was that the whooping cough vaccine was given to infants in Japan. They stopped temporarily giving it to infants and started giving it to two year olds, then after a few years they introduced the DTAP, so somewhere on that curve there should be an arrow – and this is not my curve, I lifted it. There should be an arrow that says "DTP vaccination at two years old started". They have missed an arrow actually.

Q There is an arrow missing?
A Yes, which is quite important because I think the total cessation was only a matter of a year or two so an arrow should come around 77/78. It may not be that late.

Q If it is potentially a bad point I will leave it. In any event, what one can see is that there are definitely dips in that graph – yes?
A Yes.

Q If we turn back a page, which is infant mortality, it shows, does it not, not even a blip on that graph in relation to what were obviously peaks and troughs of deaths?
A The curve, as you say, in Appendix 4, just seems to be a continuous fall with no change.

Q I think the point Dr Donegan is reminding me of and the point I should draw to your attention is that Dr Donegan's report at page 21 describes a reduction in the total number of deaths, not just of course those relating to pertussis?
A That was exactly my point, yes.

Q Can I just show you a paper which you may or may not be familiar with? I will try and do this very briefly. I have to accept that it is of tangential relevance, but, nevertheless, let me just give it to you, if I may. If it is produced later, then at least Dr Elliman has an opportunity to deal with it.

THE CHAIRMAN: It should be D9. (*Same handed*)

MR STERN: I am going to deal with it relatively briefly. You may or may not be familiar with it?
A I have read it but I cannot in detail recall the contents.

Q I will not say it is not scientific. Can I ask you to look in the background section, if I can guide the Panel through what I perceive to be the relevant parts of it? Obviously by the time you are re-examined by Mr Kark if there are any other matters he wants to raise, then he can.

> "BACKGROUND
>
> Whole-cell pertussis vaccines came into use in Japan in 1947, and their administration became mandatory as part of the Preventive Immunization Law of 1948. Vaccination consisted of three doses given approximately one to two months apart beginning at approximately 3 months of age, with a booster dose approximately one year after the third dose."

A couple of lines further down:

> "The reported incidence of pertussis in Japan fell rapidly after the introduction of the vaccine; deaths decreased correspondingly."

Then on the right, about five lines down:

> "Implementation of the compensation system subsequently served to draw increased attention to adverse events associated with pertussis vaccine and continued use of pertussis vaccine was questioned, particularly in light of the low incidence of reported cases of pertussis in Japan between 1970 and 1975.
>
> In a two-month period in the winter of 1974-1975, two infants died within 24 hours after receiving diphtheria and tetanus toxoids and pertussis vaccine (DTP). While these events were being investigated, recommendations were made for temporary suspension of the use of DTP. Two months later, routine use of the DTP vaccine was again recommended."

A That is what I was saying.

Q DTP came back?
A The same vaccine came back, but at a different age.

Q If you look at the next sentence you will see:

> "However, the recommended age at initial administration was raised from 3 months to 2 years as a precautionary measure to avoid other coincidental occurrences; also, it was believed the incidence of adverse events caused by, or temporarily associated with, pertussis vaccine might be higher during infancy."

Over the page please.

A Can I comment?

Q Please do?
A That outlines what I was trying to drag through my memory. It says in addition it was believed that adverse events would be commoner in infancy. There is actually a lot of data to show that that is not so. If you remember back to discussing the use of a pre-school booster, it was said one would not use a conventional vaccine at that age because, as you got older the conventional vaccine actually has more adverse reactions and therefore you use a new one.

Q Carrying on with this report at page 1352, about eight lines down in the bottom left hand corner:

> "…vaccine coverage declined in the mid-1970s, and the number of doses of DTP distributed declined. Because of the recommendation that the vaccine age be raised from 3 months to 2 years a decline in vaccine administration was expected for a period of approximately 2 years. In 1977, the first year in which a cohort of eligible 2-year olds would be expected, coverage with the first dose of pertussis vaccine was 41.7%, rising to 64.4% in 1978."

A few lines further down:

> "Following the decline in vaccine use, there was a significant increase in the reported incidence of pertussis, reaching a peak in 1979 when 13105 cases were reported and 41 deaths were recorded."

Moving to page 1354, can we look at table 3 at the top, "Adverse Reactions After Pertussis Immunisation. Based on Claim Paid by Compensation System", so the Japanese pay claims. Although they could not prove a causal connection, they nevertheless paid claims for compensation to adverse reactions as a result of pertussis?
A Many countries have similar schemes whereby – this country has a similar one, whereby you first have to exclude any cause for the reaction and it has to fall into a particular category of things. As you say, it is not a proof that something has caused a reaction. It is an acceptance that it is a possibility and you cannot find anything else.

Q From what you say, it sounds as if it is a relatively confined test?
A It varies from country to country. In the States I think it is quite confined. They have a list of things against which you have to do it. This country, I think, is slightly more lax. I cannot answer for Japan. Every country will say, "This is not acceptance of proof."

Q Because otherwise – one can imagine?
A Some of these have had compensation and yet have gone to court and sued and have failed. I do not know about Japan, but in this country.

Q That is very helpful. In the table in the top left hand corner we can see vaccine

type across the top, whole-cell and then the new DTP?
A Yes.

Q The periods of time are 1970 to 1974 and 1975 to 1980?
A Yes.

Q If you go to the third line down you will see it says:

> "Severe reactions… (includes death)."

A Yes.

Q In 1970 to 1974 there were 37 deaths, in 1975 to 1980 I think there were three deaths. Then it went down to two with the new DTP?
A Yes. Do you want me to comment on it?

Q Only if you want to?
A The way that these are linked is purely in time. Infants are more likely to die than two year olds, so there will be more coincidental deaths in infants than in two years olds, which is what the 1975 to 1980 period is referring to. I have not got the data with me to say exactly what it would be, but it is not comparing like with like is the important message.

Q I think, in fairness, if you look at 1356 about seven or eight lines down, which may or may not be the point you are making:

> "Since the primary evaluation and use of acellular vaccines have occurred in children 2 years and older only limited data have been collected on the safety and efficacy of acellular vaccines in infants."

Is that the point you are making?
A Yes.

Q I will not ask you about the conclusion because, as I say, we have already to some extent dealt with that. As Mr Kark has accepted, that is not primarily what the case is about. Can we move to tetanus please. It is page 20 of your report under the sub-heading "Dr Donegan's report". Your first comment is about her report at page 27. I suppose we had better look at the bottom of page 26. Dr Donegan is talking about immunity from tetanus, I think:

> "It is thought that tetanus prone skin wounds may boost immunity but are unlikely to lead to primary immunity."

That is the point she is making. Over the page, and this is the point that needs to be underlined because this is your criticism:

> "The lack of this gut based immunity may explain the occurrence of tetanus disease in fully immunised people with adequate levels of neutralising antibody."

A

Your comment is that she fails to mention that all the authors state that this is a rare occurrence and are very supportive of immunisation. Can I say, first of all, that the point she is making is a perfectly reasonable one. Do you agree?
A It may be so, yes.

Q The point is that a lack of gut based immunity – I think we have touched on this before – may provide some explanation as to the occurrence of tetanus in those who have been vaccinated and the non-occurrence of tetanus in unvaccinated individuals?
A I think the "before" that you are referring to is when we talked about whooping cough.

B

Q It may be. I cannot remember?
A If it was it is a different disease and a different mechanism.

C

Q It is a different mechanism because this is something obviously very different?
A It is. Whooping cough is more a surface infection. Tetanus is an internal infection, crudely.

Q Tetanus you cannot catch from another, I think?
A The answer to your question is no. Enormously rarely.

D

Q For our purposes?
A In real life terms.

Q Let me ask you this: it seems, if I may say so, that every time Dr Donegan makes any point it is your view that it needs to be balanced with a point which is supportive of vaccination?
A No, that is not my point. My point was that what I understood Dr Donegan to have been asked to do is produce – I cannot remember the words – something like a risk benefit, look at the benefits and the risks and decide what was best for the child. Therefore, if you take a paper that is talking about tetanus that actually concludes, for example, that tetanus vaccine is a good idea, it seems inappropriate, if you have used that paper for another purpose, not to mention that paper, especially if when you come to talk about the efficacy of tetanus all the papers you mention or all the quotes you mention seem to be balanced against it. It is not in every case, no, but it is painting a picture.

E

F

Q The point you are making is that she does not mention all the authors. You mean the papers that are set out in reference there?
A Yes, the ones she used.

G

Q She used and had copied for the experts on the other side?
A Yes.

Q They state it is a rare occurrence. What is the relevance of it being rare? If it does not work, it does not work. It is, if I may say so, a rather layman's approach to it?
A No, because when you talk about a vaccine not working, you do not say it does or it does not work. You say it works in a proportion of people. That is quite an important difference. If you were to say: does a vaccine never work, the answer would be: that is

H

most unusual. Does it work always? That would be unusual. You quantify it. For tetanus vaccine actually it works very, very, very successfully in the overwhelming majority of people. That is what they authors said in so many terms.

Q That is not the point she is making though, is it? The point she is making is a different one. The point she is making is that there is a lack of this gut based immunity which may explain the occurrence of tetanus disease in fully immunised people. She is just setting out a possible explanation of why it is that immunised people may get tetanus. Is that so terrible?

A I would go back to what I said before. It is giving an impression because it is selective. If later on you had used that same paper to talk about how well it worked, that would be fine, but it is an overall picture of taking out particular things to suit the argument rather than giving a balanced picture.

Q If you look at few lines down under the heading "The Vaccine", it says:

> "It has been available since the Second World War and appears to have contributed substantially to reduced mortality from the disease."

That is precisely the point you are making, is it not? It is balanced by that point?

A But it does not give a reference for that one, unlike the statement…

Q It does at the end. I have only just quoted the first sentence, but it carries on?

A Okay. Yes.

Q Is that not your balancing point?

A Yes, partially.

Q Can we look at the next paragraph on page 20, which is referable to Dr Donegan's page 27, the last line:

> "Some people develop nerve damage causing either muscle weakness or altered sensations."

A Yes.

Q Your point in relation to that is this: the reference she provides at tab 34 does not contain this statement. I think the reference is wrong, is it not? In any event, in your references it is at D17?

A Yes. At least I assume so, because I do not know what Dr Donegan was referring to.

Q It is an error in the tab number references. Let us not waste time on that. Can we look at divider 17, because you have a copy there?

A Yes.

Q Dr Donegan has drawn to my attention that at page 27 she does have that document:

A

"Listed side effects (Adsorbed TETAUS Vaccine Bupivacaine Pasteur Merieux…"

etc. etc. This is a patient information leaflet?
A Yes.

B Q If we look on the right hand side, about a quarter of the way down, the copy is not great, but it says under "Side Effects":

"General reactions are uncommon but may include…"

It mentions a number of things.

C "…reactions and rarely peripheral neuropathy."

Q If we look over the page, it says "rarely." I think your criticism is that it says rarely, rather than what it was she said.
A Yes.

Q Whatever that was.
A It was just ---

D Q Some. She said some.
A Yes.

Q And you say rarely?
A Yes.

E Q Can we look over the page, please. If you look at the left-hand side, there is the sub-heading, "Does absorbed tetanus vaccine BP have side effects?" If you look at the last two lines, it says, "A few patients may develop damage to a nerve causing altered sensation or muscle weakness." The first one, it says "some" - "rarely," I beg your pardon. Second, it says "a few."
A Yes.

Q And so she says some.
F A I think "rarely" is quite different from "some."

Q What about "a few"? Is "some" different from "a few"?
A I think, as you would have said, that is for the Panel to decide, but I would think there is a gradation from rarely, to a few, to some, to common.

G Q Let us move on, shall we, to the next point. Page 21 of the your report, which relates to page 29 of Dr Donegan's report. Top paragraph, Dr Donegan's comment:

"Vaccination of 11 healthy subjects with tetanus toxoid produced the lowering of the T-lymphocyte...such as might be seen in patients with AIDS."

I am paraphrasing it now. Do you have that?
H

A I do.

Q Your point, in your statement, page 21, you agree that that is accurate, as I understand it, but you say Dr Donegan failed to mention they were temporary and the authors did not report any adverse effects due to this?
A That is so, yes.

Q That is your complaint. Could we look, please, at tab 35. Sorry, Dr Donegan's reference 35. This was a study, I think, that was not looking at vaccine safety, but the effect of vaccination on the applicability of screening tests for AIDS?
A That is right, yes.

Q In relation to this ---
A Sorry, in healthy people.

Q In healthy people, yes.
A Testing blood donors' blood.

Q First of all, this was a study that related to 20 to 50-year-olds, I think.
A Yes, they were quite old. As I say, they were blood donors.

Q I would not say it was old, by any means.
A I would say it is very young, actually, now.

Q In any event, they, of course, cannot be, or the results cannot be extrapolated to babies, or the two children in this case, can they?
A No.

Q Can we just try and follow through in relation to it? Acquired immunodeficiency syndrome obviously means that the immune system is reduced?
A Yes.

Q Therefore you become prone to infection?
A Yes. It is due to a particular cause.

Q Because most people with AIDS do not die of AIDS, as such, but die of ---
A An infection.

Q So that is the significance in relation to that, that it does produce a lowering of the T-lymphocyte which may allow for infection to enter the body?
A I think that is the important point, because there is no evidence from this study that that had happened. As you will remember previously, we tried to look at whether having an immunisation did make you more susceptible to infection. The best evidence that there was to date was that there was not a significant increase.

Q Yes. I am finding this rather difficult to read, but on the first page of this report, page 204, right at the bottom of the right-hand side, it says:

> "The results presented in this letter demonstrate that abnormal T-lymphocyte helper/suppressor ratio can be detected in healthy persons after immunisation with a widely used antigen. Therefore this test is of limited value for screening blood or plasma donors, especially for those in hyperimmunization programs."

A It is saying that in healthy people it is not a reliable test.

Q Yes. Can I deal with the last point in relation to tetanus, before we have a break. Page 21 of your report referable to her page 29, the last sentence is the criticism you make:

> "In a severe and tetanus prone wound, tetanus immunoglobulin may be given intramuscularly and intravenously in established cases of tetanus to produce immediately raised level of antibodies."

Your complaint is, you say:

> "This is true but it may be too late as the toxin may already have bound to tissues, a point Dr Donegan herself makes."

Essentially, you agree that that is possible?
A Possible.

Q Indeed, as I understand it, it is standard treatment?
A It is standard treatment for someone who has developed tetanus disease.

Q Yes.
A But would not be recommended as a way of preventing someone die from tetanus.

Q No. She has set out there all the various options and included in that is the provision of what would happen if you did catch tetanus, either because you were vaccinated and that was unsuccessful, or because you were not vaccinated?
A That is right. If one was forced to the limit, you would have to rely on that.

Q Do I understand that mercury, or thiomersal, was removed from the vaccine in 2004?
A A number of vaccines contained it. It was removed from all vaccines in 2004 that were used for the routine childhood programme, in this country.

Q At the time that this court case was going on in 2002/2003, there was thiomersal in the vaccine?
A Yes, there was. In the paper you tabled from 2001, the chief medical officer, had a whole page on that.

MR STERN: Yes. I have not dealt with that yet. That is the end of tetanus.

THE CHAIRMAN: Would you like a break now?

MR STERN: I would personally like a break, yes.

THE CHAIRMAN: We will take a break and come back at half-past three and continue with the polio section.

(The Panel adjourned for a short time)

MR STERN: Polio, please. Page 22 of your report. The first point we make is under "My comments on Dr Donegan's report," which is referable, therefore, to page 31 in her

report. Again, I think we better start at the bottom of page 30:

> "The incidence of the disease continued at moderate rates through the early twentieth century until the 1940s when enormous increases in the incidence of paralytic disease occurred which were thought to be due to excessive hygiene, meaning that children were not coming into contact with the virus and developing immunity to it at a young age."

Then this is the point that we need to look at:

> "It also coincided with the widespread use of antibiotics which were initially all injected intramuscularly and massive vaccination campaigns against diphtheria (1940 onwards), tetanus (World War Two: armed forces personnel..."

Then there are the dates and there is a bit of a mix-up. I will not repeat all the mix-up, but there is a mix-up with the dates there. Basically, we can see how it goes. Your comment, page 22, as I say:

> "Dr Donegan suggests that the rise of poliomyelitis was related to the introduction of diphtheria, tetanus and pertussis vaccines and produces a figure to support this contention."

I am not sure where that figure is.
A It is figure 32.

Q It is on the graph.

> "From the figure, the incidence of polio rose rapidly 1947/8. This coincides with the introduction of none of these vaccines, so it is difficult to understand what the relationship may be. There is a relationship with injections as Dr Donegan states and all these vaccines were given as injections. [However the] 'provocation polio' followed soon after the injection, so if this were a factor, the incidence of polio should have gone up immediately the vaccines were introduced which is not the case."

Can I just take you back to Dr Donegan's point, because Dr Donegan is talking about the widespread use of antibiotics, and the vaccination campaign.
A Yes.

Q I just wanted to make sure you were aware of that. Just looking at page 32, do you accept that, looking at this graph, the increase of paralytic polio is temporally connected to the introduction of intramuscular injections?
A No.

Q Whether vaccination or antibiotic?
A The graph does not include any data about antibiotics, so it would be difficult from the graph to draw any conclusions about antibiotics.

A

Q If it is right, as we can see, that the beginning of the arrows represent - that is to say, not the pointy bit, but the...
A The blunt bit.

Q ...blunt bit at the end is the point of introduction of the vaccination?
A That is so, yes.

B

Q So we have diphtheria in about 40s. I know that it is not all in a day or all in a year. I know it is a bit more general than that. Tetanus, a few years later.
A To the armed forces.

Q To the armed forces, yes. I was about to do that. It is actually written on the graph here.
A Yes.

C

Q To the members of the armed forces; 1951, to selected areas of the country; then 1961, nationwide?
A That is so, yes.

Q That clarifies the mix-up that Mr Kark was having. Then a few years after that, the pertussis vaccination was introduced. Leaving aside antibiotics then for a moment ---
A Can I say something about pertussis?

D

Q Yes.
A Whereas the start of the diphtheria, yes, a high proportion of the population would have been receiving it in 1940, in 1950, there will be a very, very small number receiving pertussis. It was only really that common in the mid-50s that children were getting pertussis immunisation.

Q Where do we get that from?
A I have not presented that data, I am afraid.

E

Q Just as a matter of temporal association, nothing else, do you not accept that that is, in some way, connected?
A No. Should I say why?

Q Yes, please do.
A Well, the diphtheria vaccination was introduced - as we have said, it drifted in.

F

Q Yes.
A About 1941-42, the whole population of children would be getting it. I can see no jump up in polio until about 1947-8. That is six years afterwards, so I cannot see a link with the diphtheria. If we take tetanus, yes, it was given to the armed forces, but that is a relatively small part of the population. In 1951, even, it was only given to selected areas of the country, but, by 1951, we had already got past an enormous jump in cases of polio.

G

There is no arrow here, that I can see, has a logical link with that increase in polio.

Q Okay. That is your evidence on it. I do not think there is much point in pursuing that any further. Can we deal then with the next point, which is also page 22 of your report, at the foot of the page, "Dr Donegan's statement on page 31," so going back to page 31, "that after the vaccination was introduced, it was necessary to have laboratory evidence of polio infection before it could be notified is incorrect." That, we can see, is in the second rather large paragraph in relation to this particular vaccine. About halfway

H

down, it says:

> "The requirement for laboratory diagnosis of polio also removed from the figures cases of polio caused by other enteroviruses like..."

It mentions a number of them. Above that we can see:

> "Before the introduction of the vaccine polio was diagnosed on clinical grounds and paralytic polio by the presence of paralysis."

A Yes, that is so.

Q

> "After the vaccine was introduced new stringent parameters were set for the diagnosis of polio including the presence of the virus in stool and serum samples and paralysis present for 60 days."

You say it is not necessary or was not necessary to have laboratory evidence of polio infection?
A For notifications, which are all the graphs that we have looked at thus far, I think, for all of the diseases are on the basis of notifications by a doctor that they suspect an illness. When you actually go to a number of these tables and charts in official publications, they will have beside them asterisks, sort of subsequently not confirmed to be, but the published data on notifications, which is different from diagnosis, will be on a clinical - a doctor's impression, shall we say.

Q Could you just look at, perhaps, the notification form? That will probably help. Perhaps if you could be given a copy of it now.

THE CHAIRMAN: This will be D10. *(Same handed to the Panel)*

MR STERN: Did you not get a copy?
A It is coming, I imagine. *(Same handed)*

Q You actually said yesterday when polio was around, intramuscular injections were associated with paralysis?
A I did, yes.

Q Yes, I thought you said that.
A There is a condition called provocation ---

Q Just speak up.
A Sorry. There is a condition called provocation polio, and that is what it is.

Q This is the "Notification of an infectious disease." Can we look in the lower right-hand block. You will see, "Notifiable disease. Poliomyelitis (acute)." Then the type or form, so paralytic or non-paralytic.
A Yes.

Q Just help us, please, then how one assesses that?
A As I say, it would be a clinical diagnosis. I have no idea how you would arrive at the diagnosis of non-paralytic polio, but for paralytic polio, it would be a clinical

diagnosis of someone who has a paralysis. It is usually asymmetrical, so it does not involve, say, both legs. It would usually be one leg, of that nature.

Q The point I was seeking to ask you about, the way in which you contest non-paralytic, presumably, is from a laboratory test? How else does one do it?
A I do not know, actually. There are very rare reports of non-paralytic polio, even though - do you remember we had a discussion about diphtheria and throat swabs?

Q Yes.
A Laboratories will often test stools for polio as part of a routine blanket thing. I do not know how clinically you would diagnose non-paralytic polio.

Q As I say, the requirement for laboratory diagnosis – maybe that is just the way Dr Donegan deals with it – as you say, the only way you can make a distinction between paralytic and non-paralytic is to have a laboratory diagnosis of it?
A No, it is not making the distinction. You can make a clinical diagnosis but to pick up non-paralytic polio I do not know what clinical presentation there would be to do that.

Q Obviously, to pick up paralytic polio one---
A Makes a clinical diagnosis.

Q But non-paralytic you do not know how to do that?
A No, but the graphs are referring to paralytic polio.

Q Obviously, it is a notifiable disease and one has to actually set that in the box?
A One does, yes.

Q The obligation on a doctor, a GP, is to actually complete this?
A Yes.

Q Presumably to the local public health people, I do not know?
A Sort of, yes. Technically they are a consultant in communicable disease control – that sort of person.

Q I think you have copied the second page so we can see who it goes to – the London Borough of Brent Food Safety and Pest Control?
A Which employs a consultant for that purpose.

Q A doctor is under an obligation to, as I say, notify non-paralytic polio?
A Yes, if they make a clinical diagnosis of it.

Q But you have got no idea how that can be done?
A No.

Q Could we look at page 33 of Dr Donegan's report? Under the subheading "The Vaccine", the last three lines of the first paragraph:

> "The oral polio vaccine is regarded as an ideal form of vaccine as it most closely mimics wild infection and induces a mucosal reaction as well as antibodies in the blood. In the UK OPV is used in the

childhood immunisation programme."

A Yes.

Q So Dr Donegan is setting out there what the ideal form of vaccine is in relation to polio, as she sees it?
A I was going to say it will depend upon time and place, but that is appropriate for the time and place that was in question, yes.

Q That is what we are looking at, obviously. I do not think you actually referred to that in your report as being a point that Dr Donegan was actually supporting the vaccine, if I can put it in very general terms?
A Dr Donegan actually says "The oral polio vaccine is regarded as an ideal form"; it does not say "I regard it as an ideal form", which is, I think, a different statement entirely.

Q Can we look, please, at page 23 of your report, second paragraph down beginning "Polio has been reported in highly immunized populations", referable to Dr Donegan's page 34, paragraph 1. It is a long paragraph. Perhaps we can just look at this again:

> "As the World Health Organisation struggles to achieve its aim of worldwide eradication of polio it is notable that epidemics of paralytic poliomyelitis have occurred in highly vaccinated populations and, tragically, immediately after a polio vaccination has occurred."

That is accurate, is it not?
A It is accurate.

Q Then she deals with:

> "As India struggles to meet the polio deadline, several cases have been reported of children contracting polio even after receiving up to a dozen doses of the vaccine. In the Oman outbreak it was notable that the region with the highest attack rate (of paralytic polio)…had one of the highest (vaccine) coverage rates, whereas the region with the lowest coverage had a low attack rate… In a polio outbreak in Israel in 1988 in a highly vaccinated population"

- I think that is a quote we have actually seen in one of the other pieces of research?
A We have talked about that, yes.

Q We have talked about that.

> "People vaccinated with inactivated polio vaccine served as reservoir for poliovirus multiplication and transmission to susceptible individuals. Such people have low intestinal mucosal immunity and excrete poliovirus for periods ranging from days to several weeks. The spread was also linked to the greater susceptibility of young adults previously vaccinated with OPV."

A

Your criticism, I think, is set out there:

> "Polio has been reported in highly immunized populations, a fact Dr Donegan mentions… The implication is"

- again, we are on implications –

B

> "that the vaccine is ineffective. In fact, this is not the case. Sutter *et al* calculated that the vaccine reduced the risk of paralysis by 91%."

Then that is Dr Donegan's reference at divider 46. Having read it through, shall we take these points stage by stage, as it were? Dr Donegan's reference 46, which is the Sutter study in Oman – yes?

C

A Yes.

Q It is a 1991 report in *The Lancet* and we can see at the top left hand part of the paper:

D

> "From January, 1988, to March, 1989, a widespread outbreak (118 cases) of poliomyelitis type 1 occurred in Oman. Incidence of paralytic disease was highest in children younger than 2 years… despite an immunisation programme that recently had raised coverage with 3 doses of oral poliovirus vaccine among 12-month-old children from 67% to 87%."

A few lines down is the point that you are making:

E

> "Three doses of OPV reduced the risk of paralysis by 91%."

You did not actually indicate, I think, in your report that it required three doses to reach 91%?

A No, because that is the standard. I have not done it with any of the vaccines because I assumed that we were talking about giving the standard number for whatever course was appropriate.

F

Q About four or five lines further down:

G

> "Accumulation of enough children to sustain the outbreak seems to have been due to previous success of the immunisation programme in reducing spread of endemic strains, suboptimum efficacy of OPV, and delay in completing the primary immunisation series until 7 months of age. Additionally, the estimated attack rate of infection among children aged 9-23 months exceeded 25% in some regions, suggesting that a substantial proportion of fully vaccinated children had been involved in the chain of transmission."

Is that not also a relevant point to include in the paper?

H

A The chain of transmission does not mean to say that these children had polio, it

A means they were in a position to pass on the polio. So it was not necessarily that they were not themselves protected, which is quite an important difference. So when talking about what is the benefits for the individual child from the vaccine, presumably one would talk about what protection they are going to get one way or the other, which is the 91% figure.

Q Looking at the background on the right-hand side:

B

> "The Expanded Programme on Immunisation in Oman began in 1981; administration of OPV was recommended at 3, 5 and 7 months of age at specific health centres, with a reinforcing dose at 19 months. Because coverage with 3 or more doses had only reached 67% by 1985, a more extensive infrastructure was gradually developed in 1986; this used outreach and recall activities by mobile teams, and required that every contact with curative care institutions should be used as an opportunity to vaccinate children who were behind schedule."

C

So it was a pretty extensive vaccination programme?

A Trying extremely hard, yes.

Q Over the page, so it is 716 at the top:

D

> "Coverage increased further to 88% in 1987.
>
> After a five-month period in which no cases of poliomyelitis were identified, an outbreak became apparent during the early months of 1988."

E So there is an 88% vaccination coverage, which you have already told us is fairly high, I think?

A One would aim higher than that. It is not bad, but it is not your target.

Q There is an outbreak and:

F

> "Cases were reported from 6 of the 7 administrative regions of Oman, including remote villages with total populations of up to 1000."

Then a little further down, about five or six lines:

G

> "87% of case-patients in Oman had received at least 1 dose of OPV and 50% had received at least 3 doses."

So that is the background of the situation. If we move, please, to page 717 under the "Results" section halfway down on the left-hand side:

H

> "No additional cases of paralytic poliomyelitis were identified retrospectively in health centres and hospitals. Searches in the 167

A

villages which comprised the catchment areas of 16---"

MR KARK: I am sorry, I can see some of the Panel are having difficulty. Two of the pages have been reversed, I think.

THE WITNESS: Yes.

B

MR STERN: I am very grateful, thank you. I would have ended up talking to myself.

THE WITNESS: We have got it right now.

MR STERN: You must have thought I had completely lost the plot.
A I thought I had lost it actually.

C

Q Hopefully we have all now got 717, halfway down on the left-hand side:

> "No additional cases of paralytic poliomyelitis were identified retrospectively in health centres and hospitals. Searches in the 167 villages which comprised the catchment areas of 16 randomly selected health centres also failed to detect additional cases. The 118 cases patients reported previously were thus regarded as the

D

> total number of paralytic cases, and were assumed to be representative of all cases that had actually occurred."

Then we come to "Case-control study" in the second paragraph:

> "The 70 case-patients were closely matched for age with"

E

- whatever the number of controls were (there is a bit missing).

> "79% of controls lived in the same village as the corresponding case. Likewise, there were no significant differences in vaccination status between the two groups."

Then on the right-hand side we can see "Clinical Efficacy of OPV in Preventing Paralytic

F

Disease, Oman, 1988", and the adjusted figure after three doses was 91%?
A Yes.

Q We can see it is much lower with two?
A And very poor with one.

G

Q I am just not quite sure why there are two references to three doses – there is one adjusted and one unadjusted. It may not matter very much.
A I would have to read through the paper in detail, but basically the principle is there may be things that are different between the two groups that may explain it and you allow for that when you adjust.

Q Moving on further down, you can see:

H

A

> "Estimates of vaccine efficacy are shown in table II. A primary series of OPV (3 doses) reduced the risk of paralysis by 91% (adjusted estimate); two doses reduced the risk by 80%. Because these estimates were based on discordance (dissimilarity) between the vaccination status of case-patients and their controls, and because most case-patients and controls in this analysis had received the same number of doses of OPV, 95% confidence intervals were wide."

B

Can we now turn, please, to page 718? The right-hand column under "Poliovirus transmission among vaccinated children", about three or four lines down:

> "There was no correlation between vaccination coverage and attack rates by region; the region with the highest attack rate…had one of the highest coverage rates…whereas the region with the lowest coverage…had a low attack rate…"

C

A That is correct.

Q That is a fairly significant point, is it not?
A I think the two sentences taken together are important, very important.

D

Q Is there a hidden message---
A It is not hidden at all – it is in my report. If you had just said the lowest attack rate was in the population that had the highest immunisation rate and the highest was in the population that had the lowest, one might jump to the conclusion that therefore there was a link between the two, but the sentence "There was no trend" actually demolishes that because in fact it does not seem to be that it is related.

E

Q I think in fairness your report just says that Sutter calculated the vaccine reduced the risk of paralysis by 91%; unless I have missed it I do not think your report actually deals with any other part of it?
A I thought it did.

Q I may have missed it, but that is my recollection.
A No, it appears that in a quick read-through that is correct.

F

Q That is why I am going through it. Page 719, which I think is the final page of the discussion:

> "Our findings confirm that the outbreak of poliomyelitis in Oman had one of the highest attack rates of paralytic disease that has been reported during the vaccine era, with transmission lasting for more than 12 months. Among the"

G

(and I assume that says)

> "most disturbing features of the outbreak was that it occurred in the face of a model immunisation programme and that widespread

H

A

> transmission had occurred in a sparsely populated, predominantly rural setting. Whether the mass vaccination campaigns were effective in reducing further spread of the outbreak could not be determined because the incidence of disease had already begun to decline.
>
> Although we may never know the causes of the outbreak, several factors seemed to be important in the build-up of susceptible children less than 2 years old. First, rapid increases in vaccination coverage before the outbreak may have reduced or interrupted endemic circulation of indigenous strains, diminishing the contribution of natural infection to overall immunity levels in the general population. Secondly, the number of susceptible infants was further increased by delays in completing the primary immunisation series until 7 months of age rather than 3.5 months of age as currently recommended."

B

C

I think you will find the third point about four lines further down:

> "The clinical efficacy of 3 doses of OPV (91%) was lower than that observed in industrialised countries, which contributed to a further reduction in the effective levels of immunity in the target population."

D

So although 91% to a lay person may sound very high, as I understand it from this report it is not actually a significant figure?

A Oh, it is very significant, yes. If you had 91% of the population protected you would be very pleased. You would be even more pleased if you had 100% protected. So it is a very significant figure. That is my reading of what it is saying here.

E

Q Over on the column on the right:

> "Additionally, we did not find any deficiencies in the cold chain that could account for these findings."

F

Then at the end of the following paragraph:

> "Because sanitation and hygienic practices in rural areas of Oman were relatively poor, the inoculum---"

G

A I apologise for interrupting. Then it goes on to say:

> "Although our methods may not have been sensitive enough to detect minor fluctuations in freezer…"

That is quite important because polio vaccine is the most fragile one. It is very important to keep it cool.

H

Q They do say there that they could not account for these findings. They may be minor fluctuations, but in essence that is what the report says. Obviously I am not reading the whole thing, but if you want to draw that to our attention, you have done so. In the next paragraph right at the end:

> "Because sanitation and hygienic practices in rural areas in Oman were relatively poor the inoculum of wild polio virus may have been large enough to overcome the usual levels of secretory antibody that would otherwise protect vaccinated children from infection."

The outbreak of poliomyelitis actually seems to have occurred in one of the regions with the highest immunisation programmes?
A Yes. Certainly for part of the time it had the highest uptake, yes.

Q You considered that it was appropriate to summarise that paper by inserting that Sutter calculated that the vaccine reduced the risk of paralysis by 91%. Do you think that is a fair representation of this paper?
A I think what we were looking at in the case of these two children is what would be the chance – what effect the vaccine would have on them of reducing the chances of getting polio. I think, having re-read this paper, your criticism is correct. I should have said this was 91% in this population, but it probably would have been, as in one of the paragraphs you alluded to, higher in an industrialised population because there was not a burden of wild polio. Perhaps I should have said 91%, but we could expect higher in the UK.

Q The Oman paper is not relevant, as you say, to the particular position that these children found themselves in in the UK?
A The reason I quoted the Oman paper was because Dr Donegan quoted the Oman paper. It was not necessarily one I would have gone to of my own accord.

Q You are criticising her. Although she has said nothing inaccurate, you are criticising her for not including the fact that Sutter calculated the vaccine reduced the risk of paralysis by 91%. That is as I understand it?
A That is correct and that is the bottom line.

Q What I am saying is that this paper is not fairly summarised, if you do not mind me saying so, by that particular point?
A I cannot think of another response to give, other than that the bottom line is that, of the children who had the vaccine, it reduced the chance of them getting polio to 99% of what it would have been without the vaccine.

Q Can we look at the next paper? Your point in relation to the next paper is that it concluded that the Albanian outbreak was due to programme failures and did not suggest that the vaccine was inherently at fault. That paper is at tab 47?
A Yes.

Q Could you help us with where it is, because I have not seen it, that the authors of this paper concluded that it was due to programme failures? I am sure you will be able to find it?

A I doubt it, because it is quite a long paper and I would need to look through it properly.

Q Looking at this, this is a study in relation to Albania, which was at that time, and still is, a country with considerable poverty?
A Yes.

B Q Interestingly, Italy did not actually find that there was any increase in polio, although there were a considerable number of Albanians who travelled to Italy. Do you remember that in this paper or not?
A No. I would need to read the paper again.

Q Let me draw your attention to the point. At page 1917 in the top right hand corner, about halfway down:

C

> "The high standard of the vaccination policy in Italy is the possible reason why no cases were reported in that country, despite the large immigration flow of Albanians during and following the epidemic period."

D A Yes. What they are saying is that, because they are immunised in Italy, then you bring in some people who are unimmunised, there is less chance of the disease spreading in that population.

Q They are saying that is a possible reason?
A Yes.

E Q Looking at this paper, if we can, going back to the start at page 1912, halfway down on the left hand side:

> "In Albania, the latest large outbreak of poliomyelitis occurred in 1978, when 71 cases associated with either wild type 1 or type 3 poliovirus strains were reported. Routine vaccination with a three-dose regimen of the oral poliovirus vaccine was reinstated for newborns in 1980, and the vaccination coverage rate was estimated to be high (92 to 95%) until 1990. Virological surveillance of acute flaccid paralysis was conducted in Albania from 1980 through to 1995; a total of 93 AFP cases were reported, and 11 of them were classified as vaccine-associated poliomyelitis. The isolation of only Sabin poliovirus strains from these patients and from their healthy contacts suggested that circulation of wild poliovirus in Albania during this period was very limited… However, seroepidemiological investigations performed in Albania in 1980 through 1990 and with Albanian immigrants in Italy in 1991 showed that 15 to 30% of the surveyed adult population was susceptible to poliomyelitis, suggesting the existence of gaps in the immunisation programs.
>
> The apparent lack of circulation of wild poliovirus in Albania was

F

G

H

A

> likely due to the absence of virtually any contact with other countries until 1990. The opening of Albania's borders to foreigners in 1991 exposed the population to the risk of imported poliovirus from areas where polio is endemic due to the settlement of people from Western Europe or the passage of people to Western Europe."

B

At page 1913 in the top right, we can see under "Results" that it deals with the early paralytic cases. I do not want to go through those in any detail. At page 1914, in the third paragraph down, it deals with the ages of patients ranging between 2 months and 52 years with 78% being between 11 to 35. It was low among children indicating the efficacies of the NIDs.

> "On the contrary, a relatively high incidence was shown among infants aged less than 6 months."

C

At page 1916 on the right hand side there is "Discussion". At about three lines down;

> "The outbreak started soon after the NIDs, and the temporal association between vaccination and the appearance of poliomyelitis cases was initially misleading in defining the etiology of the disease."

D

Towards the end of the next paragraph:

> "The possibility that the virus had been circulating in the country for a long time and that it was sustained by the weakened herd immunity cannot be excluded.
>
> The highest incidence rate was found among young adults suggesting a major failure in immunisation practices before the year 1980. A minor peak in the incidence was, however, also found among infants younger than 6 months of age who were born after the NIDs and before the mass vaccination campaigns began in October 1996. This may be at least partially due to the lack of maternal antibodies."

E

F

A Thank you very much. You have pointed out the bit that suggests it was a programme failure.

Q That is the bit, is it?
A Yes.

G

Q It goes on:

> "However, since some of these patients were vaccinated only according to the routine schedule, this suggested that during an outbreak routine immunisation is less effective than mass vaccination."

H

A Then it says:

> "The limited number of cases which occurred in the 1 to 5-year old age group provides evidence of the effectiveness of NIDs targeted to children up to 5 years of age…"

I think that deals with what I want to say about that. Tab 48. This is a paper which, I think, in its summary three lines up from the bottom says:

B

> "Epidemics can occur in areas of high vaccine coverage"

which you have already agreed and which I need not delay you on. Can we go to tab 49? In your comments in relation to this paper you say:

C

> "In India the authorities believed that at least part of the problem was inappropriate storage of the vaccine."

If we look at tab 49 I think the authorities denied that, but UNICEF believed it?
A That is true, yes. UNICEF is the main part of the expanded UN organisation that oversees vaccines in the less industrialised countries.

D Q At divider 50, which is the last paper in this section:

> "An outbreak of paralytic poliomyelitis caused by type 1 poliovirus between July and October 1988, prompted mass vaccination of the whole Israeli population under the age of 40."

Essentially, what this paper shows, I think, is that there were two views as to the cause of this outbreak. Do you remember that?

E A Yes.

Q They wrote separate papers in relation to it?
A Yes.

Q I think it is probably summarised on the left hand side:

F

> "The focus of the outbreak (12 cases) was in the Hadera subdistrict, one of two subdistricts where enhanced inactivated poliovaccine had been the only poliovaccine used for infants since 1982. 9 of the 15 victims were 15 years or older, and 9 had previously been immunised with at least 3 doses (OPV). The authors are divided in their interpretation of the findings. One group considered that the likely causative factors were the greater susceptibility of young adults previously vaccinated with OPV as well as transmission of wild poliovirus to susceptible people by children with low gut immunity against poliovirus after vaccination…"

G

So, one was saying reduced gut immunity as a result of vaccination?

H A That the vaccine type was not appropriate to the wild virus that was doing the

rounds.

Q The other group believed that the causative factors were exposure to other factors like contaminated sewage?
A Yes.

Q Can we turn to your report at page 24? In the second paragraph you deal with Dr Donegan discussing a possible link to an SV40 found in early polio vaccine and the subsequent development of tumours. This is referable to page 34, but more to page 35, as we will see, the possible link in early polio vaccine and the subsequent development of tumours. You say:

> "The evidence on the topic is far from conclusive as the author of her reference states."

It is there and I am not going to read it out. The Panel will already have seen. Dr Donegan's phrasing at the end of this section, that is at page 35, so the part you need to underline, as it were, is the last sentence:

> "It thus remains possible that a late adverse effect of the polio vaccination programme is emerging."

That is the point that you are dealing with and your criticism is that what is not clear from her discussion is that this is something that, even if it were to be true, only applies to polio vaccines produced many years ago. That is your point?
A That is true.

Q First of all, if we turn back to page 34, this is all part of a paragraph dealing with the 1961 inactivated polio vaccine?
A It starts off:

> "In 1961, inactivated polio vaccines (IVP) was found to contain live SV40 virus…"

Q That is what I am saying. This is all part of the same paragraph of that?
A It is, yes.

Q There is then set out how that arose?
A Yes.

Q At the bottom of the page:

> "SV40 has been found in people far too young to have been immunised with the documented contaminated vaccines…"

A Yes.

Q If they are far too young it does tend to suggest that this is obviously referable to an earlier period. I accept it is not stated there, but is it not overwhelmingly obvious from

this?
A I do not think it is overwhelmingly obvious. I think you have to read it forensically.

Q People far too young to be immunised obviously implies that it is no longer in circulation, does it not?
A It could do, yes. I will accept, yes.

Q It goes on:

> "…so it is possible that it is still being transmitted through the vaccine…"

A How could it be transmitted through the vaccine then if we are talking about something that relates to children who are too young to have been affected?

Q It goes on to say:

> "…through the vaccine or having been incorporated in the human genome, vertical transmission…"

in other words, from parents,

> "…immunised with the contaminated vaccine to their children."

A But I do not see how it can be transmitted through a vaccine if we are saying that the vaccine is no longer contaminated.

Q No. The parent has received the vaccine. It is then vertically transmitted to the child?
A It says here:

> "…transmitted through the vaccine or having been incorporated…"

not transmitted through the vaccine and…

Q Or having been incorporated in the human genome, in other words gone into the human being who has got it. Vertical transmission?
A Yes.

Q It is perhaps not for us to argue that at this stage. It then says:

> "<u>It thus remains possible that a late adverse effect</u>…"

A Yes.

Q It is obviously a reaction to something that was done some time ago, is it not?
A That is the question, because it says:

"…it is possible that it is still being transmitted through the vaccine…"

in the second line down on page 35. That suggests that it is something that is still going on.

Q That is your interpretation of it. Can we look at the reference of Dr Donegan at tab 51 please? I do not think this paper actually says either that it is no longer a vaccine that is being given. I think it is just taken as read. Let us look at it.

"*Contamination of early polio vaccine may be linked to rare tumours.*

The introduction of the Salk parenteral vaccine in the mid-1950s led to a dramatic decline in the incidence of poliomyelitis. By 1961, the majority of young adults in Britain and America had been immunised…"

Three lines up from the bottom of that paragraph:

"There are no reliable data about the proportion of batches that were contaminated with live SV40, and estimates range up to 30%. Early worries that the containment might be implicated in the development of human cancers have recently resurfaced."

In the next paragraph about three or four lines down:

"Except for one study, which reported an increased incidence of neural tumours in children of mothers vaccinated during pregnancy, all studies were essentially negative."

Perhaps I can go through this paper, because it is, I think, the study that Dr Donegan was referring to on the previous page, which is another point that we need to come to in due course. At page 34, about six lines up from the bottom, it says:

"An increased incidence of tumours of the nervous system has been reported in one study in children of mothers vaccinated during pregnancy."

That is where it comes from, I think.
A It is, yes.

Q I will see if I can try and deal with two points at the same time.
A It does say in the paper, "Except for one study, which reported," et cetera.

Q In one study, that was what she has written. "SV40 has now re-emerged as a potentially tumour causing virus." Then over the page, please. The end of the middle paragraph:

A

> "No large-scale studies have been undertaken, control tissue has often been inadequate, and the findings have not been replicated in all laboratories."

Then four lines down:

> "It thus remains possible that a late adverse effect of the polio vaccination programme is emerging, although any risk of cancer is likely to be more than outweighed by the benefit of vaccination to the postwar generation."

B

So that is obviously the part that she has included. This is, I think, a March 1998 paper? Yes?
A It is, yes.

C Q Can we just look at your reference 19. This is the study that you say is a recent study, which you have produced. Yes?
A Yes.

Q I think, again - I stand to be corrected - but I do not think Professor Kroll or Dr Conway referred to this?
A I cannot recall it, no.

D Q In any event, this paper that you have referred to at divider 20, this is a study ---
A Sorry, is it 19 or 20?

Q Sorry, did I say 20? I meant 19. Thank you very much. This is January 1998, I think.
A That is when it was published, yes.

E Q The context: the vaccine contaminated with the live SV40 was used extensively in the US between '55 and '63; it has recently been detected in several rare human tumours.
Objective: to determine the risk of various cancers among Americans who, as children, received the SV40.

> "The results: Age-specific cancer rates were generally low and were not significantly elevated in birth cohorts exposed to SV40-contaminated vaccine. Specifically, compared with the unexposed, the relative risk of ependymoma..."

F

Ependymoma, I think, is a type of cancer, is it?
A Of the brain.

G Q

> "...was not increased in the cohorts exposed as infants or children, nor did the exposed have an increased risk of all brain cancers. Osteosarcoma incidence also showed no relation to exposure as infants or children. Last, mesotheliomas were not significantly associated with exposure, although the cohorts studied have not yet reached the age at which these tumours tend to occur."

H

I think part of the problem here is that the study stopped at a particular time, which obviously ---

A It would allow you to be fairly certain about some cancers, but not about others.

Q They say there was no significant increase in the rates of certain cancers. That is the conclusion they come to.

A Yes.

Q So far as mesothelioma is concerned, they could not come to a final conclusion?

A They could not be certain about that, no.

Q Page 25 of your report. This is referable to a point you are making here, that an increase incidence of tumour - it is page 25 in your report. Let me just get the reference. I think it is the point that I drew to your attention just before at page 34. About six lines up it says, "An increased incidence of tumours." That is the point I drew to your attention to try to deal with them both at the same time. I think we have already looked at that paper. Maybe we did not.

A I do not think we did.

Q No, we did not. It is 21 of your reference, is it not?

A Yes.

Q No, we did not. Thank you very much. If you could look at that reference 21, please. First of all, just before we look at it, we had seen that one study which did refer to that particular point.

A The particular point, I think, we are addressing now is ---

Q Sorry, it is my fault. Page 34, about six lines up, the part that reads:

> "An increased incidence of tumours of the nervous system has been found reported in one study in children of mothers vaccinated during pregnancy."

A That is right.

Q We looked at that just before, that there was a reference to it. Do you remember?

A Which one was that? Sorry.

Q I think it was Dr Donegan's reference 51.

A I do not know that that talked about vaccine given to mothers having an effect on the children. Oh, no - it is. It is. It is in the middle of the ---

Q It is. I drew your attention to it to try to save time. Maybe I have not done that. I do not want to go over that again. We will just briefly look at your paper, 21, please. Just looking at the abstract:

> "In a follow-up study 50,897 pregnancies, poliomyelitis and influenza immunizations, and viral infections were evaluated as possible risk factors for the development of malignancies in the offspring born between 1959 and 1966. Ascertainment of malignancies was based on clinical follow-up during the first year of life and on mortality experience covering the first four years of life.

A

> In 18,342 children whose mothers were vaccinated during pregnancy with killed polio vaccine there were 14 malignancies and in 32,555 non-exposed children there were 10. In the vaccinated group, nine malignancies occurred in children whose mothers were immunized during the first four lunar months of pregnancy. Time clustering of administration of the vaccine was evident in mothers whose children developed malignancies. There were seven tumours derived from neural tissue in the exposed children and one in the non-exposed children."

B

Just if we could turn, please, to 232, halfway down on the right-hand side:

> "No malignancies occurred among the children born to 3,056 women who received polio vaccine. Among 2,291 mothers immunized with influenza vaccine, one child developed an

C

> astroctyoma of the spinal medulla...Discussion. The present data suggests that injections of killed polio vaccine in pregnant mothers were associated with malignancies, and tumours of neural origin in particular, in the offspring born between 1959 and 1966."

That is the period we are concerned with. Yes?
A Yes.

D

Q

> "Based upon the frequency of malignancies in children born to non-exposed mothers, about 5.6 cases would have been expected in the exposed group, whereas 14 were observed."

Over the page at 233, the left-hand side, halfway down, there is a paragraph begins:

E

> "No obvious confounding was detected in the data. In particular, findings were not explained by differences between hospitals, by race...In the absence of randomization, however, it remains possible that some unidentified maternal characteristic, related to the risk of malignancies in the offspring, was independently related to receipt of killed polio vaccine.

F

> Since there appears to be no other satisfactory explanation for the association between killed polio vaccine and malignancies, the possibility that it is causal should be considered."

Then, just on the right-hand side at the bottom right:

G

> "However, the children received the vaccine by the oral route and the virus has so far only proven oncogenic in animals when given parenterally. Our observations with respect to live attenuated polio vaccine are consistent with this finding. It is possible that SV40 may only be oncogenic in the human foetus when the vaccine is given to the mother by injection. This possibility is reinforced by experimental evidence in newborn animals..."

H

So, on the face of it, it seems - you are looking quizzical.
A I am, because my complaint was that the relationship between polio vaccine and tumours was purely if it does exist, and you have read out some things that say it may not. But if it does exist, related to injected polio vaccine, which we did not use in 2002, therefore has no relevance to the vaccine you would be giving the children in the case that is under discussion.

Q That is a separate point. Relevance is a separate point.
A Oh, sorry.

Q I am just dealing with the criticisms you have made in your report, rather than additional ones. Relevance is a separate point, but, which, obviously, I am not shutting you out on making that point.
A Right.

Q The question is whether it is accurate. That is what we are dealing with.
A Okay.

Q I think we have dealt with the other paper that I wanted to deal with.

MR STERN: Madam, that may be a convenient moment, I hope.

THE WITNESS: Could I put in a plea that I am beginning to flag.

MR STERN: Well, you are not alone.

THE CHAIRMAN: Very well. We are starting a little bit earlier tomorrow. It is only fair to bear in mind your state of minds. We will adjourn now and reconvene at nine o'clock tomorrow, with the expectation of stopping at one.

MR STERN: Thank you very much.

(The Panel adjourned until 9.30 am
on Friday 10 August 2007)