SCOTTISH HOSPITALS INQUIRY

Hearings Commencing
19 August 2025

Day 6
27 August 2025
Professor Peter Hawkey

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10:03

THE CHAIR: Good morning, everyone. I think we're able to begin with our only witness today. It is Professor Peter Hawkey.

MR MACKINTOSH: Yes, my Lord.

THE CHAIR: Good morning, Professor.

THE WITNESS: Morning. Morning, your Lordship.

THE CHAIR: Now, as you understand, you're about to be asked questions by Mr Mackintosh, who think you've met.

THE WITNESS: Indeed.

THE CHAIR: But first, I understand you're prepared to take the oath.

THE WITNESS: Yes.

Professor Peter Hawkey
Sworn

THE CHAIR: Thank you very much, Professor. Now, our timetable is that we would probably take most of the day with your evidence. We usually take a coffee break at half past eleven, but – and can I emphasise this – if you want to take a break at any other time for whatever reason, and we don't need to go into the reasons----

THE WITNESS: No.

THE CHAIR: -- just give me an indication and we'll take a break. So please feel that you're in control of the situation.

THE WITNESS: Thank you, your Lordship.

THE CHAIR: Now, Mr Mackintosh.

MR MACKINTOSH: Thank you, my Lord.

Questioned by Mr Mackintosh

Q Now, Professor, I wonder if I can take your full name.

A Professor Peter Michael Hawkey.

Q What's your current occupation?

A I am a consultant microbiologist for the Scottish NHS, looking after the Shetland Health Board, and I'm Chief Scientific Officer of Alcurenex(?) Ltd, a company dedicated to discovering new antibiotics against multi-resistant gram-negative bacteria.

Q Thank you. Now, you provided your CV attached to what we have clinically referred to as the HAD Report.

A Yeah.

Q Now, that's in bundle 44, volume 1, document 1 at page 153. Now, what we'll do is we'll put it on the screen, but-- and I think it's worth reserving that, you'll need to tell me if when I put something on the screen isn't readable to

you.

A Yes, yes, I can read that.

Q We can zoom in to half pages as we go, but I'm hoping that you're familiar with your CV.

A I am pretty, yes.

Q What I'd like to understand is how you would describe your principal research interests.

A Principal research has always been around gram-negative bacteria, and in fact my first research project on gram-negative bacteria was in 1980, the investigation of an outbreak in a ward caused by Providencia stuartii, a multi-resistant organism. Thereafter, I have worked in the area of Clostridium difficile and MRSA, but if you look at my publications of 315-odd publications, 50 per cent of those are on gram-negatives, and 17 or 18 will be descriptions, big papers, on major outbreaks caused by multi-resistant gram-negative bacteria.

Q Thank you. Now, you mentioned your current role in Shetland.

A Yes.

Q I think it's important to put it into context, so how many days a week do you work----?

A I work Mondays through to Wednesday lunchtime. I'm the infection control doctor and the consultant microbiologist for Shetland Health Board. I'm based out of Aberdeen, so they employ me up and second me permanently to Shetland. I work from Norfolk remotely and I'm a response for all aspects, environmental and otherwise, in infection control.

Q So you are the only infection control doctor, or----

A Yes, absolutely.

Q You don't have colleagues who are on the scene, as it were?

A No, no. It's a role I don't mind doing because when I was head of everything in Birmingham, I was the principal infection control doctor for Birmingham teaching hospitals.

Q Right, and so you are, along with the nurses, the IPC team in Shetland?

A Absolutely, they're an integral part. We work very closely together.

Q Right, okay. Now, and you headed the IPC team in Birmingham----

A Yes.

Q Which hospital was it in Birmingham again?

A Initially, I worked at Heartlands Hospital, and then the two trusts fused, so I then moved to the Queen Elizabeth Hospital in Birmingham.

Q Right.

A Prior to that, when I was a professor in Leeds, I was head of infection control and chair of the Infection Control Committee for Leeds Teaching

Hospitals Trust.

Q Possibly one of your successors might be Professor Mark Wilcock?

A In fact, I appointed him there as a senior-- my senior lecturer when I was Professor.

Q Right. Now, what I want to do is just identify your reports.

A Yes.

Q I'll put them on the screen, but I'm sure you're familiar with them. The first one is what we have called the HAD Report, which we're looking at. If we go to page 5. That was produced jointly with Dr Samir Agrawal and Professor Lydia Drumright. Am I right?

A Correct.

Q Right. Then there's the response document, which is bundle 44, volume 5, document 2, page 20, and this was again produced jointly but in July of this year.

A Yes, correct, yeah.

Q Then we sent you two questionnaires.

A Yes, HAD 1, HAD 2.

Q Yes, HAD Questionnaire 1, which is bundle 44, volume 2, document 1, page 12, and that's in the form of a questionnaire and your answers, some of which are by you individually, some of which by Dr Agrawal individually, some of which by Dr Drumright, some of which are collective.

A Correct.

Q Then a supplementary questionnaire, from which the response document has almost sort of been spawned, is in bundle 44, volume 5, document 1, page 4. Now, are you willing to adopt these four documents as part of your evidence?

A Absolutely.

Q Thank you. Now, if we can take that off the screen, what I want to do is to think about the division of labour within the HAD Report project, primarily for the purpose of checking that I'm asking the right questions of the right person.

A Yes.

Q Now, before I do that, did you watch or listen to the evidence of your colleagues Dr Agrawal and Dr Drumright?

A I did. I've seen almost all of both of their evidences because it's important because we worked as an integrated team.

Q Right, so if we look at the report in its structure, probably actually helpfully by putting the index on the screen.

A Yes.

Q If you go to page 12 of bundle 24, volume 1. Go to page 12. I'm not going to go through this line by line, but we'll just have them on the screen for our

and your----

A Yeah.

Q So if we put the executive summary to one side for a moment, the introduction, Chapter 2, Chapter 3 and Chapter 4, to what extent are you the right person to ask questions about those?

A I am the right person because predominantly-- well, I wrote-- certainly wrote first drafts, which were then commented on by my colleague Dr Agrawal to a degree, but I'm the principal author of those chapters, correct.

Q Then if we go on to page 13, the water chapter, Chapter 5, could it be that the principal author of that?

A Sorry, page 13?

Q No, when I call out a page, I'm calling out a page for my colleagues who are behind you----

A Oh, I see, okay, got it at the top.

Q So, Chapter 5, "Water", are you the principal author for that?

A Yes, but I've also lent particularly on Dr Agrawal in relation to anywhere-- any areas where that began to impinge on haematology, oncology and his experience as a consultant physician.

Q Thank you, and then Chapter 6, "Ventilation", would largely be him?

A It-- Totally him really.

Q Totally him.

A I mean, I made some comments, but I am-- he is the expert on ventilation----

Q I'll ask my colleague to switch onto page 14 of the bundle. Now, if we look at Chapter 7, am I right in thinking that effectively it has three parts? It has 7.1:

"Are the water testing results consistent with there being 'widespread contamination'?"

A Mm.

Q 7.2, epidemiology exercise involving bloodstream infection data.

A Yes.

Q On the next page of this document, 7.3, "What does the available sequencing show?"

A Yes.

Q Would you be the right author for 7.1 and 7.3?

A Absolutely, and my-- I forgot my colleague Dr Drumright, of course, wrote all of-- prepared-- did all the data analysis and prepared drafts for us to consider and discuss of all of the epidemiological data.

Q I will still talk to you about the epidemiological----

A Oh, yeah.

Q But mainly in the context of the results.

A Yeah.

Q Then Chapter 8, "Ventilation",

is that primarily Dr Agrawal's work?

A Absolutely, correct.

Q Right, well, take that off the screen. What I want to do is to-- Well, actually, sorry, can we go to page 151 of that bundle? Now, this is a declaration.

A Oh, yes.

Q Have you had previous experience of being an expert witness?

A Yes, I've spent 35 years as a medical negligence expert witness in-- mainly in the area of-- obviously infections but also sometimes in relation to infection control.

Q Thank you. Presumably, therefore, you've come across declarations of this sort before?

A Yes. In fact, the CLO said, would it be appropriate to put a declaration in there because my duty is always to the court as an expert, and I regard that in this setting as the same sort of duty, to be unbiased and interpret the data as best I can.

Q Well, I wanted to ask you a couple of questions about the nature of your duty to, in this case, the Inquiry now.

A Mm.

Q We've used, perhaps loosely, the question of the extent to which an expert is obliged to help the fact finder understand the questions they have to answer. Would you concur with that idea as part of what you're trying to do?

A No, I'm not helping anyone. I'm looking-- and this was our approach, was to look at an incident that had happened or a purported incident----

THE CHAIR: Right, could I just take this at dictation speed?

MR MACKINTOSH: Sorry, do----

A Oh, sorry.

THE CHAIR: Right, you're not----

A I have a tendency-- Sorry, your Lordship----

THE CHAIR: You're not helping anybody.

A No, we-- my feeling here is my whole approach to this was really to look at-- to understand what had happened as far as we could, retrospectively, from what information we either had or could in some cases----

MR MACKINTOSH: No, my question, Professor Hawkey, sorry to cut across you, is, do you understand your position to help the inquiry?

A Oh, absolutely----

Q Right.

A -- because you're seeking the truth.

Q Right. So----

A Well, if that can be sought.

THE CHAIR: Professor, you've just said you're not helping anybody, so----

A Oh, I see, sorry. I meant in terms of people who'd instructed me, because the Central Legal Office

obviously approached me and instructed me with various questions, okay, and then in turn they handed us on to yourselves, and you in turn posed questions to us, you know? I wish to approach those in as unbiased a way as possible.

MR MACKINTOSH: But how would you describe the extent to which it's your duty to help the inquiry----

A Oh----

Q -- particularly-- let me get to the end, particularly the chair, ultimately, to understand the issues and to reach conclusions on the issues that face that particular factfinder? How would you understand your duty in that area?

A To look at data, to look at results and other people's reports and present an opinion. If necessary, sometimes explain some of the more complex areas and to suggest what might have happened, what seems plausible or not plausible.

Q Thank you. Now, the next question----

THE CHAIR: Could I just----

MR MACKINTOSH: Sorry my Lord.

THE CHAIR: In sort of teasing this out a little. Now, you do see your role as helping, I mean, to be frank, me?

A Yes.

THE CHAIR: Right. Now, does that include, the helping me, the way in which the report is set out and the material which is within that report?

A Yes, and we-- I mean, it's a highly technical area. Understanding bacteria is a whole new language of just how they're named, which is why CLO suggested – and I thought it was a reasonable suggestion otherwise I wouldn't have taken it-- wouldn't have taken them up on it – well, putting in a section which was criticised in CNR, how are bacteria named? What are these different types of gram-negative bacteria? That's why I wrote that section, which is for illustration and enlightenment.

THE CHAIR: That's Chapter 3 we're talking about?

A Yes, Chapter 3.

THE CHAIR: Right. We may come to that, but your purpose was for enlightenment.

A Exactly.

MR MACKINTOSH: So, what I think is probably a good idea to do now is to look at your letter of instruction----

A Yeah.

Q -- and just discuss some of the material. To be fair, you already covered it in HAD questionnaire one----

A Yeah.

Q -- which is, for reference, bundle 44, volume 2, document 1 at page 15. I'm not going to go through my questions because written questions are

always phrased in a rather laborious way because you're not there to say, "No, I didn't mean that." But let's look at the letter of instruction. Bundle 44, volume 1, document 4, page 239. Now, just to put everything in context----

A Yeah.

Q -- when you were asked to get involved, was Dr Agrawal already involved?

A I was approached initially by somebody I can't----

Q I don't think names matter in this context.

A No, no. Somebody in the Health Board who said, "We've received-- we've had this issue," which I wasn't aware of, "We've had a series of reports," I think, would I be-- about gram-negative bacteria, would I be prepared to provide an opinion on them, and I said, "Yes, I will." At that point, I had no further contact directly with Glasgow Health Board at all, and I was contacted by [redacted] CLO.

We said-- and you can see in this letter, but he said-- I said, "Well, it's obviously complex. I can deal with infection control and microbiology, but the clinical aspects are not my area," haematology, oncology, and he said they'd had some connection and work with Dr Agrawal. Now, I know Dr Agrawal, not well, but prior to this, as a very good, competent haemo-physician at Barts, and I said, "That's fine." So, at that point, we then got together to talk about how we might approach this problem.

Q While we're mentioning Dr Agrawal, I suppose a brief question. You would have heard me asking him questions about the extent he had expertise in pediatric haemato-oncology.

A Mm.

Q Did that question of whether he had appropriate expertise to cover the whole scope of this investigation occur to you, or am I misunderstanding the nature of expertise?

A I-- No. I-- Obviously, children from a pharmacological and a treatment point of view are very different to adults; they're not just mini-adults. When it comes to infection, I'm not-- and I believe that Dr Agrawal expressed the same sort of opinion, there the differential is much less, I think, and, in fact----

Q I appreciate----

A Yeah.

Q -- that that may be your view, but do you feel that, to the extent that Dr Agrawal does not have expertise in paediatric haemato-oncology, which I've discussed with him, that this issue doesn't arise for the purposes of this----

A No, it didn't concern me at all.

Q Right, okay.

A No.

Q Obviously, Dr Drumright then becomes involved.

A Yes. So, we began to look at this and I'd read-- obviously read through the CNR and read through some of the other water reports, and----

Q So, which other water reports?

A There were a-- there was a small bundle of documents that were provided along with the CNR when we-- the two of us got those, and I felt, as did Dr Agrawal, that maybe we needed to take-- the approach we could take would be look in a more broad sense, to look at time spans and possibly look-- and look at different patient populations but still all obviously compromised patients with haematology-oncology problems and then-- and that would involve a lot of statistics and although I understand statistics I am not a statistician, and he mentioned that he'd worked with a very good statistician who he'd met in Cambridge, I think, subsequently, Dr Drumright.

That's how we became involved with Dr Drumright. She kindly agreed to help us with statistical support, and she was an ideal person because she spent six years working-- I believe, six years at Imperial College with the Infection Control team there, applying-- working with infection control doctors and nurses in Imperial, applying epidemiological methods to infection control. So, she's not just a statistician. She is someone who understands and has been immersed in infection control.

Q Now, what I thought it would be helpful to do would be to look at the appendix to your letter of instruction----

A Mm, well.

Q -- because it is phrased in the form of seven questions.

A Yeah.

Q So, to page 242. What I might do to assist you is to ask my colleague to zoom into the top half of the page, questions 1-4 are visible but nothing below that.

A Yeah. Yeah.

Q Now, if this letter-- I'm sure it is complete and correct. It was issued to you in November '22?

A Yes.

Q So, to what extent did your ideas on how you would look at this matter develop after these questions were sent?

A They did, because some of those questions are relatively easy to answer. Other ones, particularly when talking more specifically about the GGC setup, much more difficult to understand how one was going to approach that, and that's when we thought, well, we need to-- if there was a problem, we would expect

to see an increased rate of particular types of organisms, perhaps, but we needed to look at that data in more detail.

Q So, if we go to the bottom half of the page, please, and Question 5. So, one of the questions appears to be 5(b):

"Is there an increased level of infections consistent with there being 'widespread contamination' of the water system:
i) Evidenced by an increase level of infections from these "marker organisms"?"

So, could it be that this idea of looking at data was already inherent at the beginning?

A Oh, absolutely----

Q Right, okay.

A -- and we just expanded its extent.

THE CHAIR: Sorry, my fault, Professor.

A Yes, sorry?

THE CHAIR: You've said that having been presented with a list of questions, some more difficult than others, your thinking developed. Did the questions develop or have the questions always been as they appear on this screen?

A I think-- I think they were always as on that screen essentially and we've treated it, I suppose, rather more as a scientific exercise to look----

MR MACKINTOSH: So, you've looked at different methods of answering the same----

A Exactly, exactly.

Q Right, okay.

THE CHAIR: Okay.

MR MACKINTOSH: Now, what I want to do is go back to the top of the screen and I want to look at Question 3 in some detail because it's a topic that keeps coming around. So, the first thing is, obviously-- I'm going to pass over Question 1 because 1 appears to be the answer is no.

A Yeah.

Q But if we look at Question 2:

"What constitutes a contaminated hospital system (particularly in reference to existing legislation and guidance)?"

And Question 3:

"If there was "widespread contamination" of the hospital water system (whether this was due to ingress contamination, regressional contamination, or contamination at installation and/or commissioning)…"

There are then two questions: what would be evident through water testing, and what would be the expected findings? Now, what I want to do in a moment is have a conversation with you about what you understand by the concept of widespread contamination. Before I do that, I'd like to look at the

footnote. So, if you go to the bottom of the page, footnote 1 is a reference to a document called the HPS Report:

"Summary of Incident and Findings of the NHS Greater Glasgow and Clyde: Queen Elizabeth University Hospital/ Royal Hospital for Children water contamination Incident, and recommendations for NHSScotland."

Now, firstly, did you read this?

A No.

Q Why not?

A Well, I did glance at it, but I felt I wanted to approach this problem independently. This is, obviously, an-- it's an investigation and they've looked very-- you know, they've looked at things, but I felt we wanted to look at this independently.

Q So, you've just told us a fact that's not in your report, that you were originally approached by someone from the Health Board who explained there'd been a series of reports?

A Yes.

Q This is presumably one of that series of reports.

A Well, I don't-- it wasn't actually the Health Board person about the report. It was CLO.

Q Oh, right. Well, if we look at this-- well, let's ask you the question first, and then we'll look at the document. So, we go back to the top of the page. What do you understand the person who was asking you the question meant by "widespread contamination" in Question 3?

A Question 3. Well, it's not a simple-- contamination in a water system. I'm not a water engineer or an expert in water systems. I'm a microbiologist. However, there are very-- the water system becomes-- There are two aspects of contamination, first of all. There's the legalistic aspect of contamination from a point of view of drinking water standards, okay?

Q Well, yes. We're going to come back----

A Coliforms, counts of Enterobacter, Enterococci, etc. So, that's that. But then you have the issue of other organisms which at the-- at that-- certainly, if we go back to the late teens, 2017-18-19 were not yet sort of, if you like, very widely recognised. They've known that they could be transmitted from water but their role and position in a hospital water system was really much-- was under research and research and development. In fact, that is still going on as-- at the moment, to try and understand. Because you can have a biofilm with Pseudomonas, maybe a few Stenotrophomonas in a water tank supplying a whole load of cold-water supplies in a hospital.

In my understanding and my opinion, yes, that can be a source and that's when we talk about ingress contamination, because you have to ask yourself, where have these organisms come from? The only place it can come from is down the public water supply. If you look at what occurs in the public water supply, you do not see Enterobacter. You certainly don't see E. coli because it wouldn't be potable quality water. So, this is----

THE CHAIR: When you say you would not see it----?

A It's just not there.

THE CHAIR: It's just not there at all?

A No, generally. No.

MR MACKINTOSH: So, can I look at Question 3, because I did ask you a question which you've not yet answered, and we'll come back to it----

A Okay.

Q -- which is what you understand by what "widespread contamination" means but look at Question 3. The way it's phrased is:

"If there was "widespread contamination" of the hospital water system (whether this was due to ingress contamination, regressional contamination, or contamination at installation and/or commissioning)…"

Which one of those possible

scenarios you're being asked about is the one where it comes in from the public water system?

A Ingressional.

Q Right. So, could you-- if we accept, for the moment, that "contamination" is the right word, presumably regressional contamination would be a means by which a water system could acquire these organisms other than from the public water system?

A Yes.

Q Yes and, similarly, at installation, you might get contamination?

A Indeed, installation, and that rose out of incidents in Northern Ireland, in a Special Care Baby unit. I used to be a member of, founding member of, the English ARHAI, responsible for infection control, and we had a lot of sessions at the time and tried to produce guidance on how one might look at, particularly in this case, Pseudomonas, particularly, and the relationship to what are known as thermostatic mixer valves, which have-- nowadays, they've changed the design of them but, at that point, they had types of plastic and rubber in them which enabled organisms like, particularly Pseudomonas, but to a certain extent perhaps-- other organisms to grow on this valve and then, of course, contaminate the water, and this is a widespread problem in all healthcare facilities----

Q And this is the Horne Optitherm tap?

A Yes, that's a particular make. I'm not particularly familiar with that make, but there are lots of different makes, yeah.

Q Returning to the question, this question-- I mean, first thing I want to check, I'm not being foolish. Is this question asking you to assess how the existence of widespread contamination would be evident? In essence, that's what it's trying to do.

A It is.

Q Yes. So, what do you understand is being meant, by the person who asked you this question, as "widespread contamination"?

A Well, we-- right or wrongly, we chose to look at the rate of infections that occur, because you will always find biofilm in taps, okay? In any ward. Does it become significant? Well, it may become significant because of the operational way in which that ward operates and that water system is used at a ward level.

Q So, the reason I ask this is because of the footnote of the document you have only skim read.

A Yes, yeah.

Q Let's look at it. Bundle 18, volume 1, document 11, which starts on page 819, and I want to look at the executive summary on page 820. 821, there we are. Now, this document describes what the authors seem to think of-- is a water contamination incident.

A Yes. It is.

Q It is a water contamination incident?

A Yes, it relates-- and this is one reason why I thought, clinically, how relevant is this? Because it focuses very much on Cupriavidus. Cupriavidus is a gram-negative organism. It's a true environmental organism in the sense that it is particularly water-orientated and you can find it in any public water supply, sometimes in quite large numbers.

Q So you feel this report is just about Cupriavidus?

A It feels like it's about----

Q Okay, well, let's go to page 825 and the summary of clinical incidence. So were you aware that in 2016 of February there was a Cupriavidus incident in Ward 2A?

A Yes, yes.

Q And that's known as the aseptic pharmacy incident. Are you aware about that?

A Yes.

Q Right.

A I am now particularly obviously since----

Q When did you become aware of that?

A Well, I suppose, really, once it was clear that our report was going to be considered by the Inquiry.

Q So, before you wrote the report, you were unaware of the 2016----

A Yes, yes.

Q -- aseptic----

A Yes, I'd seen Cupriavidus – very small numbers – and the relationship to the vast majority of infections on the ward didn't seem to me to be particularly necessarily relevant.

Q Are you aware that the opinion of the people who investigated it was a localized outbreak related to one sink?

A No, but that's interesting that they found that, yeah.

Q Yes. Then if we look at the second half of that paragraph, a mention of September '17, further single case.

A Yeah.

Q And then 2018 January, another case.

A Yeah.

Q And do you see that there's then reference to Pseudomonas in line 4?

A Yeah.

Q In February. And then Stenotrophomonas in March, three cases.

A Yeah.

Q And then Enterobacter.

A Yes.

Q Three mixed Gram-negative--

So this is not a paper about just Cupriavidus, is it---

A No, no, no, but I was aware, having read the CNR, that the CNR was-- very comprehensively looked at all of these organisms and collated those bloodstream infections in relation to that.

Q So, the problem that I'm trying to press you on is about how to use your opinions.

A Okay.

Q So, if we go back to the term of reference, the appendix, page 242 of bundle 44, volume 1, that we were looking at before, and the top of the page, the Health Board have asked you a question, and the question appears in Question 3 to be defined by reference to a concept of widespread contamination. This concept of widespread contamination remains in dispute in this Inquiry.

A Okay.

Q There have been a significant number of witnesses who think the word is entirely appropriate. There have been a small number of witnesses who think the word is not technically accurate because "contamination" is more about non-biological material in a water system---

A Okay.

Q -- and there have been a small number of witnesses who take the view

that there was not widespread contamination in the water system, from their opinion. There are also reports at the time of people who have this opinion. So you didn't read the document you were given by those instructing you that sets out the nature of this scenario, did you?

A No, no, no.

Q No. You've written a report, you've come to some conclusions and you've evolved those conclusions as we've shown you more material----

A Yeah.

Q -- to some degree. This is the question. What utility is your original report given that it was written without being aware of the details of this hypothesis that is set in this instruction?

A Well, what we did have access to was a very comprehensive data report and also results of a lot of water testing about----

Q You did.

A -- widespread contaminants, Chaput-- so-called Chaput data----

Q So the Chaput report?

A Yeah.

Q Oh, you had that?

A Yes, and in fact that was very helpful because it actually gave actual data on what their testing results were and the pattern of testing and the sort of organisms they were encountering. So there are organisms in the water system. I would say anyone who says there are no-- you know, there's no contamination, yes, there is contamination. The key for me is-- and if you went into many hospitals, you would find not dissimilar finding, I think, and that's ingressional contamination, often with Pseudomonas, sometimes with other organisms. It's how-- what measures you take to control it and how you recognise that and what impact that has on the patient population.

Q So one of the problems, I suppose, is that you had the CNR overview report?

A Yes.

Q And you read that.

A Yes, oh, absolutely, yes.

Q Yes, and I don't think there's any dispute it contains a lot of information.

A Yeah.

Q And that is often chronologically ordered so you can tell----

A Very helpful.

Q Very helpful, but it only covers the period up to when it's finished.

A Yes.

Q You then have Dr Chaput's report, which tells you when the water testing was done by month and the results. Got that?

A Yeah.

Q I wondered the effect-- what's

the effect of you not having access to certain other material? So, do you remember how in the first questionnaire – it's at volume 2, page 24 – I asked you a series of questions about documents that we've been looking at?

A Mm-hmm.

Q So I think it would be fair to say that this Inquiry has spent a large amount of time and called a large number of witnesses to discuss these documents, including the authors of most of them, people present at-- well, for almost every meeting. To take two examples, the first one on 10(a), the DMA Canyon 2015 L8 Risk Assessment, and the minutes of the Water Technical Group meetings on 13 April '18 and 20 April '18, you didn't you didn't feel they were in the scope of your remit?

A No, because what I would what I would have to do then is I'd have to go-- one would have to go back and try and, if you like, reconstruct from these documents and minutes what actually happened in terms of infection control and infection management, in the board as such, and I'm looking at it as third party who's never visited the hospital.

THE CHAIR: Sorry, what did you say about visiting the hospital?

A I've never visited it.

THE CHAIR: You've never visited it?

A Not in-- not to look at water systems or anything. I've given two expert lectures on Gram-negative bacteria there, but that was purely to the Microbiology Department.

THE CHAIR: But you haven't familiarised yourself with the water system----

A No because----

THE CHAIR: -- or the ventilation system?

A No, no, particularly not the ventilation-- well, neither of those, because that wasn't what we were led by CLO to do. They didn't say, "Come up and look at all the system," and I wouldn't feel necessarily qualified. It's Dr Walker, who I've worked with before, I believe has given evidence to you as an Inquiry. He's an expert on water systems. I've published a paper with him. He would give you a much better opinion on the state and running of those systems.

MR MACKINTOSH: So, this is the problem that I'm going to float, and I will invite you to come back to this if you reflect on it over the rest of the day, and if you think there's a better way of expressing your answer, I'm very keen to hear it. I understand that one can do a dispassionate agnostic – I think it might be Dr Agrawal's word----

A Indeed.

Q -- data analysis exercise and

produce a chart, or four, showing the rates of infections of certain microorganism groups in certain patient groups over periods of time, and if you park for a moment the fact that sometimes it's quite hard to define the patient groups and the spaces if you don't know the hospital, if you just sort of brush over that issue, you can produce possibly informative charts.

A Yes.

Q But what I worry about and what I'm keen to understand your response to is the suggestion that you then follow up that with interpretation. So, within this report there are various points when you interpret – the three of you – charts. Now, what value can the Inquiry take from interpretation of a chart or a statistical exercise carried out by, clearly, experts who don't know what was happening at the time and don't have the context in the field of epidemiology?

A Well, I think when you start to look at the field of epidemiology, that's something where Dr Drumright is the expert in understanding that. She-- she managed that aspect of our-- our work.

Q Okay, but you I don't feel that, for example, when you discuss what your-- You said for a moment ago that you thought the principal issue, the only way you could get Pseudomonas into a water system – I think it was Pseudomonas – was in ingressional (inaudible 10:41:35).

A Ingressional but also-- not-- No, I didn't say it's the only way because regressional contamination of taps is very common.

Q Right. In order to know whether there was regression or contamination of taps, would you need to know the type of tap and the way the ward – in the broadest sense – was being run in basic infection control terms?

A No, because you look at the microbiology.

Q So you feel that you can interpret the microbiology without an awareness of what was going on in the water at the time?

A We're interpreting it at a fairly high level here because, as I say, we use the concept that if there is a problem we would expect to see an increase in the rate of infections. Now, whether that's----

THE CHAIR: When you use the word "problem", what do you have in mind?

A We were-- It's a hypothesis. We look to see if there is an increase is perhaps a more accurate way of putting it, and as it happened we did see an increase at that period and now other people have found that in other analytical studies. Mr Mookerjee's work showed

there was an increase, and I wouldn't-- That was an important and interesting finding.

MR MACKINTOSH: What I want to do is I'll come back to Dr Chaput's report later, because I think you address it in the conclusions, and we're still in the early stages, so what I want to do is look really at Chapter 5, and if we could go to Chapter 5, which starts on page 51 of the bundle. No, wrong bundle. Sorry. 44, volume 1. We'll go back a bit. 45, please. There we are.

Now, you discuss in 5.2 what constitutes a contaminated hospital water system. Would it help if we zoom that into half page?

A Yeah, that would be helpful, thank you, yes.

Q Please could we do that? I might ask my colleague to generally jump to the top half of a page from now on and, if necessary, we'll move around. If we move down the page, so 5.2 is at the top of the screen. Now, you make reference to Public Water Supply of Scotland Regulations 2014 in the context of the potable water standards.

A Yeah.

Q Now, I think the next few questions are going to sound quite pedantic----

A Doesn't matter.

Q -- but I've been asked to ask them. Why do you refer to "potable" rather than "wholesome", which is the language used in the regulations?

A Oh, sorry. That's the-- That's a term I'm used to as an environmental microbiologist in England.

Q The next thing is, why does this chapter not make any reference to the, sort of, industry-standard regulatory documents about managing water systems in hospitals, just so I can check?

A Because I'm not a water engineer. I'm not really qualified to make comments on the design and construction use of water systems.

Q Well, the reason I mention that is because-- Now, I may have misunderstood but I get the impression from some of our witnesses, who are water engineers and water system operators, that water systems are managed to avoid risk, as opposed to by doing lots of testing to check you haven't got a problem. Would you agree with that, as a broader point?

A Yes. No, no, absolutely.

THE CHAIR: Sorry, Professor, my apologies. That's not quite how I understand things.

MR MACKINTOSH: I understand----

THE CHAIR: If I'm wrong about that, I want to be corrected. (To Mr Mackintosh) The way you phrased the

question was that they were to “avoid risk”. Now, my understanding – and I want to be corrected if I’m wrong – is that by their nature a, for example, hospital water system presents risk----

MR MACKINTOSH: Yes, my Lord.

THE CHAIR: -- but those responsible for managing the system are involved in managing a given and inevitable risk. Now, have I got that right?

MR MACKINTOSH: I think you have, my Lord. I think I have misspoken. So, there is an inevitable risk which would be then managed.

A Oh, yes.

Q Yes. Now, the reason I mention that is because a response to the question, “What constitutes a contaminated water system?” might well be, “Well, normally we don’t talk about contaminated water systems. We talk about the extent to which risks within the water system are not managed.” I just wonder why you didn’t make that connection to the management of water systems in this case.

A Because I’m a microbiologist and infectious disease physician.

Q So, the fact that there are hospital technical memorandum covering design, operation, testing protocols, written schemes, control Legionella, it’s not your field, effectively?

A Not my field. I’m aware of them and, at a practical level, working with my engineering colleagues in various-- in hospitals I’ve worked in in the past, but they lead on that area.

Q So, there is an area where there might be a crossover, and I’d be grateful for your assistance. So our first ex-witness in this Inquiry in Block 3 – so, that was last year – was a Mr Watson, who had been at the DMA Canyon team, and he talked about his work in the hospital from 2015 trying to manage the hospital water system.

A Right.

Q I seem to remember that he accepted, or even felt, that if you have a water system where risks of Legionella growth are not well managed because of temperature, it seems a reasonable concern that such a temperature environment might also encourage - and I emphasise “might”, might also encourage - other microorganisms other than the regulated ones to grow. I wonder if that’s, from your point of view as a microbiologist, a reasonable----

A Very reasonable. In fact, Legionella can’t survive without other organisms around it. It’s incapable of-- basically of independent existence. It needs a functioning biofilm and often we now recognise, I believe scientifically from a microbiological point of view, there

are some specific organisms which Legionella needs to survive.

THE CHAIR: Yes, and are you agreeing with the proposition that was put to you that what is true for Legionella may be true for other, potentially pathogenic, organisms?

A Yes, yes.

THE CHAIR: Thank you.

MR MACKINTOSH: What I wanted to do was to look at this section, and actually I'm going to make sure I've got the right page in front of me before I put it on the screen. It's actually on page 48. If we go to the middle of the text-- Let's stay on the whole page first just so we can get context here, Professor.

So, this is the end of section 5.2. Section 5.3 begins below it, but I'm going to ask to zoom into the middle of the screen. Do you see the line that goes, "Using highly discriminatory Whole Genome Sequencing"?

A Yes.

Q I'm going to ask my colleague to put that at the top and to widen it out as far as we can go. So, move it up. Now, it's the last sentence I want to explore with you. Now, I appreciate that I'm selectively quoting from a chapter and that you have probably drawn this summary from the whole chapter, but the sentence reads:

"In summary, although sink traps have a diverse and sometimes profuse bacterial population which is enriched sometimes by human derived materials and consequently bacteria associated with human colonisation or infection, they are not the dominant source of bloodstream infections when compared to gut or oral microbiomes of immune compromised patients themselves."

Now, the thing I'm going to ask you about is the "sink traps" bit of that sentence.

A Yes.

Q Because you'll see that Couchoud is using whole genome sequencing to assess the role of sink traps, if I've understood it correctly.

A Yes, and that was because they had no Pseudomonas in their water supply at all, in their taps.

Q So they looked in the sink traps?

A Yes.

Q But what I'm trying to understand is the extent to which-- Well, what is your mental image of this widespread contamination that you are being asked to assess whether it exists? Because-- Firstly, let's break that down so I can make sure I'm not putting words in your mouth. Would it be fair to describe that much of this report is an attempt to say, "If there was widespread contamination, would we see it in the

water testing results or the blood stream infection results?" It's, broadly speaking, what the exercise is. Yes? No?

A Yes. I have to say, I mean, the-- because-- A lot of the sampling was very *ad hoc* and not structured like a prospective research study.

Q Yes.

A And I think that weakens its value to a degree. It gives you an indication of the sort of organisms that were present, but it-- it's difficult to be very conclusive in that set of-- and I think other experts have said that previously, and I would agree with them.

Q The reason I ask that is because----

THE CHAIR: Sorry, it's entirely my fault, Professor.

A No, don't worry.

THE CHAIR: Just for my notes, you've referred to the ad hoc nature of the sampling. I just didn't catch what you went on to say.

A What did I say? Ad hoc-- Yes, so it wasn't structured. The papers I've referred to here-- because we have a problem. In real life and real outbreaks, we don't have the facilities or the manpower necessarily to always investigate them in great detail. So in practice, one looks at the literature and other people who've done careful prospective studies with time and resources to look in great detail at these sorts of environments, be they tap outlets or sink traps, and trying to correlate that, perhaps, with infection in vulnerable patients to draw some broad conclusions as to what one might see in-- in practice, in real life, and it's that's one of the difficulties of investigating outbreaks.

MR MACKINTOSH: Now, I just wonder whether there will be any difference in the approach one would take to investigate an outbreak that you suspected was built around an individual sink or an individual ward, compared to a suspected outbreak for which there is a hypothesis that it involves the entire hospital water system. Would they require different investigatory techniques to understand?

A I wouldn't have thought different investigatory techniques. It's an issue of manpower and facilities and degree, and there you would have-- they would have to make an assessment as to whether the clinical impact-- the level at which you're going to go-- go within that investigation.

Q But from your point of view, coming in retrospectively, looking at data, do you need to know whether it's a hypothetical single ward, room or sink outbreak that's being floated as a possibility or a hypothetical whole hospital system issue that's being-- Do

you need to know that it's one or the other in order to design your study?

A Which study are we talking about?

Q The HAD Report.

A Okay. Well, no, because practically it would be very difficult to do that because it's a big complicated hospital. You've got lots of individual sinks; you've got lots of individual risk factors; you've got lots of individual different patients. We felt, rightly or wrongly, that it would be difficult to try and dissect out and tease all those details, and we'd have to do it, because we're-- we're quite a long way down the tracks in time terms, by going back and looking at people's records and notes, which may or may not be consistent or appropriate.

So that's-- Our whole philosophy was to say, "Well, let's step back here. Let's see whether-- whether there was a problem, what that problem might be if we saw it in terms of bloodstream infections with organisms that are likely to come from the environment." That was the thrust of our investigation.

Q But I just wondered whether, when it comes to the topic which I hope to deal with after the coffee break of whole genome sequencing, it would be a fair criticism to suggest that you might, to some extent, have in your mind's eye a

smaller outbreak than actually it is being suggested by some people took place.

A These-- Well, the organisms that we're talking about in risk contamination here, and to a certain extent, the retrogressive tap colonisation, in the vast majority of the hospital, it doesn't matter at all. It's only in areas like Intensive Care units, Burns units and immunocompromised patients, the haematology oncology patients, that that becomes a factor. So that's a consideration, and the other consideration is that we look at the haematology oncology patients, the vast majority of their infections-- and this the CNR actually, and I mean-- It supports.

It's just the degree to which they support. 70 per cent of patients they thought were not, most probably, infected from the environment. It's about 30 per cent. So where did they get-- those-- where did 70 per cent get theirs from? They got them from their gut, okay, translocation of the bacteria from the gut into the bloodstream causing infection. So that's one common route.

Now, we immediately say, "Well, okay, how did the gut get colonised?" It could have got colonised, in some patients' cases, from a tap that has a Pseudomonas in it, but it also could get contaminated from all sorts of other areas, and there's another means of

transmission, which is very uncommon in hospitals, which we call person-to-person, and that may be directly by contact with people-to-people, by handshake or touch on the skin. Klebsiella is particularly good at doing this.

So that's one possibility, but then there's also the staff in terms of hand cleaning and management, and here, with haematology oncology patients, I'm sure-- I know you've heard already, they're very prone to line infections. They have to have long-term indwelling intravascular lines. Those entry sites, not only could----

Q Professor, we've heard a lot about that.

A But you know all about that.

THE CHAIR: Can I take a step back? If I've just got this wrong, please tell me, Professor. Mr Mackintosh has been asking you, if I've understood his questioning correctly, questions about methodology, approach, technique, in particular in relation to what we're calling the HAD Report, the report by you and your colleagues. Now, listening to your answers, it appears to me that you are telling us that this report is not directed at any particular hypothesis. Now, if I've got that wrong, just tell me.

A No, I think that's a very fair comment, yes.

THE CHAIR: All right.

A We wanted to approach it in a-- in an unbiased way.

THE CHAIR: Maybe that-- this, sort of, will save us time. The questions, as I understand it, framed by the CLA, series of questions under seven general headings, do appear to me to present, in fact, a series of, as it were, sub-hypotheses. Now, I think I'm generalising at this point. In my reading of the HAD Report, I don't see, certainly, all of these sub-hypotheses addressed. Now, that would seem to me a-- consistent with what you've previously told me, that it would----

A Yeah.

THE CHAIR: -- be fair, in looking at the HAD Report, to bear in mind that you are not addressing any particular hypothesis.

A Yes, I think that would be a fair comment.

THE CHAIR: Thank you.

MR MACKINTOSH: I wonder if we can go to the next page, page 49, and the first section, paragraph 5.3.2, in which you ask the question, "If so what would be the expected findings that would demonstrate that there is 'widespread contamination'?" You say here:

"It has hopefully become clear from the explanation above when a water system is a source of environmental

contamination and when there is spread to vulnerable patients is it generally not the whole system which has a high bacterial load. It is rather specific outlets such as tap outlets and sink traps which can be heavily colonized, and therefore represent a potential source for spread to patients."

Now, I want to show you a document which I know you didn't see at the time----

A Right.

Q -- but was on your document list, so we can take that off the screen and go to bundle 10, the minutes of the Water Technical Group, and if we can go, please, to document 2, page 9. So, you may have read this when we put it on the document list. This is a minute of a meeting that was set up just at the start of the water incident, and at this point it's chaired by an assistant director for Health Facilities Scotland.

Membership consists of a nurse consultant for Health Facilities Scotland, the principal engineer of that organisation, a number of senior managers, a consultant in public health medicine, and another infection control doctor is on the "Apologies" list, along with Ms Kane, who at that point was the co-chair of the Water Safety Group for the whole Health Board.

Now, if we move down to the matters arising, you will see the minutes described-- Stop there, please.

"The outcome of the water testing is currently being mapped onto the floor plans of RHC and Adult hospital – those present were shown samples of the work concluded at this time. The spreadsheets and drawings used together shows the rooms, risers etc that have returned with positive results and what these are.

"Discussions continued on the next stage of progress. It was suggested that the risers be next to be subjected to testing and then onto the heat exchangers. The question of the room that are shown on the floor plans with no indications of issues with the water – does this reflect they are not affected? – this means that they have not being tested [sic]. Testing is carried out on the advice of Infection Control. AR [who's from HPS] noted that it would be beneficial to have some spot tests carried out in other areas…"

Now, if we go over to the next page to "Agreed", and stop there, please, second paragraph after the bullets:

"The group asked where has already been tested – it was confirmed that not all taps and showers tested but there have been some random tests carried out from all areas of the hospital. These are noted as:-

0-3 [that's Levels 1 to 3] in RHC

4-11 [that's in the tower] in Adult

It was noted that every floor had positive and negative readings thereby this would indicate a widespread water infection."

If we go to the next minute of the next meeting, this is April 20th of 2018, and we want it on page 14, and we go to the heading-- At this point, membership, it's broadly the same, but now the leading Infection Control doctor, Dr Inkster, has joined via telephone, having not been present at the previous meeting.

A Mm-hmm.

Q Go down to the heading "Way Forward", bottom of the page:

"Every floor is showing some contamination with various species so we can assume there is a widespread contamination in the buildings. A review of the commissioning data indicates there was TVC which were off the scale but now we need to determine the way forward and solution to the contamination."

Now, I accept that's a snapshot----

A Mm.

Q -- from two meetings, relatively senior people, and these people don't-- well, some of them don't know about the existence of the DMA Canyon reports at this point.

A Right.

Q That may be important, but what I wonder is, if we go back to page 49 of volume 44, volume 1 and your discussion of what generally is generally not the whole system, which is a high bacterial load, could it be that one does need to think about a whole system as a high bacterial load in order to analyse the data and understand it, which you have produced?

A Well, it depends upon what we mean by a whole system contamination. I notice, if you go back I'm not certain----

Q Page 14.

A -- whether they were testing-- did they test storage-- water storage tanks?

Q I think at that point they might have done, but----

A Because----

Q Yes, they did. So if we go back to page----

A Okay.

Q -- 14 of bundle 10, the bit I read out was heading of "Way Forward". If we go up, "Matters Arising":

"IP provided several drawings to the site – showing locations of water into the site and the floor levels affected by the bacteria. It was noted that the spreadsheet results had shown there was now contamination in the tanks. Two tests are required on the tanks as they are split"----

A "these had always been

reported as clear"----

THE CHAIR: Sorry?

A "with exception of one report", okay.

THE CHAIR: Sorry, my fault, I don't----

MR MACKINTOSH: Which bit are you reading from?

A I was just reading from the middle paragraph.

Q Yes.

A Sorry, I'm just sort of trying to absorb that. (Reads *sotto voce*) Okay, when they say----

Q If we go to Dr Chaput's work, which of course you have seen, which is bundle 18, volume 1, document 2, and I just thought-- because since you mention Cupriavidus, we'll go to page 35. The reason I put this on the screen is just to show that I think, as you've already observed, there wasn't a lot of testing going on before-- if you go right to the bottom of the page, please-- before the start of 2018, and then there's a lot of testing.

A Yeah.

Q So, the question I'm asking is it a reasonable criticism of your approach to this topic that you worked on the basis that generally it's not a whole system issue?

A Yes, generally, but there's data here suggest that perhaps at that particular point, because tanks had been sampled, there was a tank problem.

Q But I'm just wondering whether, if we go through-- and we're going to turn in 45 minutes or so to the topic of what you learned from genome sequencing.

A Mm.

Q We've obviously got to understand what you're saying and work out how it helps answer the question.

A Yeah.

Q And I think that's why I leave methodology. If the question is, "What would you see in the context of widespread contamination, if there was widespread contamination," am I making a fair criticism that you seem to have approached your paper on the assumption that, whatever issue there was, it wasn't a whole system issue?

A Yes.

Q Right.

THE CHAIR: Right. Again, can I just pause so I can check that I have got that? Right, so what I understand you're accepting, Professor, is that, if we look at the HAD Report, the approach is to assume that, when one is considering environmental sources for gram-negative infections, (1) usual experience, or usual experience reported in the literature, is single location, and it is on the assumption that that is what you're

considering that the report proceeds on. Have I got that right?

A Yes, it depends what you mean by single location. It can be a single tap. It also can be an entire wall which-- in which sinks or outlets can become contaminated.

THE CHAIR: Okay, right.

A What we do understand is that very often, when the biofilm builds up, particularly in the traps, and there's been more work done perhaps on traps that actually on outlets from taps, you will see individual strains of the-- You don't tend to see a great diversity of organisms. You'll see one or two strains, shall we say, of Pseudomonas, and they'll be different-- maybe in a different tap on the same wall, so it's a very complex situation.

THE CHAIR: But you're accepting from Mr Mackintosh that your report was to proceed on the basis that, if one was considering environmental sources, it is either a single tap or perhaps a single location as large as a ward.

A Yes, definitely, yeah.

THE CHAIR: Are you also accepting the proposition he put to you that that might be said to be a criticism of that approach.

A Indeed, but it is interesting that the one organism that appears here as ingress contaminant is the very organism which is very common in tap water, so I can see a reasonable reason why that might be if the tank management didn't clean it out properly because it's Cupriavidus.

MR MACKINTOSH: Well, indeed. I put it on the screen. I'll take that off the screen and ask a sort of general question before leaving methodology behind. I wonder if this sentence, this concept, has any flaws in it: could it be that the sort of environmental gram-negative bacteria that you study could in a particular patient population have multiple different sources if you look at it across-- Some will be brought in by the patients, some will be patient to patient, some will come in from the water system, some will be regression or contamination. We can come up with more esoteric ideas, but there are lots of different possibilities and they could all be happening at once.

A Exactly.

Q Right, so what I want to do is look at your definition, which I think is a little bit harsh of a way of phrasing it but to keep it short, of the sort of organisms you're interested in.

A Mm-hmm.

Q So this is on page 50 of volume 1 of volume 44. Now, we can obviously read the whole of Chapter 5 if you look at the bottom of page 50 from 5.4 on which organisms, am I right in

thinking that in essence what you've done is you've looked at all the organisms and you've come up with a list----

A Mm-hmm.

Q -- which you call various things, but "environmentally relevant" is the sort of----

A Yeah.

Q -- most common phrase, and that's your work?

A Yes, but it's taken not only from a lot of experience, but also the published literature and a knowledge of the epidemiology and the way in which these bacteria behave because there's a blend between the ability of an organism to cause disease in a human.

So there are some organisms which you can find in hospital sinks, in water tanks, that even in a compromised patient you are very-- either never or very, very, very unlikely to ever see an infection, and then there are other gram-negative bacteria that have a different epidemiology which can cause infection in those highly compromised patients. And then there are other gram-negatives that can cause infection in relatively non-compromised patients.

Q The reason I ask is because other people have attempted to come up with these lists. Now, I don't see any particular value in asking you about attempts that were done after your work was done. I mean, there doesn't seem much point in that, but we know that HPS attempted various categorisations.

A Mm.

Q I wanted to see whether you had looked at this particular document, which is listed in your documents you referred to in the report.

A Yeah.

Q That is the HPS review of the NHSGGC infection outbreaks in paediatric haemato-oncology, October 2019. So, that's bundle 7, document 6, page 214. We'll look at the whole page for this one, page 214. No, not that one. Bundle 7, document 6, please. Bundle 7, not volume 7. Perfect. Now, this is listed in your document list.

A Yes.

Q Can I ask whether you read it?

A I've read it-- read the microbiological aspects of it, yes.

Q Well, you may be able to help me. Go to page 219, please.

A There is a definition, isn't there, of organisms there.

Q Well, a series of definitions.

A Yes, there you go.

Q Now, I appreciate it's short. Now, what I wanted just to do is to-- I think we know-- we've been told a lot by lots of people what gram-negative, gram-positive might mean, but there's been quite a lot of people who've given this

piece of evidence of opinion, that if you take the environmental bacterial group identified by HPS in this paper and, down at the bottom of the page, you add to it five enteric organisms to create the environmental including enteric group, that it is that group, this sort of combined group, that in very broad terms is broadly similar to your environmentally-relevant group that you've operated in.

A Yes.

Q I mean, it's not quite the same, but it's----

A Not quite the same. There is some detail-- yeah, detail I would question. Roseomonas, for instance, is only found in-- it's a mouth coloniser of humans, not an environmental organism. That's a minor point. Broadly, yes, and, again, to separate them out is interesting, and you might want to do that. But, for instance, Klebsiella pneumoniae, which is a species that causes infections, that is quite capable of free-living existence on plants, the same sort of strains.

So, is that an enteric group? Well, yes, it can turn up and colonise the human gut. But it is, if you like, not-- you might-- it's quite capable of sitting in the environmental group. So, I personally would prefer to put these almost all together.

Q Yes. So, this combined group, which is eventually is what HPS

reviewed, of the second and third bullet points together, they've called the environmental including enteric group.

A Yes.

Q You're saying that, broadly speaking, it's roughly the same as your group.

A Yeah.

Q Now, ignoring the epidemiological problems in doing this, which Dr Drumright and others have described at length----

A Yes.

Q -- pushing them to one side, does that mean there's a point of comparison, epidemiologically nervousness aside, between work done by HPS on the environmental including enteric group, and your work with Dr Drumright? Can you sort of see----

A Yes----

Q -- the possibility of reading across? Right, well that's very helpful.

A We're roughly reading across, yes.

Q Yes, roughly. What I wanted to do is just discuss at this point the concept of what we've been told are called polymicrobial cases. So, because I'm worried, I always get the words' definitions wrong, I'm going to explain what I understand, and you can tell me whether----

A Yeah.

Q -- I got it wrong. The way it's been put to us in evidence is that you might have a patient who gives a blood sample and within that blood sample, two, three, or maybe four different microorganisms would be grown, and it's been suggested that this is relatively unusual----

A It is.

Q -- and somewhat concerning, and what I want to check is whether I've got a broadly sensible definition of a polymicrobial case.

A I mean, four organisms would be highly unusual in my experience, but possible. Two? Yes. Three? There are two conclusions, which I assess it as a clinician in that setting. Is this contamination? Because when the blood culture is taken, we very-- not infrequently see contamination as a sample.

So, that's one possibility to exclude when you're evaluating the clinical value of polymicrobial bacteremia. My next thought would be, has this patient got a long line in? Because one of the things with long lines is they also develop biofilm inside the body, inside the bloodstream, and repeated injections, which is why we've got those long lines in, may result in environmental or even non-environmental, if you like, E. coli, and particularly gram-positive bacteria such as staphylococcus aureus get into that

line. They sit on the biofilm, and they sit there and they will give you a positive blood culture and potentially cause problems for the patient in terms of infection. So, that's my concept of polymicrobial bacteremia.

Q Right. So, I'm just wondering----

THE CHAIR: You've used the expression "long line". Am I right in thinking that's simply another way of describing a central line?

A Yes, yes, central line. Yes.

MR MACKINTOSH: What to ask you about that is: it's been suggested by us that the-- in fact, you just said that the number of these things might be a subject of concern---

A Yes.

Q -- you know, individual patient. I'm wondering, and there's been some evidence that-- and I'm trying to get the reference here that-- and I think it's in Ms Harvey-Wood and Dr Peters' paper from October '18. I wonder if you saw this. This is bundle 19, volume 1 page 143. If you didn't see it, I won't take you through it. Have you seen this before?

A No, I've not read it.

Q We'll take that off the screen.

A Yeah.

Q What I'm just suggesting to you is that if it was the case that there was an increase in polymicrobial

bloodstream cultures in a certain point in the events in this hospital, would that be something that the Infection Control team would be interested in as a source of concern?

A Well, in patients with lines in----

Q Yes.

A -- okay, any bacteremia is of concern, and something we always review and should be reviewed, and they would fall, probably, into that category because a lot of these patients, I would imagine, would have long-- would have central lines, long lines in.

Q What I wondered was the extent to which your data analysis of bloodstream infections, which you designed with Dr Drumright and Dr Agrawal, can pick up any growth in polymicrobial cases?

A As far as I'm aware, we didn't have a specific category for polymicrobial. There were-- we did see-- when I had looked at the data, they did see occasional polymicrobial results and, again, in highly compromised patients, that's not-- it doesn't have to necessarily be from the environment. If they have a really suppressed immune system, then, and Dr Agrawal may have touched on this, I can't remember, then you will see more than one organism invade through the gut wall and get into the bloodstream and cause an infection. That can occur.

Q Now, thinking about the sort of concept of this study, I think it's not necessary to go to the source, but I get the strong impression that the argument presented, which I think might be in executive summary, is that you would see the greatest impact of-- In fact, we'll take it from page 61, please, of bundle 44, volume 1. In fact, we'll take it from the executive summary, so we'll take it from page 6. Paragraph 2, so we can zoom in to the top half of the page. You say that:

"The greatest impact would be in severely immunocompromised patients. Hence, this report is targeted on patients with haematological, and other, cancers undergoing intensive chemotherapy and/or haematopoietic stem cells transplants…"

Now, your study looked at both adult and paediatric patients within that category.

A Yes.

Q Have I read the paper correctly to understand that you're suggesting that we would have to see a signal in the data in both groups in order to suggest there was a problem?

A No, because it depends where the groups were managed, if we're thinking environment, okay?

Q So, you'd need to know they had access to water that was----

A Not so much access to water, but the physical location. If there was a particular association with a location, one might expect to see a higher rate in that location if it had a problem. In fact, in going to look at the adults, we were aware that we could just look at Ward 2A/B, just the Children's unit, but we've got no context or understanding of what the general rate and occurrence of infection is, which is why we agreed we would request data for other sites. Particularly, as there's quite a lot of patient movement, as you've heard from previous witnesses, and also the length of time, rather than looking at a very, very narrow timeframe.

Q Yes. So, Dr Agrawal explained on the day before-- not the day before yesterday, last week – time flies when you're doing this – on Friday, that he thought-- he explained the idea was you'd look at the rate, just looking at the paediatrics for a moment, in Ward 2A, in the Schiehallion, in those patients, and compare it with the experience of, as it were, their predecessors with the same consultant team, same treatment team, in the old unit in Yorkhill. That's part of what you're describing.

A Yes.

Q Yes, and I put to him the suggestion that you might be able to look forward as well, because if you knew there were interventions to the water system that the Health Board strongly argued – and, indeed, there may be quite a bit of evidence to support this conclusion – has changed and improved the water in the water system, removed the microbial proliferation, then you actually did the study the same way, but now between before the intervention and after the intervention, effectively used the hospital as its own control. Now, did you do that?

A I think we did because we went as far as we could with the data we'd got, and we did, in fact, see, and Dr Drumright has used very good statistics to demonstrate this, a general decline and then a rise, okay----

Q But your original report didn't say that?

A Well, it's because we-- it's a piece of work in evolution, and it was very helpful to be----

THE CHAIR: Let's take this----

A Sorry.

THE CHAIR: -- in steps----

A Okay.

THE CHAIR: -- because I think Professor Hawkey may have not been given the opportunity to finish----

MR MACKINTOSH: No, I think that's fair, my Lord.

THE CHAIR: Finish what you're saying.

MR MACKINTOSH: I interrupted him.

THE CHAIR: Yes. You were talking about the trend, and general decline, then a rise. My impression was that you were then interrupted.

A Yeah, and then a fall, and that data was as a result of further analysis subsequent to the report-- her report, being accepted post-March/April, and I think that has been very helpful, because it helps-- it takes-- if you like, it moves us beyond HAD itself.

THE CHAIR: Right, and there's something useful for me in that. So, I think you used the expression that the HAD Report was, as it were, work in progress or----

A Yes.

THE CHAIR: Right.

A Yes.

THE CHAIR: Right. So, I think from that, you would not encourage us just to look at the HAD Report, but look at what has occurred as a result of the----

A Dialogue, probably.

THE CHAIR: -- interactions between the relevant professionals.

A Absolutely.

THE CHAIR: Right, thank you.

MR MACKINTOSH: Now, at the risk of-- We're making progress. I'd like to look at a concept that you mentioned earlier in the report, so it's the same

document, but it's page 20 and the bottom of the page 2.2, what is meant by an "outbreak."

A Yes.

Q Now in order to take this quickly, having shown you where the section is to assist your memory, I'm actually going to go back to the executive summary, because you summarise it, to ask you the question. So, it's page 6 and paragraph 5 of the executive summary. If you want to go back to the main document, please do. But the reason I want to look at paragraph 5 is you ask, albeit in summarised form:

"What is an outbreak? In clinical practice, an outbreak is suspected if there is an increase beyond the normally expected numbers of infections due to a specific bacterium. Relatedness of these infections in time and space provide circumstantial evidence for cross infection. A strict definition is the occurrence of two or more cases of infection caused by genetically indistinguishable micro-organisms."

Now, I've had a number of questions around this to ask----

A Right.

Q -- and I think they all boil down to this. No one really has any problem with everything apart from the last sentence.

A Yeah.

Q I wonder how you respond to this sequence of questions. So, how would you respond to the suggestion that this strict definition is in fact an overly and impractical definition given that you can't really realistically do whole genome sequencing in the middle of----

A In some outbreak infections, you can fulfill that strict criteria, and a number of outbreaks I've been involved with investigating, using not just molecular type, but older type of typing methods, you can do that. But that's why we have the earlier sentence which says, and the CNR actually described it very nicely as well, saying actually we never found any that, on our case notes review, we could say were definite. However, we did find there were associations in other categories, and I think that's the best way of looking at it.

Q Because the point I need to put to you is Chapter 3 of the National Infection Prevention and Control Manual. So, if we go to – this is not the latest version, it keeps being updated, but – volume 27, volume 4----

THE CHAIR: Sorry, bundle 47?

MR MACKINTOSH: Bundle 27.

THE CHAIR: Bundle 27.

MR MACKINTOSH: Bundle 27, volume 4, document 16, page 178. Yes. I'm assuming you're familiar. We'll zoom in so that the----

A Yes.

Q -- top half of the page is across the whole screen. So, the 3.1 definition is the top of the screen. So, now we've got section 3.1 of the National Infection Prevention and Control Manual on the screen. Thank you. Again, I'm assuming you're familiar with this document----

A Yes. Yeah.

Q -- given your job in Shetland.

A Yes.

Q Would you accept that there's no discussion in the National Infection Prevention and Control Manual of the need for organisms to be genetically indistinguishable for there to be an outbreak?

A Well-- Ah, but you see if you raid a healthcare-associated infection outbreak, which is what we're talking about, "two or more linked cases with the same infectious agent" and the key word there is "same".

Q So you would see that as an example of an indistinguishable----

A Yes, indistinguishable-- the level of identification you've had, and without getting into too much detail, one of the problems encountered, for instance, with the investigation in Glasgow was the identification of Enterobacter, so----

Q Well, we're going to come to that.

A You'll come to that, okay----

Q But I want to just----

A What I would say, the relevance is that if you apply the identification method which the lab was using, it looks like you've got more than one-- the same organism causing infection on more than one occasion or on the same occasion, but actually, if you then use a better identification technique, you find they're not the same organism. They're two different----

Q No, I understand that. I'm grateful you're making the connection with the two issues, but if we just stay at the high level of the definition of "outbreak"-- well, the definition of "incident" and "outbreak", would you accept that there are two separate definitions there and the second one doesn't refer to the need for genetic distinguishability, it's----

A Yes.

Q -- for a higher-than-expected number of cases?

A Yeah, and that's a much looser definition, which is helpful often in saying, "Yes, I think we might have a problem here; we need to do some more investigation." The first one is much more targeted and much-- if you like, a sort of-- more of a red flag.

THE CHAIR: Can I suggest that if one was trying to understand what the

manual means by the "same infectious agent", it means what appears to be the same on the basis of the information that the clinicians have available to them at the time.

A That's the practical reality, and as a microbiologist, we may see-- I may see, "Oh gosh, we've got three cases of Pseudomonas on my ward in a relatively short time period." That's the point where we institute subtyping, bacterial strain typing, because it may be that all three of those Pseudomonas are entirely different, or they may be genetically-- or not necessarily genetically, there are other typing techniques. The typing techniques which go beyond the species level say, "Actually, they're all identical."

That is a very worrying situation and tends to suggest we've got some sort of source, some transmission infection going on. That's a very important concept, and I don't-- it's a hard one to get, which is why in a way I wrote much of that earlier part of the chapter on naming bacteria and what level of discrimination we use.

MR MACKINTOSH: My Lord, this might be a good point. I haven't got quite as far as I wanted to – I'm probably about 10 minutes behind – but I wonder if it's a good time to take a morning coffee break?

THE CHAIR: Professor, as I

indicated, we usually take a coffee break.

THE WITNESS: Yeah.

THE CHAIR: Can I ask you to be back for ten to twelve?

THE WITNESS: Yes, certainly.

THE CHAIR: Thank you.

THE WITNESS: No problem at all.

THE CHAIR: I hope you'll be provided with a cup of coffee.

THE WITNESS: Yes, that'd be good.

(Short break)

THE CHAIR: Mr Mackintosh.

MR MACKINTOSH: Thank you, my Lord. Professor, I wonder if we can just look back at the executive summary and use it as a hook to ask a couple of questions about normal levels of risk. So, it's page 6 of bundle 44, volume 1. Now, paragraph 3 seems entirely uncontroversial, that:

"Infection risk is multifactorial and varies depending on: the microorganisms ability to cause disease ... its natural habitat ... ability to spread ... susceptibility of the host to infection. If an increase in infection rates is observed, this is not necessarily attributable to the built environment given this complexity."

I don't think I'm aware of anyone who said otherwise.

A No.

THE CHAIR: Could I ask, just for----

A Yes, please.

THE CHAIR: -- my understanding, would you include dose, in the sense of the amount of bacteria to which the patient is exposed? Is that a concept you would accept?

A Yes, it can be, and even in relation to the environment. So, if there's a sink trap that has a very heavy growth of a particular organism, and you've got a very vulnerable patient, then the probability or poss-- probability of that patient being exposed to enough organisms to get into their line or get into their GI tract is higher, I would suggest, yeah.

THE CHAIR: All right, and I think part of my interest in that question is, does it follow that if you have an infection control mechanism which is aimed at dilution of potential bacterial concentration, that may have a beneficial effect?

A Yes, and that's the principle of trying, for instance, to disinfect drains or to reduce the load, bacterial load. More often, one of the more effective ways sometimes is to interrupt the route of transmission. That's a very important concept, yeah, to prevent those of patients meeting those organisms in a vulnerable way.

THE CHAIR: Thank you. I'm sorry, Mr Mackintosh.

MR MACKINTOSH: I wanted to look at the references to "normal" in the next two sentences, and try and explore whether they are-- what they mean. I have a suspicion that some people might conflate the two and that may be good; it may be bad. So, you say in 4:

"To assess if there is an increased risk of infection, a normal level of risk must be established."

Now, what do you mean by a "normal level of risk"?

A Well, this is really applying to the very vulnerable haematology oncology type of patient, where infection in every unit – whether it's in Birmingham or Barts; doesn't matter – will develop infections, and quite often sometimes those infections are caused by organisms which are environmental in their nature, and it's unavoidable because of the extremely vulnerable nature of the patient.

Q If we stay with environmentally nature-- organisms on your environmentally relevant list. When I say environmental, that's what I mean.

A Yes.

Q So if we stay with environmentally relevant organisms, am I right in thinking that would mean that, in any particular hospital unit that's dealing with these sort of patients, you would expect to have some infections in that group caused because of gut translocation, coming on the skin and those sorts of things.

A Mm, and----

Q Maybe on the environment as well.

A And in the environment, because I think it's pretty near impossible to-- Well, it is impossible to produce a haematology oncology ward that has no-- no organisms in it. It will have environmental organisms.

Q In a sense, what you mean is, although there's a-- Would you accept the idea that the ambition is to have no organisms----

A Yeah.

Q -- and no infections, but there will inevitably be some, and that is what you mean by the "normal level of risk"?

A Yes, yeah.

Q In this next sentence-- I've already asked you about the reference to whole genome sequencing, but there was, in the second sentence, a reference to "an increase beyond the normally expected numbers of infections due to a specific bacterium." Now, I take it that's a reference to the National Infection Prevention Control Manual and the data exceedance.

A Yes, and I'm more familiar with

the UK but also with-- as I'm an academic clinician, with the academic definitions of "outbreak", and I've-- you know, one's debated it over the years, so-- but it broadly falls in line with obviously what Health Protection Scotland regards as an outbreak, as we've just discussed previously.

Q Would you accept that for some bacteria in the paediatric haemato-oncology cohort there will be a bacterium where any infections is beyond the normally expected numbers?

A Oh, that's quite difficult.

Q Before you answer it, let me explain why I asked it.

A Yeah, okay.

Q So, we've had a lot of evidence from people who were involved in the clinical and infection prevention control and microbiology teams in this hospital in the Paediatric unit in '17, '18, '19, who describe when they saw a particular bacterium saying variations on the theme of, "I've never seen it before. I had to go and look it up. It's so rare. We've not had it here before." In that context, many of those people, particularly focusing on the microbiologists, have said, "We wouldn't expect to get any of these." So in that context, would you ever have bacterium for which the normally expected number is to for all intents and purposes zero?

A I think that's difficult because you can-- I mean, take the case of Cupriavidus. It's a very a cause of infection in neutropenics in comparison to the amount of Cupriavidus everyone meets.

Q Yes.

A Okay? So we see a Cupriavidus in a ward. Okay, we don't-- We can find Cupriavidus obviously in every tap and in all the water supply because it's one of those organisms which seems to survive and be distributed. Does it mean that patient acquired it from that ward because we've seen it in that ward? No----

Q Well, that wasn't the question I was asking.

A Okay, sorry.

Q It was just focusing on this specific detail point. I perhaps wouldn't have thought of Cupriavidus as the example, but are there any bacteria in this environmentally relevant group for whom any number of infections would be an increase beyond the normal?

A Yes. I mean, all of them in a sense, even more common ones. If you-- if in your unit, I don't know, you see, shall we say, 10 Stenotrophomonas a year, for argument's sake, and then you go through a period where suddenly you've now seen in a month-- you've seen five cases of Stenotrophomonas, that is

abnormal and therefore requires some degree of investigation.

Q An example that has been frequently referred to this Inquiry is Mycobacterium chelonae.

A Yes, I thought you might refer to that.

Q Yes, so we know of a case not actually in the paediatric haemato-oncology wards, in one of its patients in 2018 and another case in 2019 after the decant. We've actually found reference in blood samples to a 2016 case as well.

A Mm.

Q Now, you get the impression-- well, more than impression. The evidence of those involved in treating that case is that it meets this definition of something where any infections is beyond the normally expected numbers. Are you comfortable with people talking about it in that way?

A Yes, to a degree, because again it is an organism. If you look at its biology, it's immensely widely spread in the environment, rather like the Cupriavidus. It's a very different organism to Cupriavidus. It's so widely spread. It is in almost all wet sites. If you look, you'll find Mycobacterium chelonae. In medical terms, it's come to fame not in this context in compromised patients but a major problem in heart bypass machines because the intercooler that

was used used water, plain water, and was open to the atmosphere in the theatre, and people didn't realise. You've got heavy colonisation of the intercooler, which is open to the atmosphere, and you could generate an aerosol which then would contaminate surfaces and contaminate the patient's heart valve and they develop a terrible infection.

Q Right.

A That's where I see Mycobacterium chelonae more frequently, although now we've prevented that.

Q Now, there's another concept which has been talked about, the concept of a "normal level of infections", and I wonder if there's any concerns you have about using that phraseology, as opposed to a normal level of risk or normal infections for a specific organism, but a normal level of infections for the whole class of environmentally relevant.

A Again, it comes back: what do you regard as "norm"? Well, in some institutions, you may have a very low level, and they may be doing things in a particular way – because we're talking real world here – where they get their levels down to a much lower level than another organisation which may or may not be taking those same precautions. And the whole-- The point is, I think-- is that you've got to look at it as a whole

organisation. It's the way in which the team are operating, Infection Control, management of lines, the cleaning of things, the engineering, as we know, which obviously this Inquiry has spent a lot-- quite rightly a lot of time looking at. They're all different, so when we say a normal level, I'm slightly uneasy because what level are we going to accept? What is that level, and how heavy is it? How high is it, and also how does it relate to another similar unit?

THE CHAIR: Sorry, "How does it relate"----

A How does it relate to another similar unit? Have they got half the rate? Or maybe they've got double the rate and you're really doing rather well.

MR MACKINTOSH: To what extent is the question really, has there been a real change?

A I think that's very important. It's trends that we're looking at, and that's where our data in HAD did show, yes, at this particular period there was an increase, but there was also an increase in gram-positives, which I think was the one thing we brought in HAD. We've now dissected that more carefully----

Q We're going to come back to that in the afternoon.

A But that's where trend was very important to us----

Q Right.

A -- I think all of us, all three of us.

Q What I'd like to do is to deal with what I have called "antibiotic resistance" but what Dr Agrawal has encouraged me to call "antibiotic prescribing" as a topic.

A Yes.

THE CHAIR: Can I----

MR MACKINTOSH: Of course, my Lord.

THE CHAIR: -- with apologies? If this is too superficial, just tell me. What I've taken from your previous answers is, trying to deal with this concept of what is normal, you make the point that what is normal in one unit may be not normal in another unit.

A Mm.

THE CHAIR: Now, is it too superficial to say that, if not the best people to ask as to whether there has been a change, at least very important people to ask are the clinicians dealing with a specific cohort of patients in a specific unit?

A Yes, the clinicians are important, but also it's important that that organisation has a facility to collect and collate all of those serious infections, identify the organisms, and you-- and again you've seen evidence for it, things like exceedance limits. So, you know, maybe you only get one Pseudomonas

every month, and suddenly you've got five, so that really falls more into the remit of Infection Control particularly, who say, "Gosh, it looks like we've got a problem." But then it's obviously important to talk to clinicians when you try and understand why we've got this sudden occurrence because it can be random. It can be a random event, a stochastic event.

THE CHAIR: Thank you.

MR MACKINTOSH: So I want to talk about antibiotic prescribing.

A Mm.

Q Now, you deal with this in a number of different places in the report.

A Yes.

Q Actually, probably the best place to look, I think, might be Chapter 4, when you're discussing the CNR, and what we might do is talk a bit in general and see if we need to go anywhere else. So I wonder if we can go to page 45. Now, page 45 of volume 1 of bundle 44, it's part of Chapter 4.

A Right.

Q It's towards the end. In fact, if you take out the whole page here, please, zoom right out.

A Yeah.

Q That paragraph there, so the word in in Chapter 4 is "approach" at the bottom of the page----

A Okay, got that.

Q -- so you've got the context there. I want to zoom in on the second last paragraph, the one that starts at 2017 to '18.

A Okay, yes.

Q Now, I'm not going to ask you that question yet, but that's just where we're coming to.

A Okay.

Q So we can take that off the screen. You do seem to be asking the question of what role did antibiotic resistance play in these events.

A Mm.

Q What was the evidence that you had available to you about what was actually going on in terms of antibiotic prescribing and resistance in the Schiehallion unit in '15 to '22.

A When we were considering the HAD Report, writing HAD Report, very little in terms of that.

Q Right.

THE CHAIR: So did you have any information?

A I don't recollect.

MR MACKINTOSH: Did you have some policies?

A I can't remember off the top of my head.

Q The reason I asked that is because we asked the Health Board when we took you over to provide us with the material that they had given to you, and they explained that a workspace had

been created, which my team refers to as "the data dump", and it contains a lot of files.

A Yes, a lot of files.

Q Now, many of them contain CHI numbers, and a lot of them are of course Dr Agrawal's imaging reports, and therefore we haven't put them in bundles, but we put a list of them in volume 1 of the HAD Report on page 224. Don't worry, I'm not about to take you through it.

A Ah, right. I was just----

Q But I'm just saying that for the completion of anyone making notes. Now, the reason that-- within that list is a list of policies to do with antibiotic prescribing for adults and children.

A Mm.

Q Should we assume that you have those available to you when you wrote these parts of the report?

A Yes, I don't think I remember them being exceptionally different from ones I'm familiar with with other units.

Q If we go to page 45, which was on the screen before, of bundle 44, volume 1, you describe in the middle of a discussion about, I think, Stenotrophomonas----

A Yes.

Q "In 2017-18, there was a worldwide shortage of piperacillin"----

A Piperacillin.

Q "piperacillin/tazobactam".

A Correct.

Q Does that have a brand name?

A Tazocin.

Q Tazocin.

A Very heavily used antibiotic, particularly in neutropenic patients. It's a the first line treatment----

Q "… which resulted in many units switching to carbapenem antibiotics." Would one of the carbapenems be meropenem?

A That is the market leader. Most people would use Meropenem because it's cheap and off-patent.

Q Yes, and then you discuss, "Piperacillin-tazobactam was used in the unit for empirical therapy of neutropenic sepsis and was therefore sometimes substituted by Meropenem." I'm assuming that sentence would have its origin in the policies you'd read.

A Yes. Well----

Q Because you wouldn't have reviewed medical records or prescribing actual numbers?

A I can't remember. We did ascertain that there was some increase, but not a great increase, I think, in Meropenem use.

Q So what would've been your source of----

A Oh, I honestly can't----

Q It's just you don't mention it in

your report.

A No. I mean, I-- this whole concept came as my-- part of my own personal clinical practice in Birmingham where we had a large BMT unit, and we experienced this shortage, and we switched to using not exclusively Meropenem but a lot of Meropenem, and two or three, maybe a little longer, months into that situation, we began to see infection-- serious infections caused by Stenotrophomonas.

And Stenotrophomonas, amongst environmental bacteria, is a little unusual in that it is always resistant to Meropenem, and Meropenem is an antibiotic which kills an awful lot of different bacteria, including quite a lot of the environmentals, and we saw this increase. We couldn't-- You can never actually tie it down to, "Well, this patient had Meropenem. That one didn't," because they cross-colonise each other, etc. But we then took steps to remove or massively reduce our use of Meropenem. We used a different antibiotic, Temocillin, with another antibiotic, and we saw a decrease in the Stenotrophomonas infection. So, in a sense, that's my personal experience----

Q So that's your experience. I understand that. I wonder if we can look at the CNR rebuttal document, which is bundle 44, volume 2, volume 2. There we are, page 151.

A 151, okay.

Q Yes.

A Yes.

Q Now, do you see at the bottom of the page they, CNR panel, say:

"We had access to all versions of the policy guiding the use of antibiotics for febrile neutropenia [missing out the brackets] … in paediatric haematology oncology patients issued from August 2010 to March 2020 … There was no significant change across the four versions of the policy issued during this time. Each specified Tazocin [over the page] … and Gentamicin as first line antibiotic therapy for suspected infection, with the addition of Vancomycin or…"

Can you pronounce that for me?

A Sorry, tazobactam? Oh, sorry, where are we?

Q The second line.

A The second line. It's Vancomycin and Teicoplanin.

Q "…Teicoplanin if there was concern"----

A Yes, yes.

Q -- "about infection of the central venous line. Meropenem was to be substituted for Tazocin…if there was persistent fever at 72 hours."

Now, would you accept that there was no change in the policy in practical terms?

A No change in the policy but practically many hospitals-- most hospitals were unable to obtain piperacillin-tazobactam and therefore made up an ad hoc policy, usually, and we did in Birmingham.

Q I appreciate what you did in Birmingham but----

A Yeah.

Q -- do you know what they did in this hospital?

A Not in great detail.

Q Do you know that it's the evidence of Professor Gibson who headed the unit, that there was no shortage, they were not affected, they were fully protected?

A That's very pleasing to hear.

Q But you didn't know that?

A I didn't know that.

Q Right, can we take you----

A I didn't have a witness statement or a statement from Professor Gibson.

Q Well, just a moment before you say that.

A Yeah.

Q Professor Gibson gave evidence at this inquiry before your report was finished.

A Okay.

Q We've asked her again about it in response to your report.

A Mm.

Q What steps did you take to inquire of the people who instructed you, that is Greater Glasgow and Clyde Health Board, of what was actually done in this unit at the time?

A Well, we asked to see-- to ask, was there a change in usage and they came back and said there was-- didn't appear to be much of a change in usage of----

Q Right. So, there wasn't a change in policy and there wasn't a change in usage.

A Mm.

Q Can I show you a report prepared for the paediatric haemato-oncology consultants in August 2018?

A Right.

Q In the middle-- well, not in the middle. Towards the end-- just after decant. So, it's bundle 19, document 19, page 143. This is the document you hadn't seen before. But this was prepared by Dr Peters, who was then microbiologist for that team, and Ms Harvey-Wood, who's given evidence twice, a clinical scientist, and a pharmacist who hasn't given evidence.

Now, what I wanted to do was to look at the aim of this report. So, this was prepared at the time. Do you see the second bullet point, "To determine antibiotic resistance rates"?

A Yes, okay.

Q Right.

A Yeah.

Q If I can take you to page 161 and step out a little bit so we can see the whole chart. We've had a lot of evidence about this from its authors and from Professor Gibson. So, If I understand correctly, the vertical purple bars are the total environmental orgs by their definition.

A Okay, well, that's a very broad sweeping statement----

Q It is, but that's not the purpose of the chart.

A No, okay.

Q That, I think, is just to provide context.

A Okay.

Q But the actual chart contains-- do you see how it contains three single colour lines?

A Yeah.

Q One for each of three types of antibiotic and then, below that, dotted lines for the number of organisms who are resistant to these antibiotics. So, for example, if we look at Meropenem, just to put it into context, the line for the prescribing of Meropenem in 2015, February, just comes up below the 400 line on the----

A You mean 4 in terms of the number of blood cultures positive with a resistant organism----

Q No, but if you----

A -- if we're talking resistance? Are we talking resistance, the dotted line?

Q Well, I'm looking at-- I'm just making sure that you can read the chart.

A Oh, yes, I can. Just about----

Q So, the Meropenem prescribing comes to 400 DDDs antibiotics in February 2015. Do you see that?

A In 2015?

Q It's got the yellow line----

A Yeah, got it. Yes, yes. There we are. Yes.

Q If we look down below that, we see that the number of blood cultures – this is not a rate, this is a number – is 1 for the Meropenem resistant environmental gram-negatives at that point i.e. February '15. Do you see that there?

A Yeah, got it. Yes.

Q Then if we look at Tazocin, it has a blue line----

A Dotted.

Q -- and blue dots and----

A Yeah.

Q -- there are no infections in February '15. Then for-- I can never pronounce what Cipro will be.

A Ciprofloxacin.

Q Ciprofloxacin. Thank you, Professor. Ciprofloxacin has a rate of just over 200 DDs in February '15 and no

infections. Do you see that?

A When you say no-- you mean no resistance?

Q It's right along the bottom of the chart. You see----

A Okay, no resistance.

Q No resistance or-- Right, now, what I'm-- I'm not asking you to conduct an analysis of this now.

A No.

Q But it does appear that in October 2018, various people carried out this analysis and I will take you to the conclusions page which is on page 166, and they've reached certain conclusions.

A Yeah.

Q Then over the page, on 167, they reach summary results. The overall conclusions are 167. What I'm wondering here is what do we do as an inquiry?

A Mm.

Q We have your text in which----

A Yeah.

Q -- you have expressed your concerns based on your experience.

A Mm.

Q We have contemporaneous records of an investigation which appears to-- and we are told by its authors and by others, have excluded antibiotic resistance as a factor. In fact, If you go and look at page-- I missed out a chart to show you, page 162, a nice clear chart of Meropenem use divided by the number of gram-negative bacteremia. The peak----

A Ah, gosh.

Q -- if there is one, is in 2015 before they moved to the new hospital.

A That's an unusual way of presenting the data in----

Q No, I think that's a fair point. I think the author did say that, but the point I was just going to be putting to you is what do we do as an inquiry when faced with people at the time who say, "We looked into this, it wasn't an issue." Now, they might have been wrong, I get that----

A No, no, no.

Q -- (inaudible 12:21:26) and you who tell us we should look for things without any contemporary evidence. Who do we listen to?

A Well, I-- we-- I wasn't trying to prove-- I don't believe at any point we said, "This is why you saw an increase in Stenotrophomonas." In HAD, we said, "Actually, this might be a factor and needs looking at," basically. It's a possible explanation, and I take all your points and I think-- I don't think Meropenem usage can be accounted for as causing the Stenotrophomonas-- any rise, apparent rise, in Stenotrophomonas. There is another antibiotic on that chart, if we can go back to----

Q Yes, of course, page 161.

A Yes, which is interesting, and

that is the line for the usage of Ciprofloxacin.

Q Yes, it is.

A Yes, which is used, I think you'll have heard from Dr Agrawal, as a prophylactic agent.

Q Yes.

A The problem with a prophylactic agent, I think Agarwal touched on this, is that it can select for much more resistant organisms. The very reason why at Barts they don't use Ciprofloxacin prophylaxis, and what I see here is a marked increase, a huge increase in usage of Ciprofloxacin. So, I could put it to you that actually, maybe, excessive use of Ciprofloxacin is influencing what we're seeing here.

Q Well, yes----

A Not saying it's proven, but I think it's something to think about.

Q Well, indeed, I'd like your help in thinking about it. So, if we look at this chart and put it into context----

A Yeah.

Q -- do you see how the final entry from this October 2018 report appears to be February 2018?

A Yes, second-- or is those-- those are quarters, I think----

Q They might be quarters, you're right.

A The end of quarter, yeah.

Q So, I'm wrong. It's the end of June. End of June 2018.

A End of June.

Q Now, we are told, and I don't think there's any doubt about this, that the water incident begins in March 2018----

A Okay.

Q -- and that there is some anxiety in January, February and March, and you, of course, have now produced a HAD chart, which Dr Drumright described as having a peak in the first few months of 2018.

A Yeah.

Q I'm just wondering whether-- obviously, we can't tell what's happening on the righthand side of the chart any further because it doesn't go any further, but it would be quite difficult for Ciprofloxacin to be causing the growth, any such growth there was, in organisms prior to the peak of its use.

A No, because actually you've got to remember these patients are not just instantly-- you know, they're not short term-- Some of them go over relatively long periods.

Q No, I must have mis-asked the question because----

A No?

Q Either I've got the wrong question, or you've misunderstood me.

A I've probably misunderstood the question.

Q So, we are told by, amongst other people, you----

A Yeah.

Q -- that there is a growth in the environmentally relevant infections between the middle of ’16, which we can see where it is on the chart, and January/ February ’18 and Dr Drumright’s very keen for us to be a bit soft about that time----

A Yes.

Q -- and then it drops away.

A Yes.

Q Now, there is a peak of Ciprofloxacin in quarter 1 of 2018.

A There is indeed, yes.

Q How does that peak cause the growth infections beforehand?

A In the sense-- the only thing I can hypothesise, and it’s purely hypothesis----

Q I understand that.

A -- is that in taking the quinolone, you select more resistant organisms. Now, those resistant organisms may not cause----

THE CHAIR: Sorry, could you just repeat that----

A In taking the Ciprofloxacin, it’s an oral drug, and a number of the sort of gram-negatives we’re talking about in this context are very often resistant to Ciprofloxacin drugs.

THE CHAIR: Yes.

A Organisms like Stenotrophomonas but also Klebsiellas can develop resistance and Enterobacter. So, I’m just wondering, and would you-- you won’t see an immediate effect. So, I’m wondering actually why are they increasing the usage of Ciprofloxacin. That’s question number one. Is it for prophylaxis? It seems it most probably is. Have they got more patients? Have they got more sick patients? Are the patients sicker for longer? Are questions I would be asking, and then----

MR MACKINTOSH: Why didn’t you?

A Sorry?

Q Why didn’t you?

A I didn’t see this chart.

Q No, but you’re investigating. You raise antibiotic----

A Yeah.

Q -- resistance as a possibility and yet you don’t enquire as to what’s happened.

A Okay. It was a failing in that sense.

Q Because we now have to investigate it, so----

A No, no, no. Sure. Sure. Yeah.

Q So, the reason I was slightly snappy with Dr Agrawal when he raised this was----

A Right.

Q -- because he hadn't put it in the report----

A No.

Q -- and I've now got to work out how to investigate this.

A Sure.

Q I'm doing that months after people who were there have given evidence. So, that's why I'm wondering why you didn't investigate this-- the whole concept by saying, "I'm interested in this topic of antibiotic resistance. I know it's a problem. Why don't I find out what happened?"

A To a certain extent a limitation of time.

Q Right.

A Spent a lot of time on this. It limits what I can do.

Q I wonder if I can show you a document I'd just like to understand.

THE CHAIR: Well, unless it's staying on this point, before we-- I think there's maybe three things that interest me at the moment. First of all, I wasn't entirely sure if, Professor, you, and Mr Mackintosh were engaging simply on the point of time.

A Right.

THE CHAIR: Because I think what was being put to you was that if we assume that the chart is our best information on when things are happening, what I think was being put to you was that there was an increase in infections which were noticed and were a matter of concern by about March of 2018. Whereas, depends exactly on how you, maybe, read the chart, the peak for Ciprofloxacin use looks to be subsequent to that. Now, I just wondered if----

MR MACKINTOSH: Yes.

THE CHAIR: -- you and Mr-- That's my first concern.

A Yeah.

THE CHAIR: I just wondered if you and Mr Mackintosh were actually engaging on that.

MR MACKINTOSH: We're on the same page here.

A Okay.

Q So, let's recap. You are positing that we should consider whether Ciprofloxacin prescribing levels in the first quarter of 2018 might subsequently cause resistant organisms to prosper.

A Could be an association.

Q Right.

A It's an unusual finding to see that sudden peak.

Q Yes, and that would be something we would see in the nature of the organisms that were growing after that date.

A Yes, and in fact, you could test that fairly quickly if you've got-- well, you will have access to the sensitivity test, the antibiotic sensitivity testing data of these

organisms. Did they see more Ciprofloxacin-resistant organisms because resistance to Ciprofloxacin usually arises by a mutational process? So, your organism in your gut's sensitive, sensitive. You start taking Ciprofloxacin, and then at some undefined point during taking it, it develops resistance and now it's resistant, which is not a very typical mechanism of resistance development for other antibiotics.

Q Right. When it comes to Meropenem----

A Yeah.

Q -- am I thinking that your position is, well, you now see they've investigated it, and so in a sense, it's not an issue?

A It's not an issue, I don't think.

Q Right.

THE CHAIR: Right. I'll just mention the two points while we're at it.

A Oh, yes.

THE CHAIR: We may have heard evidence about this, but it would seem fairly uncontroversial that one possible explanation of an increased use of ciprofloxacin is a concern among clinicians about an apparent increase in infection which has got to be dealt with one way or another.

A Mm-hmm.

THE CHAIR: The other point is maybe a bit more fundamental. In the HAD Report, there are lots of pieces of information and I want to take the best----

A Of course.

THE CHAIR: -- or make the best use of it as I can. It's not always clear to me why the information is there, but if we take the example of what you say about antibiotic resistance, you raise the possibility of, specifically, the resistance as a result of the discriminating effect of meropenem, but you just leave the possibility, notwithstanding the fact that, as we've established, it would have been open to you and your colleagues to make inquiry of, for example, the pharmacy in the Queen Elizabeth, as to whether in fact what was a possibility was actually fact and, had you done so again, if I understand the evidence, you would have been able to eliminate that possibility, but in the HAD Report the possibility is left hanging.

A Yes.

THE CHAIR: Now, would you accept that----

A Yes.

THE CHAIR: -- as a criticism of the way this aspect at least of the HAD Report has been put together?

A Yes, this is valid criticism.

THE CHAIR: Right.

MR MACKINTOSH: I want to just – one topic, particularly – clear up something that I showed Dr Agrawal and

Dr Drumright, but they couldn't help me.

A Right.

Q If we go to bundle 44, volume 1, document 7, at page 248. Now, I'm going to first ask you whether you've seen this document before.

A Gosh, I've seen so many documents.

Q Maybe it would help you if I just step onto page 249, you'll see the graphical treatment----

A Let's have a look at that, yeah.

Q 249. So, there's lots of these. So, if we go back to 248, it seems to be-- top of that page, in fact. Just go to the top of that page. It seems to be report by someone called Sean MacBride-Stewart dated from January last year. It's in the folder we were given by the Central Legal Office on behalf of Greater Glasgow. It's accompanied by an email – which I'm not going to put on the screen – to somebody in the legal team, attaching it, and it has various pieces of information about use of antimicrobial agents. Now, I wondered if you'd seen this before you wrote your report?

A Not familiar with it, no.

Q Well, in that case I'll take it off the screen, okay.

A But it looks very useful.

Q Well, indeed, and it just turned up in the folder. We haven't used it yet. I want to turn to the topic of whole genome sequencing.

A Right.

Q Now, I'm going to have to remind you that, whilst I would like to think I'm a-- and I'm sure this is the case with your Lordship, we are intrigued and interested people who want to understand, I think I speak for myself and for his Lordship that we're not technically trained in the field of genetic microbiology.

A Sure.

Q Bearing that in mind, I'm going to put some things to you and I'm very keen if you'd tell me if I've got them wrong, but I would encourage you to do that in a way that keeps it short as you can----

A Yes.

Q -- at a level that we can understand. Now, we've had a lot of people give evidence that whole genome sequencing can prove a connection between two samples, either an environmental sample and a sterile sample from a patient to environmental samples, or to sterile samples, by analysing them and working out how closely related the organisms are and they measure it in something called SNPs. Have I got that right?

A Yes, single nucleotide polymorphisms, yeah.

Q So it's entirely uncontroversial

as far as we can see----

A Yes, that's----

Q -- that you can prove a connection.

A Absolutely, yeah.

Q Now, a witness, Professor Dancer, gave evidence last year.

A Oh yes, Stephanie Dancer, yes.

Q Stephanie Dancer gave evidence, and she almost set this up as a principle. She didn't quite phrase this way, but it comes across the way she talks about it as a principle, that when you are looking in the environment to find the source of a particular infection, when you find a whole genome sequencing match, you say, "I found the source, that's the end, I stop, but when I can't find the close connection I keep looking."

A Yes.

Q It seemed to be her position and a number of other witnesses' that therefore that one works on the basis that whole genome sequencing can't prove the absence of a link between a sample in patient A and patient B, and that seems to turn on the meaning of some words and that's what I wanted to ask you about. That wasn't the question, it was you see where I'm coming from?

A Absolutely, yes.

Q You've got it, right? So, if we play hypotheticals and we imagine we have a sink or a water cooler in a unit with a very vulnerable patients and two of them get the same microorganism, and you examine the samples, and they are genetically almost identical, you'd agree that is----

A That's a very important finding, yeah.

Q Yes, and if you went and found a sample from the water cooler----

A And it matched, that would be----

Q That'd be great.

A -- good.

Q If we extend that logic to a sink, the same would be true.

A Yes.

Q Right. Now, if we change the scenario slightly. It's still a sink, and there's a sample from the sink, and there's a sample from a patient, but they don't match. Would you say that that would enable you to exclude the sink as the source of the infection for that patient?

A No, you can't. You can't exclude it----

Q Right.

A -- at all on those-- just with those two data points.

Q Yes.

A What one might see is if you've got this increased incidence, shall we say, of organisms, of this one

particular species that you're typing and you see that you're-- There are two scenarios. You'll get lots of different types----

Q Of the same species?

A -- amongst-- yeah, the same species, in the bloodstream infection. So we've got, say, ten people get septicemia with Stenotrophomonas and they're all different. So we could say, "Aha, yes, that's probably not due to the environment." Well, difficult because it may be some of those patients have acquired it from the environment and we haven't found the in the environment, but what you do tend to see in outbreak reports in----

THE CHAIR: Sorry, my fault entirely, because I'm keen to follow the----

A No, please interrupt me because I'm using words I'm familiar with and I'm aware your Lordship may not have met them.

THE CHAIR: Sorry. We're thinking of a hypothesis. Six or seven patients have acquired an infection with Stenotrophomonas.

A Yeah.

THE CHAIR: One does carry out a----

A Genome sequencing.

THE CHAIR: A typing analysis and finds a number of strains.

A Yeah.

THE CHAIR: Now, I think you then said that excludes the environment or excludes the environment in certain of these strains. Now, I don't follow that step.

A Well, the reason being, if one then goes on to look at situations where we do have-- people have identified a source, an environmental source, you not infrequently in many of those accounts see that there is-- although you get different types, a type keeps on popping up, the same type. Do you see what I mean? Because when we go into the environment, we will find at least one or two different types, maybe more, subtypes of Stenotrophomonas for argument's sake, okay? And they're not-- you've not seen them in the patient.

If you like, the patients are sort of sampling the environment, but the problem is you can't be an absolute proof one way or the other. So the hypothesis being put, I think, by some people is that, "Well, okay, we look at all these bloodstream infections, they're all unrelated, so that's-- you know, that means we've just not found the holy grail of the type we found in the patient's blood in a sink because we didn't look hard enough."

MR MACKINTOSH: Yes.

A And there are elements of that

I would agree with because the investigation of the whole genome sequencing and the sampling was somewhat erratic I think it would be fair to say, and I think other people, including the CNR, and I would agree with the CNR, it was not ideal.

They didn't always know which sample it came-- what site it came from, whether they were all, but I did note in my interpretation of what I could understand from the reports on the WGS, is it seemed that a lot, maybe not every, certainly not every, a lot of the bloodstream isolates, just for Klebsiella, Cupriavidus, but the numbers are very small, but also Enterobacter, did-- they did do typing on a lot of the clinical isolates that may or may not have been absolutely in the period we're interested in and they were all different. Doesn't prove they didn't get it from the environment.

Some of those probably did get it from the environment, but what we-- not what we see typically in many other outbreaks, including one that Mr Mackintosh has seen the paper of, the Nurjadi paper.

Q I'm going to come to those in a moment.

A If you're going to come to them that's fine. Where they did eventually see and identify a definite source for this one type.

Q So just-- because I'm trying to----

THE CHAIR: I wonder if I can take advantage and just----

A Please.

THE CHAIR: -- understanding, as it were, the nature of the challenge. Now, question one. Is there any theoretical limit in the number of strains of, let's say, Stenotrophomonas that one might find in a hospital in Scotland?

A In practical terms, if you look at the literature you don't tend to find-- you won't find sort of 30 different strains in one sink. I think that's highly improbable. What most people find-- and again there's a piece of work done in Oxford which the CNR group refer to, which is a very nice piece of work where they intensively looked at the traps in three different wards over a time period, and not only whole genome sequence-- the whole genome sequence, every one of their E. coli and Klebsiella they get out there, and interestingly they found that different-- certain traps and certain sinks in certain wards had a long-term resident.

THE CHAIR: Right. Maybe I didn't put my question very well. First of all, as a matter of total principle, is there any limit on-- Because I understand bacteria are a relatively simple organism compared with other organisms----

A Well, yes, absolutely.

THE CHAIR: -- but that doesn't mean they're not highly complex.

A No, no, yeah.

THE CHAIR: But is there any limit in principle on the capacity of a particular bacterial species to differentiate into strains?

A Oh yes, very much so, and that's where we see evolutionary trees and in fact Stenotrophomonas is an example of a bacterial type which is very diverse. It produces a lot of different clades and they've diverged in their evolution a long while ago. So, there's other types of bacteria we see sometimes which are really very, very narrow in their evolutionary route, particularly in relation to sort of human infection and some types of E. coli would fit with that.

So, because it's an organism which is widespread in the environment, not necessarily the hospital environment, when you look at traps and situations there, you will find quite a lot of different types and the whole genome sequencing did find that for Stenotrophomonas. It doesn't mean some of those can't be a source, and it's my opinion that some of those trap Stenotrophomonas did get into patients in all probability.

THE CHAIR: Right. I'll try this again.

A Yeah.

THE CHAIR: We've been introduced to the notion of looking for a needle in a haystack. I'm just trying to see if I understand the size of the haystack.

A Yes.

THE CHAIR: I'm just trying to see if I understand the size of the haystack. Thus far, as I've understood you, some species will have many variants, types.

A Types, subtypes, yeah, yeah.

THE CHAIR: Types, yes, well, have many. Some species will have less, but are we talking about tens, hundreds, thousands?

A Well, the thing about whole genome sequencing is-- so we can distinguish these, if you like, families that have evolved, rather than that-- But within those families, when you get down to what Mr Mackintosh was talking about, SNPs, we can then get very, very detailed about a collection of strains living within that little family, and if we find they're only five to ten SNPs different, then we know genetically they-- they must have come from a common source. They must be very, very recently.

THE CHAIR: Yes, I think I've understood that. Right. The other very basic point is that, am I right in understanding that if you're taking your samples from the environment, the bacterial population of a particular

location may be different, may be very different, from a location which is in close proximity to that?

A Yes, that's quite possible and particularly applies to sink traps. I mean, this is almost a hierarchy here. We've been talking about biofilm on taps and ingressive contamination and retrograde-- retrograde contamination. That's-- That's, in a sense-- I won't say simpler, but it's not such a help-- a nice environment for the bacteria to proliferate and produce biofilm because it's a very small area, that interface between air and the tap-- water tap body.

A sink trap is a lovely place because you've got-- always got-- it's always wet and you've got nutrients there and, what's more, it gets complicated because various types of bacteria are being flushed down the sink. So, when people wash their hands or put things they shouldn't put down the sink, such as some human sample, you know, urine-- I'm not saying people do that regularly, but it's a much more open environment so you do see quite a-- quite a big population, and studies show that.

THE CHAIR: All right, and it seems to follow from that that where you carry out your sample is of importance.

A It is, and the other thing to consider is that there's lots of these bacteria around, but they can sit there

and not be a problem if you don't have a route of transmission back into the patient, and that's the key point. And that-- and then the Chartley Stone – we'll come back to anyway – they interrupted-- they didn't clean up all their traps at all. In fact, they went back to an even more inferior method of disinfecting their traps. What they did is they interrupted the route of transmission; end of outbreak with their Stenotrophomonas.

THE CHAIR: Thank you. I suspect I've really just interrupted without----

MR MACKINTOSH: No, I'm grateful, my Lord. I'm going to move away from principles.

A Right.

Q Well, before I do that, I'll just take one concept. Am I missing-- Should I actually be using the word "homogeneous" in these sentences? So, when I put to you that the absence of a virtually identical bacteria between two sterile samples and two separate patients proves they don't come from a homogeneous source, is that, in a sense----

A Hang on, I just need to go through that. So you're talking sterile samples.

Q Two sterile samples, same bacteria.

A Blood samples, right.

Q Blood samples.

A Two different types of organisms.

Q No, the same bacteria species.

A Oh, the same species and type, WGS type?

Q Well, we'll come onto that first, just same species first.

A Okay, species.

Q You do analysis; they're within tens of SNPs. You can then say they come from the same source.

A It's very suggestive.

Q Very suggestive of that.

A Yes.

Q They're not within tens of SNPs; they're a long way apart.

A Yeah.

Q I've seen articles, and you've quoted things, and I'm wondering-- and it's not exactly your words. I don't want to put them straight to you, but could it be that, in the absence of a close relationship between the two samples, what you can actually say is that they don't come from a homogeneous source.

A They don't come from what-- we would use the term "common source".

Q So the common source is a particular bacteria, single bacteria.

A Well, no, no, the common source is, shall we say, as you were saying-- In this context, it's a-- a disinfect-- no, a disinfectant solution, shall we say, that's become contaminated on a ward, got lots of Stenotrophomonas in it, but if they're different types then it's unlikely they're coming from that single common source.

Q Right, so I'm getting the impression, and I want you to stop me if I've got this wrong, that in this discussion of single common sources what we're thinking about is something that at some point has been quite small. It might have been spread across the hospital in a cleaning solution but it started off little because it's a little community of bacteria.

A True, true, yes.

Q So what I would like to explore with you before the lunch break is-- I don't see it as worth pressing you about the example that you can go and look at a study that has examined a single sink or a couple of sinks or a water filter, and you can see that the organisms aren't closely related and you can say, "Probably not that water filter." That doesn't seem controversial.

A No, I think that's right. Yep, yep.

Q Right, okay. But absent the aseptic pharmacy of 2016, the hypothesis that has been put to us that we're, in a sense, investigating is that it's not one water filter. It's not one sink. It is a lot of locations throughout the hospital which are reaching patients through multiple sources; taps, showers, drinking water,

and so forth.

A Well, these types of organisms-- you talk the “whole hospital”, meaning in general medical and surgical wards, you won’t be picking these up because----

Q No, but it doesn’t mean they’re not there.

A Oh, they’re there. They’re in my own hospital. All of my hospital sinks have got them in. It’s the location. It’s, if you like, the haematology oncology--

Q No, no, I understand the location point about-- It’s about the whole genome sequencing. So the thought is this – and this is why I’d like you to explain to me, in a sense, why this proposition is not correct – that if you have a community of vulnerable patients in a hospital, they might meet the water system in a number of different ways. They’ll meet it through taps, through showers, through drinking water, through things that have been cleaned with water from the taps and showers, from spray from taps and sinks. They might meet the drains from spray from the drains if they’re badly designed.

A Yes, absolutely.

Q Right. They might meet all these things in their own room, in their own ward, operating theatre, imaging location, or anywhere in the hospital they end up being. Do you accept that’s all possibility?

A Oh, absolutely.

Q Therefore, if you have a handful of Stenotrophamonas patients who have the Stenotrophamonas species found in their blood, but of widely different genetic connection – they’re not closely relatives – what is to stop you thinking, “Well, they didn’t come from the same small sample - the disinfectant, the one sink, the cold water sample - but given they’re in different rooms, they might actually come from multiple different locations.”

So one could have got it from the tap in their room, one could have got it from the shower in their room, one could have got it from another tap down in X-ray, the fourth could have got it from home, the fifth could have got it from the fact they’ve been previously colonised. Actually, because it’s possible that each individual patient can have a completely different route to get the infection, whole genome sequencing does not exclude that.

A No, it doesn’t exclude it. It also-- In practical terms, we know, going from studies and the literature, that one of the most common ways in which people acquire these organisms isn’t necessarily from the environment itself or directly from the environment, but from another patient who is colonised.

Q Indeed.

A And most units in the UK don't generally do extensive colonisation studies on these vulnerable patients.

Q Right, I want to pick out one topic about-- in general terms, it's about something you say on page 121 of volume 44 (sic), volume 1. It's the reference to the-- 121, reference to a "reasonable sample". Now, I'm just going to make sure I've got the right page, because it would be a terrible shame to put the wrong page to you.

A Yes, I can see it there, yes.

Q You can see it there. It's the second paragraph at the bottom: "However, a reasonable sample has been sequenced"-- Now, I recognise we're going to have a conversation after lunch about Professor Evans' individual pieces of work and Professor Leanord's work and what you draw from those, but it occurred to me that I should press you on this idea of a reasonable sample.

A Yes, and this comes back to a little bit of what I said a little bit earlier, that it is my understanding-- I may have got the understanding wrong, as far as I could tell, and I'm aware that the documentation of source of isolates-- and I haven't seen a list of isolates, isolate names and how that relates to when they were isolated, and there seems to be a little bit of haziness as to whether these samples were there. So the ones I felt were-- perhaps in terms of the environmental location, and also the-- there was intensive sampling, then there was very little sampling, then there was sampling from tanks in the roof, but what did get typed seemed to me to be a reasonable number of the positive blood cultures with those two organisms we talked about.

Q So, how do you know it's a reasonable number?

A Because the CNR very helpfully charts, by each year, how many isolates they had-- they perceived in their bacteremia isolates of all of the different organisms and then in turn, we-- I think this is something that Dr Drumright did. She did look back at those totals as presented in the CNR charts and her understanding of how many cases of BSI there were on 2017 on the relevant wards.

Q Because we have some evidence from Professor Wilcox.

A Right.

Q So if we think about the Stenotrophomonas that were whole genome sequenced, and we go to actually look at Professor Evans's paper, so that's bundle 8, document 46, starts at page 239.

A Not there.

Q 239. Yes. Now, this is

obviously the beginning of the paper. I wonder if we can just step over to page 242, and do you see in the paragraph 3.2, there we are, at the last sentence of 3.2:

"Over this time period, there were 23 isolates of clinical relevance isolated from blood cultures."

A We're talking Steno-- Stenotrophomonas----

Q Yes, so this is the Steno paper.

A Yeah, okay.

Q The problem is that Professor Wilcox has explained to us-- Now, he seems to have had this from Professor Leonord, that of those 23, only 15 are from within the CNR cohort.

A Okay, so I did look at this and I couldn't understand where he got to the statement. I just couldn't see it so I know----

Q I think, slightly reading between the lines, he can do this for two reasons. One because he tells me he's been told that by Professor Leonord, albeit he told that after Professor Leonord gave evidence, so that is a slight snag. But the second problem is that he has access to the individual patient medical records.

A Of course, yes.

Q So he can connect the samples in the SNP charts that Evans and Leonord has to his records. Now, we can't do that.

A And I can't do it, no.

Q Exactly. So, what I'm worried about is, I know that I need to be nervous about using anytime someone like Professor Wilcox says, "We looked at it and we concluded X, but I can't show you my working because of the confidentiality rules around the CNR."

A And I found that difficult as well.

Q Yes, indeed. So, I know to be nervous at that point, but sadly, doesn't it also mean that you're at a bit of a disadvantage? Because whilst you've got the Evans/Leonord's work, you don't have the context, and so I'm worried that when you make statements like, "There's a reasonable sample taken", how do you know that?

But because I read the Leonord-- I may have misinterpreted it, but I read that report in the way as-- I did read it and those-- What one-- I mean-- Okay, so Professor Wilcox can now say 23 in his opinion, and I'm entirely happy to take that, were relevant to this time period and were from blood cultures. My next question would be what's the denominator? So, in the period he's talking about, how many, if you like, didn't get WGS? I don't know. I haven't-- just can't do the calculation quickly but-- I

need something to look at.

I see that look at, but the difficulty is-- and this goes back to a comment that you make in the response document, where-- I think probably I ought to find it. I think before lunch it might be worth trying to just do this. In fact, no, my Lord, I think I'll do it straight afterwards, so I'll just remind you so you can look yourself. I have a recollection, and I will pull up the reference, of you commenting on something Professor Wilcox says, and suggesting that-- You talk about burden of proof.

A Yes.

Q So I will go and find that.

A Okay.

Q You might want to look in the response document yourself.

A Right, I----

Q -- and we'll speak about it at two o'clock.

A I will need access, and I don't have my computer with me, and I don't have a copy.

Q No, we'll get you a copy, we'll get you a copy.

A If you can get me a copy, I'd be very happy to look at it, yeah.

THE CHAIR: Well, we'll take our lunch break now, and we'll try and sit again at two o'clock.

MR MACKINTOSH: Thank you.

A Thank you.

(<u>Adjourned for a short time</u>)

THE CHAIR: Good afternoon, Professor.

THE WITNESS: Afternoon, my Lordship.

THE CHAIR: Mr Mackintosh.

MR MACKINTOSH: Thank you, my Lord. Now, Professor, I wanted just to jump back to Ciprofloxacin. We found the IMT minute----

A Oh, right.

Q -- which I'm not going to put to you but I'm just going to tell we found it, from 16 March 2018, bundle 1, document 17, page 66, which contains an entry on page 68, "It was agreed that as a precaution [page 68] all patients when the affected wards will be given Ciprofloxacin prophylaxis as a precautionary measure."

A Ah.

Q Do you see that, the fourth paragraph? So, we know that happened.

A Good.

Q Thank you, and what we'll do is we'll take that off the screen. Now, the reason that I-- I wanted to look at a document that you wrote, the HAD----

A Yes.

Q -- response document, particularly to-- which is bundle 44, volume 5, document 2 at page 28, at paragraph ID.2. You'd gone off and read

Professor Wilcox's statement.

A Yeah.

Q I think this is in the context, if we look back to the previous page, to your discussion of whole genome sequencing and Stenotrophomonas and Enterobacter.

A Yeah.

Q So if we move back to page 28, you say:

"In his witness statement, Professor Wilcox states in paragraph 44: 'There could be 20 different Stenotrophomonas species in the water, of which only three ever get into patients, so it is complex. Because of the incompleteness of all those levels then it is not surprising, sadly"--

The "levels" I think in this context might well be the charts.

A Yeah.

Q

"… then it is not surprising, sadly, that we were unable to produce case examples that match the definition of definite.' [You've then responded] The implication is that there will always be so many different strains of Stenotrophomonas in the putative environmental source that it is most unlikely ever to get a match. This position cannot be refuted but it relies on a negative assumption."

Now, before we go and look at the rest of the paragraph, what do you mean by a "negative assumption"?

A The negative assumption is that, because these environments with the Stenotrophomonas, if there are indeed 20-plus strains there, that you will never-- not never, but you're very, very unlikely to ever get any form of match, so therefore WGS can't give you any information about the possibility that there is or isn't an environmental source.

Q Other than a definite case.

A Other than a definite case, and we all accept the definite case is unlikely, a very definite case. But what we do see in many reports in this setting, and I give a specific example below----

Q Yes.

A -- is that actually, if you have a discrete source and it keeps on pumping out the Stenotrophomonas, and as I've described earlier, once these biofilms are established and the organism is in there in the biofilm, they don't tend to swap many types. I'd slightly disagree with Professor Wilcox's assertion there'll be 20 different types there.

Q No, I understand that a bit. I'm going to go to that paper----

A But if that happens, what happens periodically some-- you know, on two occasions – it may be separated by six months – people will have the same clone, the same subtype, of

Stenotrophomonas in their blood or causing an infection, and----

Q Because they got it from the same source.

A Exactly, and by WGSing all of the bloodstream isolates, if we-- And it's not an absolute here, I hasten to say. It's not an absolute. If we never see matching-- any matching samples at all, my opinion, my feeling here is that it makes the role of the environment a little less strong than one might think otherwise. I can't say more than that, but it's unusual, and as I say, I've given a number of examples where----

Q I'd like to go to some of the examples.

A Yeah.

Q Before that, we're lawyers, which is our strength and our weakness.

A Indeed.

Q So when we see a sentence like, "This position cannot be refuted but it relies on a negative assumption", we immediately think of the concept of burden of proof.

A Absolutely, yes, I understand that.

Q Not so much the weight of it – I don't want to ask you about that – but the direction it lies in.

A Mm-hmm.

Q So if it's true that that statement by Professor Wilcox relies on an assumption that there are many different strains in the hospital, why is there any greater problem in accepting that as a possibility than accepting that there's likely to only be one strain in the hospital-- or in the source rather.

A I'm a bit lost there. Could you sort of rephrase that slightly?

Q So in a sense you're positing, as you just described, that if you've got a water source, experience suggests there will be one strain. I mean it's not quite as simple as that, but----

A One or two.

Q One or two.

A Yeah.

Q If I understand Professor Wilcox correctly, he is positing that that in this hospital there might be 20 different strains. You seem to feel that his proposition relies on a negative assumption and, therefore, it's got some issue with burden of proof, or am I putting words in your mouth?

A Perhaps I'm using-- Perhaps my use of "negative assumption" is perhaps not totally correct, certainly not probably correct in a legal sense.

Q Yes.

A It's this assumption that you've got so many there, you're-- you can never really chase one down. Well, I know from my knowledge of the biology of the organism and studied and published on

Stenotrophomonas, something as Professor Wilcox hasn't done, that actually you see relatively narrow numbers of subtypes in these environmental sites, okay?

Q Right, and so these are the papers you want us to look at?

A Yes, yes.

Q Well, why don't we look at Guyot----

THE CHAIR: Could I just check with you? When you use the word "environmental site", you mean?

A In the hospital.

THE CHAIR: Yes, but----

A Drain, tap, that sort of thing.

MR MACKINTOSH: One drain, one tap, one----

A Yes, or-- Yeah.

THE CHAIR: That sounds quite a discreet location.

A Yes.

THE CHAIR: I mean, it's just to understand the phrases you're using.

A Some of the detailed studies have shown that you may get the same strain coming up in maybe four or five sinks in a----

THE CHAIR: Okay.

A And in one extreme case, which is the Nurjadi case, the whole of a big Haematology-Oncology unit actually wound up with one dominant clone of Stenotrophomonas beginning to emerge and take over and be present in a number of showers. In fact, it was the shower drain that was the problem. So yeah, I see elements of what-- As I say, it can't be refuted and I accept what Professor Wilcox is saying there. I'm just saying that you can't just totally dismiss the WGS data that shows that none of them are the same as each other.

MR MACKINTOSH: Well, let's look at Guyot, so it's in bundle 44, volume 2, document 38 at page 617. It's published in the Journal of Hospital Infection. Now, what I was going to ask you to do is, bearing in mind how much time we have and how I want to get to a number of different articles, can you explain how that paper supports the conclusion that hospital outbreaks or clusters of infection frequently involve a limited number of strains when a water source is identified?

A Well, it doesn't always. In this particular case it did.

Q Right.

A And it's not a universal truth at all.

Q Right.

A I think if we perhaps roll on a bit, there's----

Q Will we perhaps look at the "Investigations on source" on page 618?

A Yes. Where have we gone----

Q If we could zoom in the top half of the page, please.

A There is some-- I haven't read this paper recently-- very recently. There is some typing data. So, under "Results"----

Q Oh, go down. Here we are. It's on the top of page 619, at----

A Probably, yes.

Q -- Figure 2.

A Okay. So, this shows the instance of these outbreak strains being occurred, okay? Now, they also-- from memory, they also found a number of other-- a few other strains as well, both causing infection and in the environment.

Q Right.

A But, as you see here, this single strain keeps on popping up in patients.

Q This is the one, FR04, that's in blue?

A Yes, that's right. Which then encouraged them to go and look even more carefully at the environment – I think they had had a preliminary look – and to discover, despite sampling (inaudible 14:12:53) spaces, they found one water cooler, which had a very heavy biofilm growth of Stenotrophomonas in it that was leading to----

And the other important thing is, for this case, it was a water cooler. So, the water wasn't processed in any other way. There was no filtration, and therefore the route of transmission immediately becomes apparent. Patients drinking it, becoming colonised and, also, I think sometimes the water, from memory, was used in one or two semi-clinical settings as well.

Q So, if we just stay with-- Sorry, you explained and I'm not proposing to challenge this, that the conclusion in this paper is that what happened in this location is that FR04 became the dominant strain and the source that was affecting the patients was this water cooler.

A Yeah.

Q Now, I appreciate that's an example.

A Yes.

Q But how does that help us try to understand this particular scenario we're dealing with----

A Yes.

Q -- where it's not just one water cooler?

A No, no.

Q Well, I mean, it's debatable how big it is, but it's bigger than that.

A Yeah.

Q So, are you saying that it's not quite true to say-- well, it's the "frequently" I think is the problem. Go back to page 28 of bundle 44, volume 5.

A Yeah.

Q Third paragraph:

"Hospital outbreaks/clusters of

infection frequently involve a limited number of strains…"

Is it not perfectly possible to be the case that they could frequently do so, but there'd also be times when there wasn't a limited number of strains?

A It's certainly possible, yes.

Q The reason I keep, I suppose, pushing on burden of proof is that the Inquiry has set itself the task of trying to understand whether there is a link between these infections and the environment. It seems now certain that we'll not be able to show a direct link by whole genome sequencing.

A As indeed the CNR people quite correctly said.

Q Yes. It does seem to be the case that if we apply Bradford Hill's concepts for epidemiology, a number of those headings would lean in the direction of there being a link to some of the cases. But equally, we have this whole genome sequencing source of evidence. What are you actually saying that papers like this do to the balance of proof?

A What I think it does is there's a question of degree, and I don't-- I know we don't want to go back over the CNR or anything but there was a-- they stressed a very large number of episodes were related to the environment. I mean, don't go into the methodology stuff because you've done all that.

My feeling was, and a feeling in discussing it particularly with Dr Agrawal, who has experience managing outbreaks in HaemOnc units very similarly, was this seemed to be something of an overestimate.

I mean, we're-- we're not-- we at no point had disputed that there wasn't an environmental source causing infections, and our subsequent analysis, as we've said with Dr Drumright in our review of data goes, there was undoubtedly an increase in gram-negative organisms. Interestingly, there was also an increase in grant-positives, and that's the counterfactuals argument which I'm sure we can go on to discuss.

But we put-- at least, in discussion, we thought, well, this is only an opinion, and it's only a guesstimate, if you like, that perhaps somewhere nearer, 20 per cent rather than 31 per cent would be a more reasonable figure. But I'm nervous about this very high figure, particularly as I don't know how this was arrived at because I don't know the methodology.

Q Well, I think you know the methodology. You don't know the data.

A No, the data, if you like. Yeah. Yeah-- or no, it's the way in which that data was interpreted.

Q So, for better or worse, it's their evidence they carried out----

A Yeah.

Q -- 118 standalone root cause analyses. It's a slight exaggeration. I'm sure Professor Stevens will correct me tomorrow. But we can't see----

A No.

Q -- the tableau timeline. We can't see the medical records. We can't see their conclusions. Now----

A It's also a methodology that, as far as I can understand, has never, ever been used before----

Q I understand all that but----

A -- and I do have misgivings about how easy it is from retrospective examination of clinical notes to say, "Okay, this person got it from the environment," and just because----

Q Well, they don't say that, do they?

A No, they say, also, the impression I get is, the longer the patient was on the ward, the greater the exposure to environment. Well, yes, that's true but they use that-- seem to perhaps have used that as a surrogate-- a way of assessing what the risk was and therefore defining your cases, and I just----

Q But----

A -- feel very uncomfortable with that.

Q I wondered if there was actually as much a difference and much of a gap between you and the whole genome sequencing because I had some notes of questions that I might run out of time to ask you around----

A Okay.

Q -- your clustering methodology, but within them was this. As you've noticed, the CNR reached the conclusion that 30 per cent of cases----

A Yeah.

Q -- that they looked at were more likely than not to have a connection to the environment, and I noticed, and I'm not going to go through every single line of your report but, at a number of times in your report, you make statements-- for example, if we go to, obviously, one example, because it's Stenotrophomonas and we seem to be talking about it a lot, if you go to volume 1, page 53.

A Right.

Q If we go to the whole page, please. You have a statement that:

"…not all clusters of S. maltophilia infections in immunocompromised patients are necessarily spread from an environmental source."

That is at the top----

A Yeah.

Q -- of the page, and the CNR, for better of worse, and without us being able to double-check their work, have 66 per cent. Now, I agree that you-- I understand that you might say, "Feels a

bit high"----

A Yeah.

Q -- but are the two statements actually inconsistent?

A No, they're not inconsistent. We're into the realm of expert opinion, I'm afraid here.

Q We are, and what I'm wondering is, would you accept this as a sort of shorthand that as we go through Chapter 5 of your report, but also to a lesser extent Chapter 4, you often will refer to a number of articles, papers around a particular microorganism and say, quite clearly, well, frankly, "You don't generally find," or ,"It's not always the case," or, "The majority of the time, it isn't"----

A Yeah.

Q -- "an environmental source," and then you'll move on to the next one.

A Yeah.

Q If one goes to the CNR's conclusions, with one exception, they don't say it's all the environment. They have a sort of a large minority. So, I'm wondering what the value of this argument, if it's an argument----

A Yeah.

Q -- between the CNR team and yourselves is, given they can't show you their results in detail and, actually, in many ways, you're slightly at cross-purposes because you're both saying----

A Yeah.

Q -- "It definitely won't be all"-- One's saying, "It's a bit likely to be the environment." The other's saying, "It's definitely not always the environment," and those two don't seem to be inconsistent.

A No, no, they're not. They're not.

Q Let's go back to one of the papers that you wanted to look at. Well, I asked you a series of questions and you have prompted by wanting to look at-- I'm going to pronounce it wrong, so you're going to correct me, Nurjadi.

A Ah, Nurjadi, yes.

Q Now, this is bundle 44, volume 5, document 16, page 222. Yes. Now, before we look at this paper, can you explain why you think this is relevant to this debate?

A In many ways, it's very similar to the situation that was faced in Glasgow.

Q Right.

A These are haematology-oncology patients. It's a large German, I think, unit, from memory. Yes, German unit, with three wards, from memory, that were-- that they considered very carefully, handling very immunocompromised patients with a variety of environmental and non-environmental type infections. But they

notice, and there's a marker here, they notice this particular Stenotrophomonas that has-- sorry, Enterobacter. This is an Enterobacter, this one. Enterobacter that has a slightly unusual resistance pattern, and this crops up from time to time in patients. So, though they haven't done any detailed sequencing or typing, it's a little bit unusual. So, it prompts them then to start investigating their ward.

Q Yes.

A They start looking, understandably, at all sorts of things, surfaces, but also at drains and traps, etc., and they find that actually they've got a lot of this (inaudible 14:23:00). Some people are carrying, and this is something that I don't think was done in Glasgow, and it isn't done as a routine, but they look to see if these patients were carrying the Enterobacter, and quite a lot of people were asymptomatically carrying it. Very important because, of course, these patients could go on to develop a bloodstream infection. But then as they focused down, they began to discover it in traps, particularly the drain traps in showers.

Q Yes.

A Okay, and went, "Ah-ha, what we need to do is eliminate the organisms from the trap." So, they tried various chemical treatments and, you can see, they've got rather like you have in your documentation, you've got a timeline with interventions on it and they weren't very successful, and they're-- these sporadic infections with this one type because now they've done the whole genome sequencing, and they realise whilst they got quite a lot of Stenotrophomonas-- a reasonable number of different types in different locations in the ward, this one-- this resistance strain was found in quite a lot of different drains in different wards as well by the time the thing progressed.

So, they then asked the question, "Well, what on earth is going on here?" They show a photograph, in fact, and it was a simple plumbing design fault. Because if you look at the photograph, you'll see the drain is a large drain like that, which is open with mesh in it, or, you know, grill on it, and the shower head is immediately above the drain. They suddenly realised what was going on.

The water was pouring down going straight into the drain and splashing up, so splashing the organism out. Now, not everybody got infected. Not everybody got colonised but they then thought, "How do we interrupt that?" So, they put a false floor, fiberglass floor, into each shower unit.

Q Do we see that on page 229?

A There we are. You can see they-- the new shifted shower drain. So, they moved the drain----

Q So, on the lefthand side, they have the shower drain in the middle----

A Yeah.

Q -- and then by the righthand side, they have effectively repositioned it by inserting a floor.

A Yes. Completely terminated the outbreak. They could still isolate the same strain from the drain, but it didn't matter because they no longer had a route of transmission.

Q So, what does that tell us? I mean, it's a good example of investigatory infection control, but what does it tell us that helps us in our situation of understanding whether in Enterobacter, for example----

A Yeah.

Q -- the whole genome sequencing that we do have available, which is six environmental samples----

A Yeah. You have more-- you have more clinical samples, I think.

Q No, but for the whole genome sequencing world, we end up with 6.

A From environment, I thought WGS was taken out-- it was carried out in----

Q Well, what we'll do is we'll double-check the numbers in a moment, but----

A Okay, yeah.

Q -- just to ask the question, how does this paper help us understand the Enterobacter samples that we do have in this case and their value to the analysis exercise? How does this paper help?

A It-- I-- well, I think the way it helps, perhaps, is to be slightly more circumspect in ascribing all of the-- well, not all but a very large proportion of the Enterobacter or, in the case, Stenotrophomonas, 66 per cent of infections to the environment.

We've never denied that there is environmental transmission going on. It's a question of the degree and the occurrence of it, which is why we went back to look at rates of bacteremia, to try and understand. We identified-- and, in fact, we did identify in HAD that there was a peak. There was also a peak in gram-positives, and it was a subsequent analysis and modelling, which enhanced and refined that increase.

Q Okay.

A So, it's not telling you absolutely, "No, the environment is important," or "No, the environment is not"; what I think it's helping us understand is that we might have expected to see a signal in all the WGS typing where there were some isolates which were indistinguishable, and we saw none.

Q Well, let's go and look----

A Other than obviously the Cupriavidus and the-- yeah.

Q We'll come back to this paper, but let's go to bundle 8, document 45, page 230 which is Professor Evans's analysis of Enterobacter, and go to page 233.

A Right.

Q Now, it may be I haven't understood this, and I'd be grateful if you can assist me. So, 3.1 describes the species isolated in patients in the hospital environment. How many Enterobacter samples were subject to whole genome sequencing as a result of this exercise? You might find it on page 234 at 3.2.

A Yes, that's the environment. The environment wasn't looked at in any detail at all, and very difficult to assume anything for the environment. I'm thinking of the patient samples.

Q I understand that, but if we just go back to the paper we were looking at, and we'll go back to the front page of it, so that's Nurjadi – sorry – at 222. We see in the abstract there were 133 clinical and environmental isolates produced.

Now, I'm just wondering whether the fact that in this paper-- and if we look further on, we can see on page 224 the number of isolates recorded in the chart in the top right-hand corner.

A Yeah, that's right.

Q At one point in 2019, there are 40, nearly.

A yes.

Q So I'm just wondering the extent to which there is a difficulty with using the example from this German hospital and applying anything to the Queen Elizabeth, because in this hospital they had the benefit of large number of isolates to review but in the Queen Elizabeth we don't. So, is the German case anything other than an anecdote of what we might find as opposed to a statement of what we should rely on?

A I don't think so because we're looking at patient isolates here.

Q We are, are we? Okay.

A Not looking at the environment.

Q So how many environmental isolates were considered in the----

A I can't remember but it took them a while to get down and would be buried probably in results, I guess. I can't remember offhand. Back a page, I'm guessing.

Q So the bottom of page 223?

A Maybe. So, they identified they were getting this clone appearing. They had a lack of epidemiological overlap, despite the close relationship. (Inaudible 14:31:00) problems, really start to look in great detail at sinks and plumbing systems, and they found quite extensive contamination at that point, which had been signalled by the finding of the same type cropping up in these

bloodstream infections.

Q Well, perhaps you could find it in the top of page 226 in figure 3.

A Right, here we go.

Q So this is----

A Yes, environmental contamination, yeah, yeah.

Q So what I'm trying to understand, because I really feel I should understand this, is that if it's the case that in Glasgow there were, due to chance, only six samples, but in the German hospital there were a lot more than that, in the environmental side is there not a risk that reading across the scenario from the German hospital to the Queen Elizabeth-- it might just be that the German hospital is different?

A Well, that's always a risk in any hospital, but again, from the Enterobacter whole genome environmental sequencing in Glasgow, I don't think you can tell anything because the numbers are too small. And not only that, what you can tell is they're certainly all different because three of them are different-- different species, and then the other three are three different species, but then it doesn't help you. I'm saying here I'm looking at the patient positives----

Q Right, I see.

A -- which might be, if you like, a canary in the mind-- mine saying, "Actually, gosh, look, we've got more than one the same," but you don't see more than one the same. They're all different.

Q Yes.

A It doesn't exclude the possibility that they're coming from the environment, but it makes one less certain. It makes you, as you say, nervous about it.

Q Well, it might be helpful at this point to just step back and look at Cupriavidus from Evans. So it's bundle 8, document 44, page 223. Now, this is a timing issue, which I'm keen to understand, and again you'll have to correct me if I misunderstand something. So next page, please, and we'll move over the whole of this discussion, onto the following page, and the samples are described here. Now, my reading of this paper is that 127 environmental samples were subjected to whole genome sequencing out of 485 samples.

A Yep. It's quite a lot.

Q Is that something that rings a bell with you?

A Sorry?

Q Is that something that rings a bell with you?

A Yes, yes. I can't carry all of the figures for all of the bacteria but----

Q No, I realise that, but what I put to you is that----

A yeah, they say they've

analysed 133.

Q Right. If you go onto the next page, do you see in 3.5 it does some dates?

A Yeah.

Q What I'm suggesting is that-- What do we do with the information from this page that there really is nothing very much before March 2018 in terms of human or environmental samples? We're dealing with ones or nones. So, if we have a suggestion that there's an increase in rate of infections of environmental organisms in the run up to January 2018, and the whole genome sequencing that we do have is largely after that event, can whole genome sequencing look back in time and imagine what was in place the year before or two years before? Does it do that?

A Not really.

Q Not really?

A No, no, and Cupriavidus, there obviously was a clearly great interest in it because all these isolates were made. As a player, in terms of a pathogen, I would say it's really a very small beer(?),when you look at the Klebsiellas and the Pseudomonas and the Stenotrophomonas. Not dismissing it because I think, as we said earlier, there was a link between certainly one sample but-- And it is a very, very, very common

organism in all water, but is a very-- is really a very rare cause of infection in haematological patients, unlike Pseudomonas and Klebsiella.

THE CHAIR: Sorry, you said "a rare source of infection among" and then I just----

A Haemotology-oncology patients, yes, your Lordship. It's-- And interestingly it's only one-- there are three or four species identified and only one species seems to be ever involved in human infections. That's (inaudible 14:35:45) I cannot say it properly, but it's-- that's the one that was found in the-- in the-- all patients.

MR MACKINTOSH: Again, I suppose because of time, I'm quite keen to see if I can understand your position correctly. We've obviously dealt with the scenario where whole genome sequencing can prove a connection and that's controversial and your position is that the various studies that you've referenced and your experience over many, many years in this field, have found many examples of studies that suggest that there's a homogeneity in populations of microorganisms in the environment. Is that effectively what you're saying?

A Homogeneity? No, the-- When you----

Q Well, use the right word. Don't

let me put that word in your mouth.

A No, no, not homogeneity. What these studies show, that where you have got an environmental source or maybe one or other sources, environmental sources, you often see the same strain or subtype appear across time.

Q Would you accept that some of those studies on which you're relying are inevitably for smaller scenarios?

A Oh, yes.

Q You'd accept that.

A Yeah, and sometimes different patient groups as well to a degree.

Q I know you did a literature review. You're not the only person who's done one, but did you ever find the paper that dealt with a study at the scale of what's being suggested in the HPS summary from 2018?

A That meaning very regular environmental monitoring and sequencing all-- all isolates, I take it to mean?

Q Well, no, because there wasn't any of that going on.

A No, no.

Q So, it seems uncontroversial that after a point in 2018/2019, there was lots of environmental monitoring going on.

A Yeah.

Q We've had a witness last week who's very keen to point out it's the highest levels of environmental sampling anywhere in the UK, and that doesn't seem uncontroversial.

A No.

Q But that's afterwards.

A Yes.

Q I'm wondering if you've come across in the literature any papers, other than the one I think that was published by some of our witnesses a few years ago, of anyone investigating something of similar potential scale. I'm not saying definite scale because it's a matter of debate, but potential scale. A whole hospital, a water system that's not necessarily well managed and someone's investigating that through whole genome sequencing, as far as you know?

A There are-- Not looking at every tank in every aspect. There's a very good Oxford study which looks at traps, okay? Sink traps.

Q Is this Halstead?

A Sorry?

Q Is this Halstead?

A No, this is-- Halstead is the study I initiated and ran. No, it's Constantinides.

Q All right. Well, let's go and look at that.

A It's not-- it's one I mentioned to you but it's not actually in the document bundles I don't think.

Q No, but it's in our documents, bundle 44, volume 2, document 37 and it will be much easier if I remember what page it was one.

A Yes, because it was cited by Professor Wilcox, that's right, of course.

Q Yes, it's page 604.

A Yeah.

Q This is a----

A Very elegant study done across three wards, I think. Okay. They sampled on a rolling basis every three weeks all of the traps in these three wards, I think a three-month period. They whole genome sequenced all the-- Interestingly they found a lot of E. coli there but didn't be associated with much in the way of infections, and Klebsiella. They also did something called metagenomics, which is where you go into-- you take the trap sample and you ask the question not "What can we grow from bacteria?" but, "What is the nature of all the DNA in that sample?" And from that you can then deduce what bacteria are there without ever growing. A very sophisticated technology.

Q And this big study, obviously it has its conclusions.

A It did.

Q How does it help us?

A It helps you to a degree because what they found-- and in fact, as Wilcox was quite rightly saying, "Gosh, look, you get a lot of diversity of organisms in sink traps," and it elegantly showed that and they said in their conclusion, "Yes, we're getting organisms in here which are potential human pathogens."

Interestingly, they also whole genome sequenced all of the infected-- all of the clinical isolates in parallel. So it's, if you like, the perfect study in many ways and asks the question, "Well, okay, we've got all these Klebsiella and E. coli in the environment. They must be the ones, particularly the Klebsiellas, that are turning up in our patients." And the disappointing answer was no, actually.

Q So does the paper reach any conclusion about where they come from?

A It reaches a conclusion that just because you find-- and I'm slightly, sort of, not distorting-- I'm sort of slightly interpreting their conclusion. Just because you find a lot of potential pathogens in the environment doesn't necessarily mean they're going to be the source, and there's a need for even bigger studies and more detailed study and an understanding. And they actually allude, I think I'm right in saying, saying you need to understand the routes of transmission, portals of entry, and I think that's very pertinent to your inquiry because, yes, you've got these environmental sources.

What went on, what we were talking about-- I think Dr Drumright Wright very-- termed “counterfactuals” and these are important. It’s not just the source, the patient. It’s actually how they get there and what circumstances., and they’re dynamic, they’re changing all the time.

Q What I’m proposing to do is to move on from whole genome sequencing to that topic that Dr Drumright raised of counterfactuals.

A Yes.

Q Though I think we’ve already considered them as confounders in a different context.

A (Inaudible).

Q What I propose to do is to take you to the HAD response document, volume 5-- 44, volume 5, page 50, and we can briefly look at this and then look at the next chart on the next page. I’m staying in the paediatric BSIs, Professor-- --

A Sure, sure.

Q -- because-- Do you feel you want to look at the small aspect of the HAD Report that had a single spike in 2018 in the adult haematology? It’s not on here.

A No, I don’t-- I think, you know, your----

Q I mean, I discussed this with Doctor Agarwal.

A No, absolutely. Your main

focus is on this paediatric area.

Q Right, okay. So if we look at this chart, which is 2.F.3, now, you heard Dr Drumright’s evidence-- if you zoom up a little bit please. Scroll upwards slightly.

Now, Dr Drumright’s evidence was that there is - and she’s very keen to be careful with the dates - some form of a peak in 2017/2018, then a reduction and a low point in 2016, and she was unclear, to be fair to her, whether the dip in the linear smooth line, which she prefers that starts in early ’14, was either an artifact of the GAM model hunting the zeros in 2016 or a real dip point, change point, in early ’14. She was unclear about that, and I wasn’t proposing to ask you questions about GAM models.

A I’m glad because I don’t-- I understand the principle, but I couldn’t talk on them in detail.

Q What I want to do is I want to just accept-- I want to put that on the screen----

A Yeah.

Q -- do the same thing for the next one, and then ask you some questions. So, over the next page we have a non-environmental group, 2.F.4, and the way she described this as a peak in early ’17, perhaps a bit unclear about when the turn is there, it never goes-- It comes in from the mean, as it were, from the average. “Mean” is not the right

word. She'd be cross with me. It comes in from the linear trend indeed, and it raises off a turning point somewhere in '13 and then rises and drops away to below the trend.

A Yes.

Q Now, we'll look at this one first. What information did you have when you wrote your first report about the CLABSI line safety work done by the paediatric teams in '16 and '17 in the Schiehallion unit in order to reduce non-environmental or, as they called it, gram-positive infections?

A I wasn't particularly aware of that. I mean, it was something-- I suppose this peak that we found-- and the idea to look at the non-environmental bacteria came very late in the production of the report and the analysis. We were working against time, quite tight time scheduling, because it took a long while to get the data. When the data was got, it took Dr Drumright a while to analyse it, and then towards the very end of trying to look at this data and everything else, we were looking just at the gram negatives. We sat around and we thought, "Well, hang on, what's happened to the gram positives, whether there's been any change? Do we see any other similar signals there?" Because we know they, and everybody accepts, are not directly related at all to the environment.

Q No, indeed, in both reports.

A Sorry?

Q In the HAD Report, if we can go back to volume 1, page 116, I think.

A Yeah. You saw a peak. Yeah.

Q So in volume 1, page 115, please. No, 117. Sorry, 117. There we are. That's the non-environmental peak chart as you presented it in Figure 1. There's no peak, according to you, at this point.

A No. Okay. Yeah.

Q That's what you say in the paper.

A But there was a-- yeah. Yeah.

Q So, if we go back to volume 5, now you see a peak.

A Indeed. This has come out due to the further analysis.

Q To what extent would you say that that peak that you see in the non-environmental BSI in 2.F.4 is consistent with what you've now learnt about the concerns and then efforts made by the hospital team to address CLABSI issues?

A Well, we've discussed it amongst ourselves but also I've looked at and thought about it. I think it's a very-- it is a very plausible potential cause for that rise.

THE CHAIR: Sorry, you do or you do not?

A I do, yes. Yeah. Yeah, we're all of one mind, the three of us, in that

because we discussed it at some length.

MR MACKINTOSH: In terms of timing, did you have the opportunity to look at the reports done by Ms Rogers and Dr Kennedy into the CLABSI work in September 2019, which showed their charts over a period of time?

A I didn't look at the charts. I know Dr Drumright looked-- read that report and looked at it----

Q But if you haven't looked at it, I won't----

A -- but I haven't looked at it myself directly. I was relying on her interpretation and distillation of what it said.

Q Let's go back to the environmental ones on the previous page.

A Yes.

Q Now-- So, page 50 please. What I thought might be-- 50. Yes. What I thought might be helpful was to attempt to ask you the same questions I asked Dr Drumright.

A Yeah.

Q Now, I'm going to use a word, "some", by which I mean a non-trivial amount, not necessarily a majority.

A Indeed.

Q Now, I appreciate that you-- What do you know about the temporal change, if there is one, in the water system at the Queen Elizabeth between its completion in early 2015 and, say, 2022? What's your state of knowledge about interventions, changes, that sort of thing?

A Certainly I think it was '17/'18 when there were-- concerns were raised. There already was a lot of testing, but also things like point-of-use filters were fitted to taps.

Q When do you think the point-of-use filters were fitted?

A I'd have to refer in detail to it, but was it around about '17, about '18. I can't remember. '17/'18.

Q Can I put to you what seems to be the evidence so far so that I can just check that you-- because remember I showed you the meeting of the Water Technical Group from April 2018?

A Yeah, yeah.

Q In that minute you would also find a reference to the fitting of point-of-use filters that month, so it's March/April '18.

A Okay. That's right, yeah.

Q And the hospital opens to paediatric patients in June of '15.

A Yeah.

Q And the water system is filled at some point in '13.

A Yeah.

Q And handover takes place in January '15 . Now, using the concept of "some" here, to what extent is what we

see here consistent with some of this peak-- of some of these infections, actually is a better way of putting it, being caused by patients being exposed to the water in the water system?

A I think it is-- it is consistent, yes. It certainly is consistent. Yeah, and this isn't an unusual finding in some units, as you've seen from the literature.

Q If we look at some of the counterfactuals Dr Drumright discussed, we pass over ventilation and move to-- we've dealt with lines.

A Yeah.

Q She raised the question of single rooms causing problems with infections. Is that something you've come across?

A Yes, indeed. Single rooms put a-- place a great strain on nursing staff, obviously. They are value-- useful from an infection-- conventional infection control point of view because they restrict the movement of people in and out, and contact with the patient, but they can lead to nurses having to dash around from one room to another and they can't easily see what's going on, sometimes, in another room, so it is certainly a pressure.

Q Do you see any issue with-- I mean, I talked to the idea of plausibility with Dr Drumright. To what extent would you agree or disagree with her idea that-- which developed, I think, over her evidence. Initially she categorised line safety, single rooms and nursing numbers as separate counterfactuals, but I got the impression to some extent she saw them eventually becoming, really, one counterfactual, and I wonder where you might stand on that sort of debate.

A Well, certainly nursing pressure and nursing time is important for patient care and care of lines. Care of lines is a very important aspect and this is where it may-- you know, the organism can-- can ultimately be derived from the environment but not in a direct way from-- directly from water.

Q She gave an example someone might wash something under the water and then use it.

A That's a very direct form, but an indirect form would be another patient, unrelated patient, who is exposed to the source, becomes colonised. A lot of these gram negatives, particularly Klebsiella, when you become colonised as a patient you have, if you like, sort of an aura of Klebsiella around you, and this was shown in the 1970s by a very-- and is the basis for us using alcoholic hand rub, actually, nowadays, and so your skin becomes colonised. This is true of haemo-onc patients, as well, and paediatric patients, and therefore people touching your skin, if they don't operate adequate hand hygiene, will touch

somebody else's another patient's skin, and that patient then becomes colonised with the Klebsiella, okay?

And because we put our hands in our mouth, and children, you could argue, put their fingers in their mouth perhaps more than maybe we do as adults, you then get gut colonisation and, bingo, they've got a bloodstream infection. Same strain, came through a silent third party, a colonised patient. It may have come from that sink over there, went through the third party's gut colonisation onto a surface or a nursing care, and if you're under pressure, from a nursing point of view, maybe your hand hygiene isn't always as good as it should be. Maybe when you come to check-- sort out somebody's line you haven't necessarily fully washed your hands. You haven't used the alcohol hand rub or your no-touch technique is not so good because you're hurried, so I can absolutely see how that could drive infection.

Q So, am I right in thinking, from what you just said, that these single room nursing issues not only can drive non-environmental infections of the sort we've seen on page 51, but to some extent could also drive environmental infections?

A Yeah, yeah.

Q If we think about another counterfactual which is to do with team dynamics, now, I'm assuming that you've not made a big inquiry into the team dynamics of the Queen Elizabeth Hospital.

A No, I know very, very little about it.

Q No. So, I'm just going to put something to you, which is that if there is an issue of internal team dynamics, it is not restricted to one team. There seems to be-- there have been evidence, that we have to decide the value of it, of problems in the Infection Control team in states management relations between those teams and other teams; Microbiology, Higher Management.

A Yeah.

Q I want to come back to the idea of a normal level of infections here. If we look at this chart and we look below the blue line.

A Yeah.

Q Is that, sort of, for this hospital, or hospitals because there's two here, the normal or am I getting my problems mixed up?

A I think maybe we're trying to simplify it a little too-- What the blue line does demonstrate is a line of continuous, relatively slow improvement, and that's generally what we often see in this setting as we get better at managing infections, we get better at our infection control, and

that's--

Q What I'm trying to ask is that, to what extent do these charts-- can these charts be interpreted as showing something is unusual, because it's above the mean, but is-- not quite normal but relatively unsurprising because it is below that?

A Well, yes, because I feel this analysis does-- and this has been very helpful and has changed our view, certainly my view, of the sort of situation, because it demonstrates this clear peak in around about 2018 or so, and there's something going on there. And it doesn't just infect the environmental organisms but it affects other organisms as well, so that's why, when we discuss this amongst ourselves and-- we we were very quite excited by it, actually, because it puts a different perspective which you can't get from the situa-- the reports we'd seen. So that's-- we felt we'd found something interesting and novel, dare I say it.

Q Right. Before we come back to the novelness of it, I wonder if we can go back to the original HAD Report, volume 1-- bundle 44, volume 1, section 7.10----

A Right.

Q -- which is your conclusion section on the epidemiology. So, it's page 118. Now, there's a series of bullet points and we'll look at the ones on the

next page, and so it's the second bullet point I wanted to ask you about:

"Among paediatric haemato-oncology patients, we see an ... 2fold decrease in incidence and cases of bacteraemia attributed to environmentally relevant microorganisms following transfer of services from Yorkhill to QEUH; lower incidence at QEUH was statistically significant."

Now, you're using the same data set for Figure 22, which is on the previous page, as you're using in Figure 2.F.3 in the HAD response document we just looked at. So how is it you didn't find the peak when you looked at it when you wrote the original report?

A That really is a question for Dr Drumright. I'm not the statistician who produced it. I mean, there's-- if you eyeball that blue line, there appears to be a bit of a peak there. Just-- you know, just barring statistics, there is a bit of a peak there, but when it was analysed by her, it was found to be not significant.

Q Moving away from complex statistics, do you find anything of interest, which I think has been observed by a number of people, that on that chart, at Yorkhill most of the time there are often zero months?

A Yeah.

Q At the new hospital in blue, there were some zero months at the

beginning and there are zero months after late 2020, but there are no zero months for the intervening not quite four years.

A Mm.

Q Is that something unusual or not, or I'm just imagining that here?

A No, no, no. It looks as though there is a bit of a signal there, and I suppose for the benefit of retrospectively looking at this chart, you can see that the regression line-- I think it's a regression line (inaudible) some type of regression line, actually starts at a projected higher rate than the original Yorkhill line, so it's a step in it----

Q Yes, I mean, I----

A -- which I take to be due to that tendency to higher values in that period of '17, '18.

Q Now, in your----

A In missed that, if you like, statistically. I didn't think, "Oh gosh, we need to challenge the stats." I relied on obviously Dr Drumright.

Q You mentioned a moment ago that you felt that the conclusion in the HAD Report about the peak in 2018 was novel.

A Was what, sorry?

Q Was novel, was new.

A Well, novel in the of the way it's been analysed and there's the use of these models to actually clearly demonstrate.

Q Had anybody else found it before you did?

A I don't-- I'm not aware of it.

Q Because you----

A Not to the degree of statistical rigor that it was found by Dr Drumright.

Q Because we looked at the HPS October 2019 review in the context of the microbial organisms.

A Mm-hmm, yeah.

Q That's bundle 7, document 6, page 250, I'm hoping is the right page. Excellent. You said you read this focusing on the microbiology.

A Yes.

Q I just wondered if we-- I wondered if you looked at a particular figure which is on-- if we actually go to page 214 because this is the redacted version. We don't want to look at this one. If we go to page 230, Figure 6. Now, did you look at these SPC charts when you were doing the original work?

A Yes, I remember looking at them. I mean, in a sense, there's-- they've-- you've got a period of exceedance also in 2014, '15. Then it dropped down and then it came up and was----

Q Well, the----

A If you eyeball it, it looks pretty constant----

Q We're told by the author----

A The blue line. We're looking at the blue line, aren't we, in the bundle?

Q Yes. We're told by the author that exceedance is above the yellow line.

A Mm, above.

Q So there's only one exceedance, which is '18.

A Yeah, yeah, sorry.

Q I'm just wondering if you looked at this chart, which is environmental including enteric group, and the next one, which is gram-positive at the bottom half of the page, we've had various epidemiologists and microbiologists say that there is a similarity in trends or shape between these charts, your charts, those of Dr Kennedy, even Mr Mookerjee. I'm wondering whether the signal was actually there to be seen when you wrote your original report.

A Well, there's no test of statistical significance, as far as I'm aware. Is that right? These are just pure plots of data right with exceedance now. Am I right in presuming that?

Q Other than the then it's an SPC chart with a----

A Oh, yeah.

Q -- warning limit, no there isn't.

A Yeah, no, so very dangerous to make assumption on that without proper statistical analysis, which is why we needed Dr Drumright's skills to analyse the data.

Q Okay, right. I think what I might do, my Lord, is I might do a little bit of clustering and then ask to take my 10-minute break a little earlier because I've slightly cut a few corners. The way, Professor, it works here is that I ask the questions, but this room full of lawyers who are out of shot from the point of view of the YouTube video, they propose questions, amongst other things.

A All right.

Q I'm proposing to take you through a couple of chapters of evidence but stop a little bit earlier than we normally do in case there's anything that's significant that I've missed because I felt we've covered what we need to cover, but others may have different views.

A Indeed.

Q So what I want to do is turn to the HAD Report, section 7.2.2, which is page 67 of bundle 44, volume 1. This is your clustering analysis.

A Yes.

Q Now, the first question is a little bit cruel, but it may short-circuit matters. I got the impression that Dr Drumright had rather resiled from this in the response document and she'd moved towards a statistical methodology----

A Yes, yes.

Q -- looking at (inaudible).

A I mean, in throwing these ideas and evolving the ideas of how to look at data and perhaps try and see what's going on, cluster analysis is one tool.

Q Yes.

A And she was able to say, "Well, I can have a go." I do have a vague recollection that we-- she was not keen-- well, not "not keen". There are caveats around it, and I'm aware of those, and I think we did it more-- well, my feeling was I did it to be exhaustive and just see if there was anything to find in that-- by using that approach, but weren't looking to be an absolute answer---

Q Is there any difficulty in doing a clustering analysis with the limited information that you had available to you?

A Yes, there was.

Q Because I hope I'm not being overly simplistic, but one gets the impression that notwithstanding its weakness that we can't see its conclusions in detail, the one thing you can say about the CNR is they had a lot of information.

A Mm.

Q You didn't have a lot of information.

A Yes.

Q Does that put you at a bit of a disadvantage against them in terms of the merits of the two exercises?

A Well, we were never against them, and actually one of the things I think-- coming back to me, one of the things that prompted us to have a go at a bit of cluster analysis was because they specifically drew attention to a cluster of Stenotrophomonas clustering, and I think it was a Klebsiella occurrence. And one of them – I can't remember if it was Stenotrophomonas or Klebsiella – they applied a very simple statistical test and said, "Ah-ha, looks like that might be significant." So, in a sense, that drove us forward to just at least explore that.

Q Right, because what I'm wondering here is that your clustering thresholds here, which are time and space driven, there was more information available to you had you chosen to ask for it presumably, from the Health Board.

A I guess so, but again there that's very much driven by Dr Drumright, this section on cluster analysis, because she knew what data she wanted or to apply whatever testing she wants to apply.

Q Because one of the observations that Professor Stevens made last year when he gave evidence, he was talking about the concerns that the Health Board corporately had with the case notes review.

A Okay.

Q Did you have access to those concerns?

A I don't recollect them, no.

Q In that context he observed that the Health Board could've carried out their own case notes review.

A Yeah.

Q Now, I'm not going to ask you about whether the Health Board should have done that because you're not responsible for the Health Board.

A No.

Q But I am asking you, given that you-- I mean, if we look at the introduction, so if we go to page 17, you say in terms at the end of this introduction that you "do not consider that the CNR is of assistance". I wonder whether you gave any thoughts to effectively attempting or proposing to attempt something as sophisticated or at least data heavy as a clustering exercise a bit more like the CNR, where you could get more information.

So, one of the things that the CNR had was something called a tableau timeline, where had someone plot for them all the interventions in the patient's life, where they'd been, what drugs they had, and they put that into a graphical form so they can move around in time and understand how patients related to each other. We've not seen it, but it sounds terribly complex.

A It does, and I would say, does it reflect the real risks, in a sense, of your-- the exposure to a particular shower or closures of this or that, and when you don't actually know which ones are likely to be the contributing source? That's the worry with that approach----

Q Well, I understand that, and so I wonder what your reason is for not attempting something more like that than what you did in the clustering exercise by getting more information?

A I think we were a little constrained by the time and resource available really.

Q Right, I understand. Now, I want to go to something that the case notes review authors have said because it occurred to me, whilst it may contain a truism, it might be interesting.

A Mm.

Q So bundle 44, volume 2, document 15, page 127. Now, this is the end of one of their sections.

A Okay.

Q But if we look at the big paragraph at the end, the second sentence, it said, "Basic infection control analysis clearly showed clustering of some types of infections in time and place." I think that's-- where you haven't seen the infection control minutes and things, we have.

A No.

Q

"The occurrence of repeated, unrelated infections with the same microorganism is very unlikely [this is in the context of cluster analysis]. What is the chance that clusters, occurring in time, of children managed in the same wards all developed BSIs caused by bacteria of the same species that had no common source(s)? It is implausible that, on repeated occasions, patients who developed a BSI were the source of BSIs in other patients. It is more likely that there were common sources of the bacteria involved that either colonised (and then infected) or directly infected the children."

Now, I suspect that somewhere down that paragraph you stop agreeing with them, but I'm quite intrigued to see which bits of it you're willing to-- or even the whole paragraph. Where do you fall out with them? It's quite interesting to see what the points are.

A In a sense, I suppose, one of the caveats is they talk about the same organism.

Q Yes.

A I want to go back into WGS because we know all about that, but in the case of Enterobacter cloacae, because of the type of identification system, they said, "Oh, we've got a cluster of Enterobacter cloacae here."

No, because you could subdivide that into four or five different species, so it then becomes implausible that that's a cluster of the same organism. That's that approach, and it's----

Q Unless there's a drain with all the species in it.

A Well, yes, but that, again I think it's possible, but it becomes-- but why-- okay, so you've got-- all the Enterobacter come out this this week, shall we say?

Q Yes.

A And then you then suggest that in two or three weeks' time when there are an exceedance of Stenotrophomonas, they will come out from the drains. I don't know. It becomes a bit of a stretch in my mind.

Q I mean, what about the idea that there is a water system which for better or worse is being managed in the way that has caused the people who manage it or assessing it to feel its high risk in temperature and these sort of things?

A Okay.

Q If that's all happening at the same time across the water system and if the peak of infections is at the same time, i.e., early '18, what's the chance that an appreciable sum of the infections that are found in '17 and '18, early '18, in that unit have occurred through this sort of

mechanism of, “They’re all happening at once; therefore, there must be a connection”? Is that a logical tool we should----

A I don’t like the, “Oh, well, they’re all happening once; therefore, it must be connected” because that’s a connection of-- you’re trying to pursue a definite causation there. I accept and I agree with you that some may well have been derived from an environmental source, and I suppose in a sense the-- not the proof, but if we go on to all the interventions that were taken and then we look at later rates, my understanding is those are lower than they were at that point.

Q So after the intervention?

A After the intervention, if we’re looking ’21, ’22, that sort of year, the right hand side of Dr Drumright’s graph----

Q What does that tell us?

A Sorry?

Q What does that tell us?

A Well, it tells us that this occurrence occurred and it’s gone away.

Q But does that tell us anything about the cause of the----

A No, it doesn’t tell us the causation necessarily, no.

Q Does it tell us about association?

A It tells us an association, but as you rightly say, it could be some of these counterfactuals. It could be that improvements in line care led to a marked improvement. We know that environmental organisms can, not infrequently, be involved in line infections.

Q I think I probably want to wrap this section up by asking for your help.

A Okay.

Q So, we’ve heard about Bradford Hill. Are you familiar with this work?

A A bit. I’m not. I wouldn’t say I-- it’s one-- as a molecular biologist and infection specialist, it’s not one of my top priorities of----

Q I suppose the alternative is you obviously consider the management of infections as an Infection Control doctor as well?

A Yes. Oh, yes. Yeah. Yeah, absolutely.

Q If the Inquiry is faced with answering a question about the extent to which anything that we find that is deficient about the water system may or may not have had an effect on patient safety, in the absence of some really quite impressive whole genome sequencing of the level found in our Oxford study----

A Yes, yeah.

Q -- in the absence of that, but in the presence of some epidemiology data from various people, including

yourselves, in the presence of a lot of contemporary analysis, opinion, memory about that from people who were involved, what do we do? Do we just hold up our hands up and say, "Well, we can't reach an answer. I'm terribly sorry. It was all a waste of time"----

A No, no.

Q -- or do we try and reach a conclusion, and if so, how do we do it?

A Ah, well. That's a big question. I don't know. I suppose you have to take a view on all of the evidence you've seen. Unfortunately, it's not a strong legal case of proof and it's not clear and it comes back to, I would imagine, trying to consider what is the most probable, plausible and reasonable explanation for what was observed.

Q Could there be more than one explanation?

A Yes, I think there almost certainly is more than one explanation. That would be my personal view. In much the same way as Dr Drumright was exploring with line infections, team (inaudible 15:14:16), teams, nursing shortages, maybe, you know, this, that, and the other. Yeah.

Q Now, I want to look at a couple of sources of material that I'm relatively certain that you haven't seen, but I need to make sure you haven't seen.

A Right.

Q Can we go to bundle 44, volume 2, page 25? This is the list of things that were outwith your remit.

A Yes, yeah.

Q Now, I think some of them, you've now looked at.

A Yes. I can't remember exactly which, I must confess. I don't know.

Q So, I wondered the extent to which-- I mean, most of them relate either to the management of the water system----

A Yes.

Q -- or steps taken to change things in the building. The ones I want to focus on are G and H; that is the Innovated Design Solutions reports.

A Okay.

Q Now, I wonder what you knew at the time you were preparing this report about whether parts of the hospital were being rebuilt?

A They both didn't impinge on my consciousness, that's certainly----

Q So, you weren't aware that money was being spent rebuilding the whole Paediatric Haemato-oncology unit?

A Not really, no. No.

Q Had you been aware, do you think it would have helped to know what was being done?

A Are we thinking here in terms of ventilation?

Q These are ventilation reports,

yes.

A Aspergillus risk, etc.?

Q Yes.

A Not my area, I'm afraid.

Q Then at J----

A Yeah.

Q -- it's a rather dry title.

A Yes.

Q

"The NHS GGC Review of Issues Relating to the Hospital Water Systems' Risk Assessment".

We know by its principal author, Mr e NHS GDC review of issues related to hospital water systems risk assessment. We know it by its principal author, Mr Leiper. Did you know that GGC had carried out a review of the issues relating to the water systems risk assessment in late 18, early 19?

A It was not-- it was not put in front of us by CLO. I mean, they-- there was-- they had a letter of instruction, but also, they said, "We'd like you to concentrate on the-- just generally look at this area, look at data, etc.," and also going back and looking in detail at other people's risk assessments, detailed minutes of infection control, I felt uncomfortable trying to do a retrospective critique, analysis of how an outbreak had been handled because I would need to know a lot more. I'd have to visit the site. I'd have to look at all of the physical

structure and look at the risks that are involved, the patient loads, and that just didn't fit into the timeframe we had, really.

Q Now, hold that thought, because I was actually going to show you one more document on this----

A That's all right.

Q -- before you-- I was expecting you to say something like that, which is K, which is the HFS Water Management Technical Review for March '19. Now, you haven't read that either?

A No.

Q Now, there is a difficult question which I would welcome your help with, which is, to what extent can an expert witness be criticised for not looking at material they are not supplied with?

A I think it would be difficult to criticise people that----

Q Can I----

A If they're not being supplied with the material, then it's very difficult.

Q Can I posit a possible exception to that and see what you think about it?

A Yeah.

Q If the witness is an experienced professional in a field----

A Yeah.

Q -- as I think in your field---

A Yeah.

Q -- you clearly are, would it not be reasonable to think, "Well, I would

know that there are documents of certain sorts out there." So, you work in the UK in the field of environmental microorganisms. You know that water systems are subject to management plans. You must have known that there'd been somewhat of a public scandal about this hospital, and so there'd been other investigations.

A Yeah.

Q So, is it cruel or unfortunate to suggest that you should have looked for more information because you probably ought to have known about it?

A Well, no. You've got to go back to the thesis we adopted. We didn't want to be prejudiced by that.

Q Right.

A Therefore we wanted to look at it in our own way, looking, particularly, at infection data etc. Not go out and look in detail at why somebody did this or this temperature was too high there. That's----

Q I mean, one of the issues that came up with Dr Drumright was the occupied bed day data----

A Okay.

Q -- and an inconsistency between the occupied bed day data supplied to NSS and Dr Kennedy for their studies in 2019 and supplied to you for your HAD numbers.

A Right.

Q Now, the issue arose because that occupied bed day data comes from the Public Health Scotland system.

A Right.

Q Well, the stuff supplied to NSS and Dr Kennedy does, and it may be that the data supplied to you also does, but it's just cut in a different way. I suppose you couldn't possibly criticise an academic from Washington State for not knowing there's a Public Health Scotland database of reported bed day data.

A Well----

Q It'd be quite hard to.

A Unless you had detailed knowledge of the way in which bed day data is defined etc., in Scotland versus even England but-- then, yeah, they wouldn't-- you wouldn't know that.

Q Do you know about that?

A No, not particularly. No, it's not really my area of expertise, I'm afraid.

Q So, it's been suggested that I should ask these questions.

A Oh, right.

Q In the Questionnaire 2 we gave you, so that's volume five, page 18, Answer 49, we asked you a question about the CLABSI associated bloodstream infection work. Central Line Associated Blood Stream Infection work, CLABSI. We referred you to Dr Kennedy and Dr Rodgers' presentation and Ms Rodgers'----

A Yeah.

Q -- statement or at least part of it, and you responded:

"It was not our remit to review all reports from the Inquiry. We were asked to use the data made available to us from the NHS on bed days and microbiology results to determine if there was evidence that the QEUH put people at additional risk of HCAI, especially BSI and Aspergillus infections. We have now reviewed the documents mentioned above…"

A Yeah.

Q How do you respond to the suggestion that, as an experienced microbiologist, you should have challenged the adequacy of this remit?

A I don't know. I don't-- I don't think I should have-- we should have necessarily, and I in particular should have necessarily----

Q Because it's been suggested that-- Is it scientifically robust to compare infection data between hospitals without context of the nature of the hospital, the patient groups, the water system, etc.?

A Well, how-- I'd say to those people, "Well, what is the context that's going to alter the data so greatly?" Other than the obvious ones that we have that it's a different location. We know that, and the patient mix is very similar.

Q There's been evidence that some witnesses are of the view that the Yorkhill building for the children----

A Right.

Q -- was a rather old building and therefore could be expected to have a higher rate of-- sorry, a greater problematic water system than the new building.

A That's an interesting point, and I've reflected on that, and if you look at the Halstead paper which you mentioned, which was a large study which Dr Beryl Oppenheim at QE and myself got a grant from the Department of Health to look, okay, at Pseudomonas intact in highly vulnerable populations of patients, and in this case, these are those that are requiring intensive care or burns treatment----

Q Why don't we get that on the page?

A Yeah.

Q Bundle 44.

A It's Halstead. FD Halstead.

Q Now, that's not Halstead. Okay.

A Yeah.

Q It is-- I'll find it eventually. Just give me a moment.

A Yeah, yeah. No, please.

Q Bundle 44, volume 2, document 77, page 1217.

A Right, let's see.

Q No, I've done something wrong

there.

A No, that's----

Q 44, volume 2. Give me a moment just to find it myself. Page 1227. Now, sorry, I was asking you about----

A Yes.

Q -- is it scientifically appropriate to compare----

A Yes.

Q -- two hospitals without having the context and you were referring to Halstead?

A Yes, the reason being, these four large UK hospitals, one of them is a very-- really, a very new building and the others, one was a medium-age building, and the other one was another sort of moderate age, and the other one was really a very old hospital, rather similar to Yorkhill. The hospital that had the lowest rate of occurrence of Pseudomonas in their water systems in the Intensive Care units, was the oldest hospital. The newer hospital had the highest rate.

Q I appreciate that's what they found in this case. Does that follow in all cases?

A Not in all cases, but it means you can't take the general statement, "Oh, it's an old hospital, therefore it'll have a problem with its water system." That just doesn't follow.

Q No, I think at the point where the witnesses have said it had more of a problem-- well, it had a "spring bloom", according to one of our witnesses, Ms Harvey-Woods.

A Well, I'm not a water expert. By a "spring bloom", do you mean the occurrence of algae in the potable water supply?

Q I can't say any more than that----

A No, well, I think-- but I would not generalise that just because it's an old hospital, it will have problems with its water supply. It's a lot more to do with, as we've been discussing, the way in which the distribution system is handled, maintained, the nature of it, and the hospital that had the very low rate had something called a copper-silver system to prevent the occurrence of Legionella. In this publication, which I was the joint communicating author of, we speculated that maybe that was where-- perhaps that had an influence on this very low rate in this hospital.

Q Would you need to know, for example, how the water system at Yorkhill was managed and how the water system at the new Queen Elizabeth was managed and whether one used secondary treatment or not, in order to make a fair comparison between the two in infection rate terms?

A I don't think so.

Q No, you feel that it's a helpful

comparison?

A No, because that's-- it's all part of the general engineering environment. I can't consider that and make an opinion on it because it's outside my area of expertise.

Q There have been two documents that I have mentioned. I want to just check whether you-- I think the answer to both questions is you haven't read them, but I want to be sure I've got it right.

A Okay.

Q One was the three documents, the Innovated Design Solutions reports on the ventilators in 2A and 2B. Have you read those?

A No, because ventilation areas is not my area of expertise. That's Dr Agrawal to ask that one.

Q The others were the DMA Canyon and Intertek reports on water. Have you read those?

A No.

Q No, and I think you've answered why you didn't read DMA Canyon, but why did you not read the Intertek report, which investigates the water system?

A When was this report produced?

Q If we go back to bundle 44, volume 1, we were on the right page. It's Questionnaire 1. Volume 2 actually, and it's page-- (After a pause) No, I didn't put it on the document list.

A Okay.

Q I won't put it to you.

A I can't have read it then.

Q How do you respond to the suggestion that by designing this study in a way that either was agnostic or avoided bias or didn't look at the context – those are three ways of describing it – actually the effect is that you're willfully ignoring contemporary data on the contemporary state of the environment in the hospital, but still giving an opinion?

A We're giving an opinion on what we felt an approach to using data on infection rates might help us understand whether there was an abnormal occurrence.

Q When it comes to the use of infection rates, why did you not look in more detail at other people's attempts at the same exercise? So HPS compared the rates of infection in Yorkhill with the RHC, albeit for a shorter period. Why not look at those?

A We wanted to look at the data ourselves.

Q My Lord, this is a little bit early but I think I've asked all the questions I need to ask, but I think there would be some benefit in having the ten-minute break now because if I haven't, it's going to be a longer chunk of questions that I

need to ask.

THE CHAIR: Yes, we'll take a break. Can I just take the opportunity of clarifying? I apologise----

A No, no.

THE CHAIR: -- if these are rather simplistic questions. My underlying theme is going back to what I should take from the HAD Report, having regard to what you've said about it in your evidence today.

Now, in the HAD Report, from time to time we see you emphasising the importance of understanding a route of potential pathogenic-- well, that's redundant. A route of possible infection and a (inaudible 15:29:55).

A Yeah.

THE CHAIR: Now, am I right or am I wrong in approaching matters on this basis? If for the purpose of the question one assumes that the domestic supply water in a particular ward – let's take 2A – is a potential source of infection because of the presence in that water supply of a variety of microorganisms.

A Yeah.

THE CHAIR: Now, if patients – paediatric patients in this case – are washing their hands, having showers, younger children having baths, patients and their parents drinking from that (inaudible) supply-- Now, that appears to me as the layman that that covers the requirement of a mode of transmission, assuming there's something to be transmitted, and portal of entry because one may be drinking the water, one may be breathing in aerosol water, one's eyes may be splashed. Is there something I'm missing?

A No, one thing is the number of organisms-- I think you hinted at it or Mr Mackintosh did. The number of organisms in any particular quantity of water is quite important, okay?

THE CHAIR: Does that go back to dose?

A Dose, exactly. So, you know, if you're running a bar, it's the degree of contamination, the amount of organisms which are available and come off that biofilm if it's in a tap, and the degree of dilution in a bath, for argument's sake. And with regards to the portal of entry, yes, you could drink it or eat it, but you'd also be exposed to just very similar organisms in the-- outside of the home environment.

Very many people come in pre-colonised as well with those organisms. So, again, dissecting out, just because you're finding it in those systems or in that tap, there is a potential risk there. Absolutely, don't disagree with that at all, but to assess what the degree of influence that has on the infections that are preserved is much more difficult.

THE CHAIR: I think I understand that.

A Yeah.

THE CHAIR: It's just I'm going to your report, I'm seeing repeated reference to the need to understand route and portal.

A Yes, yes.

THE CHAIR: From my layman's perspective, it seems to me obvious that there is a route and there is a portal.

A Oh yes, yes, yes. Every haematology-oncology ward, every patient has that potential, particularly-- lines are particular and you notice lines-- a lot of these bloodstream infections came from lines----

THE CHAIR: Well, yes. I didn't mention that.

A -- they can be environmental organisms, though we did interestingly see this rise in the Gram-positive Staph-aureus type organisms, probably mainly line related, but it is always a risk.

THE CHAIR: Now, another theme in the HAD Report is the importance of bearing in mind gut translocation as a mechanism whereby the blood becomes, as I understand it, a carrier and therefore infect of microorganisms that have originated in the patient's digestive system.

A Correct.

THE CHAIR: Right. Now, the origin of microorganisms-- Well, as I understand it, we all have our – and it's a good thing that we do have – a microbiome with billions, if not trillions, of microbes.

A Oh, yes.

THE CHAIR: However, am I right in thinking or am I wrong about this: that microbiome will be contributed to by the microorganisms we encounter? For example in drinking water, in showers, in baths and so on.

A Yes, and also be modified by our exposure outside the hospital environment, very much by food, and also we often-- some of the key organisms like Klebsiella and Enterobacter and Pseudomonas-- and even now it's recognised that Pseudomonas colonisation in the gut is more common than we originally thought. So those may well be long-term carried by a patient who, prior to developing their leukaemia, actually has the organism already there, sits there quietly. They've then become neutropenic, so their immune system is totally suppressed.

So now the barrier that prevents those organisms getting out, as you say, into the blood, the organisms move – we call it translocation – across the bowel wall into the bloodstream, cause an infection, a so-called endogenous infection, and a--

The majority, I think as Dr Agrawal has said and he's absolutely correct, the majority of infections we see in haem-onc patients are often usually endogenous. It doesn't prevent-- as you're rightly saying, my Lord, you can-- you can be in that ward and you can have swallowed the Stenotrophomonas from a tap and then become gut-colonised. You wouldn't know. Nobody's going to test you.

It wouldn't be reasonable to screen those patients, but then a week or a month or six months later, you then develop neutropenia and bingo, you've got that organism, which is why, in a way, I am very-- I am somewhat nervous, Mr Mackintosh, about this concept that you just look at clinical notes and decide whether something came from the environment or not. I'm afraid I'm much more pessimistic than that. I don't think you can, but it doesn't mean the risk doesn't exist and I think plausibly my opinion would be that, yes, some of these patients will have acquired organisms from the environment.

THE CHAIR: And it seems to at least slightly qualify the sharp conceptual distinction between the exogenous and the endogenous.

A Exactly.

THE CHAIR: Right.

A Exactly.

THE CHAIR: Now, I think, finally, or at least finally at this stage-- How do you encourage me to read Chapter 3 of the HAD Report?

A In what way?

THE CHAIR: Well, I think in one of the responses you describe the sections as being vignettes dealing with----

A Oh, right----

THE CHAIR: dealing with----

A Yes.

THE CHAIR: Now, how should I use Chapter 3?

A I would hope that Chapter 3 gives you an understanding-- We've been banding these names around very glibly, Stenotrophomonas, Pseudomonas. Our hope was with-- we were-- or our hope was-- with the little vignettes is to give a feeling for what the normal niche-- what its pathogenic potential of those different bacteria is and the sort of harm and trouble they can cause in these sorts of patients or in these of settings, potentially. It's not an absolute guide to say this is a villain and that is an innocent bacterium. As you're only too well aware, it's very much a grey spectrum and in different settings bacteria behave very differently.

THE CHAIR: Yes. I mean, I've read the chapter and will re-read it, but I'm not sure why I'm doing that and the reason I say that is possibly twofold. One point is that I don't see any line of

argument and don't appear to be being led----

A No, no.

THE CHAIR: -- to any particular conclusion. The other point is that, having started with a discussion about a species, the text goes in another direction, for example, to stress the value of whole genome sequencing.

A Yes, I mean, I think there is the debate we had a little earlier on this afternoon about what is "same". Very easy sometimes for people and some of the reports around saying, "Ah, we've seen a cluster of the same bacteria," and what I think we wanted to do there was to say, "Well, hang on, what do you mean by "same"? What level are you going to go down to? What level are you looking at?" You'd be presenting when someone says it's Enterobacter cloacae, are they all one? All 26 of them, for argument's sake, are all E. cloacae? Therefore, if we see three of them in a month, it's exciting, but actually if you look a little more closely, maybe one's a hormaechei, one's an asburiae and one's something else.

Now, your point, Mr Mackintosh, is that okay, they could all come from the environment. Yes, but again I would say, in terms of the examples I've given, it leads you a little bit against saying these all must have come from the

environment. So there's no-- Maybe some of them haven't, because if we did have a big problem we would perhaps see the same – truly the same, by WGS subtyping – cropping up as causing infections. I'm not saying that's an absolute rule, but I find it odd that we don't see that. It doesn't-- and I don't think it does rule out the role of the environment, but perhaps the environment isn't the only role.

THE CHAIR: Right.

MR MACKINTOSH: My Lord, you've given me the opportunity to realise I've missed something out. I wonder if we can go to section 7.1 of the HAD Report? That's bundle 44, volume 1, document 1, page 62. Now, this is a short section of just over two pages discussing are the water testing results consistent with being widespread contamination?

Now, when I read it, this chapter, I did wonder whether you were in effect arguing that Pseudomonas aeruginosa-- it effectively enables you to draw-- you can draw inferences from that one microorganism.

A I wouldn't wish to draw too many inferences. It is-- I found it interesting that I would have perhaps have expected to see a little more Pseudomonas aeruginosa in the makeup of the infections because it is an

organism which is really well adapted to surviving in hospital, in water systems, but also it has a really relatively high degree of, a relative high degree of pathologists to the extent that it causes problems in those with almost normal immune systems sometimes.

Q I just wanted to put two things to you. One is the water testing results that Dr Chaput prepared.

A Right.

Q So, that's bundle 14, volume 1, document 2, at page 21, at least I hope it is. (After a pause) No, it's not at all. We can take that off the screen. I'll try it a different way, which is bundle 18, volume 1.

A Yes.

Q That's a relief. Can we go back to page 21, please? Now, this records the number of water samples and tests carried out in Table 2. I think you looked at this report.

A Yes, yeah.

Q -- and we noticed that in Pseudomonas for the first three years of the hospital's operation – it's worth saying that the hospital is handed over to the Health Board in January; it's almost a complete year in 2015 – there are less than 400 tests done a year. It then rises up just shy of 550 and then there's a big step up to the current regime and I just wondered, does the number of water testing results being carried out in '15, '16, '17 at around perhaps 30 a month, in a building this big, rather reduce the ability to use Pseudomonas as a way of finding out what's going on?

A My question, I don't think I'm very-- I'm necessarily terribly clear about it, but the key is where those tests were done, because it only makes sense, in the sense of Pseudomonas-- and this is why there's been English and Scottish-- as I said, at the moment, it's an experimental system to look at certain key areas for Pseudomonas, so we're looking at operating theatres. We're looking at----

Q Well, we can see that on page 28.

A It's on 28, it tells us where they're----

Q Figure 4.

A That's good.

Q So they don't test the basement tanks, either side of the filters or the hospital in general very much, but the testing, such as there is, is in high risk.

A High risk. It's all high risk. Well, that's where it's very appropriate to have it, and will give you a much clearer indication of what's going on, because these are the areas where the Pseudomonas in that water, or in that tap or drain, have a good chance of

potentially causing an infection. If we're on a general medical ward or a general surgical ward, they have virtually zero chance of causing it because (a) the patients aren't that susceptible but (b) the potential for portals of entry and routes of transmission don't exist, so the patients on the ITU, particularly, got lots and lots of lines. Not just long lines: they've got maybe wounds, they've got other situations, and-- and they may be on a ventilator and then spread into a ventilator to give Pseudomonas, and pneumonia is a very difficult and common problem. So, I'd say that's entirely appropriate to focus in high-risk areas.

Q Dr Chaput, who's the author of this paper, gave evidence last week.

A Right.

Q What I've just said comes from column 152, 153 of her transcript. That's for the benefit of my colleagues.

THE CHAIR: Sorry, could I just take----

MR MACKINTOSH: 152, 153, my Lord. Now, I think she's talking in a slightly different context, but with that health warning, she says something like this:

"You cannot just extrapolate Pseudomonas oreganoza and Legionella to all other gram-negatives because they're very different organisms."

A Well, particularly Legionella, which is a very specialised and unusual organism because it's route of transmission is solely by the air, so-- we've established and Dr Agrawal has established, in fact, ventilation in terms of gram-negative transmission really isn't a big deal.

Q Yes, but I suppose if you can't extrapolate from Pseudomonas oreganoza, what's Chapter 7.1 trying to do?

A No, because I said Legionella. If I talk about Pseudomonas, then that is much more similar to Stenotrophomonas. In fact, taxonomically in Chapter 3----

Q So you think you can extrapolate?

A -- you'll see they're very, very similar organs.

Q So your view is you can extrapolate?

A You can do a degree of extrapolation, yeah.

Q I think that's probably all I need from that, Lord. I think this might be a good time to do our short break.

THE CHAIR: As you will have followed, Professor, Mr Mackintosh wants to, essentially, check with the room.

THE WITNESS: Indeed, I understand.

THE CHAIR: This shouldn't be more than ten minutes.

THE WITNESS: No problem at all.

Thank you.

(Short break)

MR MACKINTOSH: My Lord, just two questions.

THE CHAIR: I'm told perhaps two questions, Professor.

THE WITNESS: All right, your prerogative.

MR MACKINTOSH: Professor, so these relate to the use of antibiotics as a prophylactic.

A Yeah.

Q From the perspective of the patient, can there be long-term consequences that arise from long-term prescription of antibiotics as a prophylactic, perhaps to the patient's microbiome?

A Yes, is the answer. Yes, particularly some types of drugs. Ciprofloxacin is guilty in a sense of damaging your flora quite substantially, and this is where medical opinion is pretty much split. There are protagonists for Ciprofloxacin prophylaxis, and undoubtedly there is an argument that it reduces the number of infections. I'm of the camp of Dr Agrawal's view as a haematologist oncologist, in that If you use it all the time, the infections you do encounter (a) you may not recognise them very easily because they're masked by the low level of antibiotic, and (b) when you do encounter them, there's a greater chance they're going to be either resistant to Ciprofloxacin or other multi-resistant-- or in fact some environmental bacteria like Acetobacter(?), which we haven't talked about, is intrinsically resistant usually to Cipro, so you'll be confronted with a much more difficult to treat infection.

Q Does this apply to, well, in general haematology oncology patients and paediatric ones in particular?

A I wouldn't say it applies to paediatric patients in particular. It applies to both of those patients, and it applies to other patients taking long-term antimicrobial drugs.

Q I'm just going to just check one thing that arises from that before we finish. I don't want to put a document on the screen without thinking it through. When you say "the long-term prescribing of Ciprofloxacin"----

A Yeah.

Q -- would that be as part of a sort of policy-driven plan?

A Oh, policy.

Q Yes.

A Absolutely. It's always policy, so----

Q So the policies that you looked at for this and the CNR looked at, did

they suggest that was the general approach as opposed to the specific approach?

A I think it was, yes.

Q Right. You----

A And my own-- For instance, when I was in Birmingham, we didn't use Ciprofloxacin prophylaxis.

Q What do you feel about the use of Ciprofloxacin *in extremis* in reaction to a perception of increased infections?

A A lot of the environmental organisms were-- This is the choice of what we call empirical therapy, when you don't have a-- you've got a neutropenic patient, temperature, an infection----

Q Or you can have a lot of neutropenic patients.

A Yes, indeed. You then-- what I would-- You should be looking at what the susceptibility pattern of the organisms you are encountering, or Stenotrophomonas or Pseudomonas, and decide what might be an appropriate, best guess antibiotic to treat a patient that's developing the infection.

Q And do you have any issues about the use of Ciprofloxacin in that scenario?

A No, not at all. If somebody is deemed-- "Oh, let's use Cipro because it's good against environmentals." I'd be a little worried about that. Let's look at what's causing infections, what's the susceptibility of those. Let's tailor our empirical therapy or our second-level empirical therapy to target those organisms, and I have been in a situation with one outbreak where we-- In fact, it was a Pseudomonas outbreak on an Intensive Care unit. This particular clone, and it was actually an environmental source, very bizarre, it was one tap which had the wrong water temperature on it, and this is 1988, long before we started thinking of these things, and we had repeated bloodstream infections.

The source was this one tap. All the other taps all had Pseudomonas. This had Pseudomonas in one strain in that one, and it was being transmitted because nurses against anybody's knowledge, and I spotted them doing it one Easter Monday-- Easter Friday, were taking a little bit of the water and putting it in the pressure monitoring device to get a better signal. And in that water was Pseudomonas in close proximity to their arterial line, and they were then getting-- So coming around, this particular strain was resistant to Piperacillin-tazobactam.

Q Right.

A So, we then instituted an empirical policy of giving Cipro.

Q Thank you. I've got no further questions, my Lord.

THE CHAIR: Nothing further occurs

to me. Professor, that is the end of your evidence.

THE WITNESS: Thank you.

THE CHAIR: Therefore, you're free to go, but before you do that, can I say thank you for your attendance today, the evidence today, but also the work that has gone behind that evidence, including your engagement subsequent to the provision of the HAD Report? So thank you very much indeed, Professor.

THE WITNESS: Thank you, thank you, and I wish you good luck with your Inquiry as well.

THE CHAIR: Thank you.

THE WITNESS: Thank you.

(**The witness withdrew**)

THE CHAIR: Now, I think the plan is to resume tomorrow at 10?

MR MACKINTOSH: With Professor Stevens and with Mr Connal.

THE CHAIR: Right, well, can I wish everyone a good afternoon and evening? All being well, we'll see each other tomorrow.

(Session ends)

16:08