Bundle of documents for Oral hearings commencing from 19 August 2024 in relation to the Queen Elizabeth University Hospital and the Royal Hospital for Children, Glasgow

Witness Statements – Volume 12

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Scottish Hospitals Inquiry

Supplementary Questions for the CNR Expert Panel

Professor Mark Wilcox

1. It appears from the Public Health Commentary authored by Dr Emilia Crighton, NHS GGC Director of Public Health and submitted to the CNR in February 2021 that she and NHS GGC then considered that it would be useful to carry out additional epidemiological analysis and specifically that:

   a. An analysis comparing infection rates within the NHSGGC Unit to the combined Aberdeen and Edinburgh Units was carried out by HPS in 2019 Bundle 7, Document 6, Page 214) should be included in the Case Notes Review; and

   b. That that the use of statistical methods (like indirect standardisation) would be more suitable to assess the chance of a real excess number or cluster to avoid the cognitive bias of “Clustering Illusion”.

   How did the Expert Panel respond to this Public Health Commentary in general and the request that additional epidemiological analysis be carried out?

A a. The brief we were given was to examine specific Gram-negative blood stream infections, i.e. those caused by bacteria that could be associated with the hospital environment. Our brief was not to determine the infection rates per se. The latter are of only indirect relevance to our focussed brief. Furthermore, it is well known that comparing infection rates between different hospitals / units is fraught with challenges relating to differences in case mix, illness severity, ascertainment of infection, and propensity to (risk factors for) infection. It is, therefore, not straightforward to interpret similarities or differences in infection across hospitals / units, and indeed is prone to missing data and assumption errors.

b. The answer to this question partly requires a knowledge of (advanced) statistical analysis that is beyond my expertise. However, I am clear that the approach we used to determine/describe clusters of infection cases (critically, in time and place) was appropriate to the brief we were given. I do not believe that this approach was subject to 'clustering illusion'.

2. Can you provide further details beyond what you stated in your earlier statements as to the role that NHS GGC or its staff had in (a) defining the remit of the Case Notes Review, (b) setting the selection criteria for cases within it and (c) the decision to include all Gram-negative bacterium in the scope of the review?

A I do not know the answer to these questions. I do not recall that the development of / input into our brief, as described in 1a. above, was described to me.

3. Why does the CNR Overview Report not contain any comparative data on infection rates?

A My answer here is essentially the same as set out in 1a. above.

4. If a comparative epidemiological analysis was to be carried out to compare the rate of infections in the patient cohort covered by your review knowing what you now know about the Schiehallion Unit and its patient group how would you go about selecting comparable hospitals to compare it with and do you have in mind any particular hospitals/units with which a comparison could be made?

A The scenario described is not the brief we were given. In short, to answer the scenario described, a propensity analysis could be used. This is a relatively complex process whereby a range of risk factors that can affect (in this case) infection rates are measured in the units being compared. The data are then adjusted to take account of any differences in the rates of these risk factors. Such analyses can part- but not wholly-overcome crucial confounding factors that can bias comparisons between groups of patients. Notably, some risk

factors for infection that differ between/across units may be unknown and/or cannot be adequately controlled for in such analyses.

5. In applying your methodology to the cases in the review what consideration did you give the possibility that any particular infection was a commensal infection arising from a colonised patient by reference either to the particular circumstances of the infection, the epidemiology of the infections observed in the hospital and any published papers about the prospect that particular bacterial was more or less likely to be arise from colonised patients?

A My answer here is contained within 4. above. It is likely that such a risk factor will not be measurable across different patient groups as systematic screening of patients will not be carried out to determine bacterial colonisation; if it is carried out, then the granularity/depth of such data will not be sufficient to determine true differences, and/or the extent/quality of screening will differ between units/patient groups.

I believe that the facts stated in this witness statement are true. I understand that this statement may form part of the evidence before the Inquiry and be published on the Inquiry's website.

Scottish Hospitals Inquiry

Supplementary Questions for the CNR Expert Panel

Professor Michael Stevens

1. It appears from the Public Health Commentary authored by Dr Emilia Crighton, NHS GGC Director of Public Health and submitted to the CNR in February 2021 that she and NHS GGC then considered that it would be useful to carry out additional epidemiological analysis and specifically that:

   a. An analysis comparing infection rates within the NHSGGC Unit to the combined Aberdeen and Edinburgh Units was carried out by HPS in 2019 (Bundle 7, Document 6, Page 214) should be included in the Case Notes Review; and

   b. That that the use of statistical methods (like indirect standardisation) would be more suitable to assess the chance of a real excess number or cluster to avoid the cognitive bias of “Clustering Illusion”.

   How did the Expert Panel respond to this Public Health Commentary in general and the request that additional epidemiological analysis be carried out?

A These comments were made both in the Public Health Commentary provided as Appendix 1 to NHS GGC’s response to our draft report and in the main body of its response to the draft report. My response to your questions is: a) we agreed that we should include a section critiquing the HPS 2019 report in our final report. This was inserted in the final report as Section 8.2.3 (page 93); and b) we understood the possibility of ‘clustering illusion’ and the need to avoid the ‘association is not causation’ bias. Our decisions about the possibility of a link between an infection and the hospital environment were nevertheless influenced by the clustering we observed. This is described in section 3.6.6 (pages 43-45) of our report, and also in Section 4.3.5 (pages 56-57). Standardised statistical techniques, including indirect standardisation, are

available for comparing the incidence rate of ‘events’ between populations even if they have differing characteristics. However, data from a reference population is required for such calculations and I was not aware of appropriate reference data for infection rates in paediatric haematology-oncology patients against which data collected at NHS GGC, or another treatment centre, could be compared.

2. Can you provide further details beyond what you stated in your earlier statements as to the role that NHS GGC or its staff had in (a) defining the remit of the Case Notes Review, (b) setting the selection criteria for cases within it and (c) the decision to include all Gram-negative bacterium in the scope of the review?

A I am unable to provide further details about the involvement of NHS GGC or its staff in a) agreeing the remit (as reflected in its Terms of Reference) of the Case Note Review or b) setting the selection criteria for cases within it. With regard to c) I wish to point out that all Gram-negative bacteria were NOT included in the scope of the review. Gram-negative non-environmental bacteria (such as E. coli and Proteus) were not included.

3. Why does the CNR Overview Report not contain any comparative data on infection rates?

A Although the HPS 2019 report shows SPC charts for infections in paediatric haematology-oncology patients at NHS GGC using data points expressed as rates per 1000 occupied bed days, we did not have access to similar incidence rates for infection in paediatric haematology-oncology patients at other treatment centres for comparison. I should emphasise that whilst evidence for a difference in infection rate compared to another treatment centre would have been of interest, our review was less about infection rate and more about the nature and pattern of infections, and whether there was evidence to suggest that some of these might have been acquired from the hospital environment. I would also like to reiterate an important point of emphasis about the HPS 2019 report (also referenced in section 8.2.3 of our final report) specifically that the comparison made by HPS with the Children’s

Hospitals in Edinburgh and Aberdeen was based on whole hospital data, i.e. the data were not restricted to haematology oncology patients. Moreover, the data for Edinburgh and Aberdeen were combined for the purposes of this analysis. This then does not provide direct experience of the haematology-oncology population with their associated risk for blood stream infection. Importantly, however, the report states (page 17) that between June 2015 and September 2019 the rate of environmental with enteric infections was statistically significantly higher at RHC Glasgow than for Edinburgh and Aberdeen combined. Despite the caution with which HPS themselves treated their findings, this report is not consistent with the reassurance that NHS GGC seems to have derived from it.

4. If a comparative epidemiological analysis was to be carried out to compare the rate of infections in the patient cohort covered by your review knowing what you now know about the Schiehallion Unit and its patient group how would you go about selecting comparable hospitals to compare it with and do you have in mind any particular hospitals/units with which a comparison could be made?

A At the time of our investigations and the writing of our report, I was not aware of any routinely collected data about the incidence and type of infection in haematology-oncology patients in other, potentially comparable treatment centres in the United Kingdom. Creating this resource would be the necessary first step to undertake a prospective study to explore variability in rates of infection. The data collection would require an agreed protocol to define the types of infection to be recorded (much as was done to define the infections to be included in the Case Note Review) and a minimum clinical dataset to identify key characteristics of the patients involved (for example, age, gender, diagnosis, cancer treatment etc.), type of infection and patient outcome: an approach similar to that which we initiated for retrospective data collection within the Case Note Review. The number of children and young people with infection within each treatment centre and the casemix (principally the age range of patients, the nature of their different diagnoses and modalities of treatment – particularly the presence of a bone marrow transplant

programme) would need to be defined as a way of selecting treatment centres most likely to offer appropriate comparison with NHS GGC. Centres of similar size and complexity in terms of number of patients and casemix would not be found in Scotland. The treatment centres in Edinburgh and, in particular, Aberdeen, are much smaller than Glasgow and have a less complex case mix. Centres in England with characteristics which might serve as appropriate comparators to Glasgow would include Manchester, Birmingham, Bristol, Cambridge, Leeds and Newcastle.

5. In applying your methodology to the cases in the review what consideration did you give the possibility that any particular infection was a commensal infection arising from a colonised patient by reference either to the particular circumstances of the infection, the epidemiology of the infections observed in the hospital and any published papers about the prospect that particular bacterial was more or less likely to be arise from colonised patients?

A We discussed the possibility of endogenously acquired (patient derived) infection from commensal bacteria at several points in our report (see Section 3.6.6, page 44; Section5.6, page 68; Section 8.2, page 88).

I believe that the facts stated in this witness statement are true. I understand that this statement may form part of the evidence before the Inquiry and be published on the Inquiry's website.

Professor Michael Stevens
16 October 2024

Scottish Hospitals Inquiry

Supplementary Questions for the CNR Expert Panel

Gaynor Evans

1. It appears from the Public Health Commentary authored by Dr Emilia Crighton, NHS GGC Director of Public Health and submitted to the CNR in February 2021 that she and NHS GGC then considered that it would be useful to carry out additional epidemiological analysis and specifically that:

    a. An analysis comparing infection rates within the NHSGGC Unit to the combined Aberdeen and Edinburgh Units was carried out by HPS in 2019 (Bundle 7, Document 6, Page 214) should be included in the Case Notes Review; and

    b. That that the use of statistical methods (like indirect standardisation) would be more suitable to assess the chance of a real excess number or cluster to avoid the cognitive bias of “Clustering Illusion”.

    How did the Expert Panel respond to this Public Health Commentary in general and the request that additional epidemiological analysis be carried out?

A We reviewed the Public Health commentary in detail and amended out report in response to the feedback. There are 36 references to HPS contained within the CNR. We considered that a further request for epidemiology as it fell outside the Terms of Reference for this review. Chaper 2, section 2.2 , 2.3 and 2.4 of the CNR.

2. Can you provide further details beyond what you stated in your earlier statements as to the role that NHS GGC or its staff had in (a) defining the remit of the Case Notes Review, (b) setting the selection criteria for cases within it and (c) the decision to include all Gram-negative bacterium in the scope of the review?

A a) I cannot say how much input NHSGGC had in defining the remit of the CNR. The cohort was defined using, I believe, the HPS 2019 analysis (Review of Haemato-oncology data) with which the panel agreed with the caveat we would continue to review throughout the process

b) setting the selection criteria for the review was already confirmed at the first meeting with the panel and therefore have no knowledge of any prework undertaken by NHS GGC. This is defined in section 3.2.1of the CNR

c) The cohort did not include all Gram-negative bacteria in the scope of the review. Escherichia coli being the most common Gram -negative See section 4.3.5 of CNR and Appendix D

3. Why does the CNR Overview Report not contain any comparative data on infection rates?

A The panel was asked to answer a specific set of question these can be found in section 2.1 of CNR:

1. How Many children in the specified population have been affected, details of when which organism etc?
2. Is it possible to associate these infections with the environment of the RCH and the QUEH?
3. Was there an impact on care and outcomes in relation to infection?
4. What recommendations should be considered by NHS GGC and, where appropriate, NHS Scotland , more generally to address the issues arising from these incidents to strengthen infection prevention and control in future?

5. If a comparative epidemiological analysis was to be carried out to compare the rate of infections in the patient cohort covered by your review knowing what you now know about the Schiehallion Unit and its patient group how would you go about selecting comparable hospitals to compare it with and do you have in mind any particular hospitals/units with which a comparison could be made?

A This is a question more appropriate to an epidemiologist, however I would suggest selecting hospitals with a similar demographic, population size, similar specialist oncology tertiary centres across a UK wide network to provide a larger cohort . I would also like to include a study of other wards across QUEH site to determine if there is a similar pattern of infection across the organisation not specifically within this patient cohort

6. In applying your methodology to the cases in the review what consideration did you give the possibility that any particular infection was a commensal infection arising from a colonised patient by reference either to the particular circumstances of the infection, the epidemiology of the infections observed in the hospital and any published papers about the prospect that particular bacterial was more or less likely to be arise from colonised patients?

A We discussed the possibility of infection arising from other sources in particular in section 3.6.6 of the CNR, Categorising the likelihood of an environmental source for an infection. We considered the possibility of external sources from other hospitals or outpatient departments or from home where there was an opportunity. Many of these patients had been inpatients for a number of weeks and therefore with a similar infection in another child in the same locality, it is more likely to have been transmitted. Our objective was to find the most likely source of infection as we were unable to confirm the source.

I believe that the facts stated in this witness statement are true. I understand that this statement may form part of the evidence before the Inquiry and be published on the Inquiry's website.

Scottish Hospitals Inquiry

Post Oral Evidence Statement

Dr Teresa Inkster

In relation to ‘picks’ and the sequencing report prepared by Professor Leanord and Derek Brown dated 18 January 2023, which can be found at **Bundle 6, page 1195**, in the course of carrying out a DNA analysis, particularly by whole genome sequencing, one or more colonies or ‘picks’ will be selected for that process.

1. Q. Are you aware of any published material which discusses the number of such ‘picks’ which should be used to ensure reliable results or conclusions? If so, please identify any such publications, and if possible, attach copies or links to your reply.

A. I am not aware of any publica on that concludes exactly how many picks are enough to ensure reliable results or conclusions. I am however, aware of several publications which discuss the limitations of selecting a single colony pick including examples where greater than one colony pick has been undertaken. These are listed in the table below along with the relevant parts of the paper and copies are a ached. I would like to highlight that the issue with colony picks was discussed with Professor Leanord in January 2021. Dr Michael Weinbren, Consultant Microbiologist and Clinical Lead for water at the me with NHS Assure, requested changes to the research application for Cupriavidus WGS to include multiple picks from water samples. This was acknowledged by Professor Leanord and included in the research application as a secondary question. The application states ‘Current national guidance asks laboratories to select a single colony from an agar plate for typing of positive water samples. This approach may underestimate exogenous acquisition of waterborne pathogens. Outbreaks may be polyclonal, particularly if mature and extensive biofilm is present in pipework/outlets. Not detecting a polyclonal outbreak is a lost opportunity for future preventative measures .’ Emails and the application form have been provided to the Inquiry. (Cupriavidus CoE WGS proposal 221220 Final v3 Al edits (**Bundle 27 Volume 17 document 35**) Email chain between M Weinbren and A Leanord regarding WGS protect 17-19 January

2021 **(bundle 27 volume 17 document 36)**

Publication	Relevant sections
Vallés J, Mariscal D, Cortés P, Coll P, Villagrá A, Díaz E, Ar gas A, Rello J. Pa erns of colonizationon by Pseudomonas aeruginosa in intubated pa ents: a 3year prospective study of 1,607 isolates using pulsed-field gel electrophoresis with implications for prevention of ventilator-associated pneumonia. Intensive Care Med. 2004 Sep;30(9):1768-75 **A50508336**	In the discussion sec on the authors state 'This study is also unique in subculturing at least four colonies that were representative of the different morphological types of PA present on each culture plate. It allowed the origin of the strains to be identified and reduced the risk of underestimating exogenous colonization'
Visca P, Goldoni P, Lück PC, Helbig JH, Ca ani L, Giltri G, Brama S, Castellani Pastoris M. Multiple types of Legionella pneumophila serogroup 6 in a hospital heated-water system associated with sporadic infections. J Clin Microbiol. 1999 Jul;37(7):2189-96	In the discussion sec on the authors state 'Second, sampling bias can occur, and a large number of environmental isolates should be genotyped to ensure that all types of legionellae present in the sample are recovered and characterized.'

Mäklin T, Kallonen T, Alanko J, Samuelsen Ø, Hegstad K, Mäkinen V, Corander J, Heinz E, Honkela A. Bacterial genomic epidemiology with mixed samples. Microb Genom. 2021 Nov;7(11):000691. **A50808339**	Introduction sec on states 'Standard genome based epidemiological linking of cases requires accurate genome sequences for the pathogens derived from high coverage sequencing data for pure-colony isolates. The isolates are obtained by an enrichment and separation step in the form of a plate culture and subsequent colony picks based e.g. on morphology and colour. Typical workflow of genomic epidemiology may thus necessitate multiple colony picks per sample with the corresponding DNA library preparation and sequencing steps done individually for each of them. DNA isolation, library prep and sequencing require a significant amount of laboratory effort and me per colony, and lead to increased costs since the price of library preparation is becoming comparable to the cost of sequencing itself.'
Stoesser N, George R, Aiken Z, Phan HTT, Lipworth S, Quan TP, Mathers AJ, De Maio N, Seale AC, Eyre DW, Vaughan A, Swann J, Peto TEA, Crook DW, Cawthorne J, Dodgson A, Walker AS; TRACE Investigators Group. Genomic epidemiology and longitudinal sampling of ward wastewater environments and pa ents reveals complexity of the transmission dynamics of bla$_{KPC}$-carbapenemaseproducing **A50808334**	See diagrams page 8 Figure 5 for the number of colony picks taken. This paper in general highlights the complexities of WGS in wastewater environments.

Enterobacterales in a hospital se ng. JAC Antimicrob Resist. 2024 Sep 3;6(5):dlae140	
Tang P, Croxen MA, Hasan MR, Hsiao WWL, Hoang LM. Infection control in the new age of genomic epidemiology. Am J Infect Control. 2017 Feb 1;45(2):170-179. **A50803442**	Discussion sec on 'Tracking transmission dynamics, however, can be hampered by the diversity of organisms that can be found within a single host. Sequencing of multiple colonies of the same organism isolated from a single person showed that these individuals can carry multiple unrelated types of that species, such as diverse sequence types of MRSA, extendedspectrum β-lactamase–producing E coli or vancomycin-resistant enterococci. SNVs within a single sequence type have been seen in MRSA, A baumannii, and K pneumoniae, and this has been described as a cloud of diversity. These findings imply that a single colony isolated from a single patient may be insufficient to reconstruct the chain of transmission between otherwise epidemiologically linked patients. This diversity is not exclusive to infected patients; asymptomatic carriers can also harbor a diverse set of potential pathogens that can be silently introduced into health care facilities and linked to outbreaks. These organisms may have a unique biology that makes them adept at establishing a foothold in health care settings.'

Van Goethem N, Descamps T, Devleesschauwer B, Roosens NHC, Boon NAM, Van Oyen H, Robert A. Status and potential of bacterial genomics for public health practice: a scoping review. Implement Sci. 2019 Aug 13;14(1):79 **A50803448**	Discussion sections; The most highlighted issue is the fact that WGS, as is equally the case for conventional typing methods, cannot stand on its own and that epidemiological data (including me, place, and exposure data) should complement the WGS results to identify a common source or link cases during outbreak investigations. False conclusions could be drawn from WGS data alone since it is possible that epidemiologically unrelated isolates are highly similar at the SNP level. Another reported issue was the potential misinterpretation of isolate relationships given the diversity of isolates that can be found within a single host (e.g., following long term carriage) or environmental reservoir. It was stressed by several studies that it is important to account
	for this “cloud of diversity” by increasing the number of samples taken from the suspected source.

Jay-Russell MT, Mandrell RE, Yuan J, Bates A, Manalac R, Mohle-Boetani J, Kimura A, Lidgard J, Miller WG. Using major outer membrane protein typing as an epidemiological tool to investigate outbreaks caused by milk-borne Campylobacter jejuni isolates in California. J Clin Microbiol. 2013 Jan;51(1):195-201. **A58088338**	Methods sec on; Multiple (8 to 12) pure colonies of presumptive C. jejuni were picked from each plate to increase the likelihood of finding the clinical outbreak subtype and stored on Microbank dry beads Discussion: Our analysis also emphasizes the importance of selecting multiple pure colonies from individual samples during C. jejuni outbreak investigations for successful molecular subtyping, as described previously in the human and veterinary literature

Ruppé E, Olearo F, Pires D, Baud D, Renzi G, Cherkaoui A, Goldenberger D, Hu ner A, François P, Harbarth S, Schrenzel J. Clonal or not clonal? Investigating hospital outbreaks of KPCproducing Klebsiella pneumoniae with whole genome sequencing. Clin Microbiol Infect. 2017 Jul;23(7):470-475. **A58088343**	Discussion; Perhaps if we had considered other sites for sampling and selected more than one strain from the culture, we might have identified the strain that had been transmitted to HUG2 and HUG3. Currently no specific guidelines recommend the typing of more than one strain per patient. These findings suggest that when typing with WGS, the collection of multiple strains from more than one anatomic site could be justified.’

Quick J, Cumley N, Wearn CM, Niebel M, Constantidou C, Thomas CM, Pallen MJ, Moiemen NS, Bamford A, Oppenheim B, Loman NJ. Seeking the source of Pseudomonas aeruginosa infections in a recently opened hospital: an observational study using whole genome sequencing. BMJ Open. 2014 Nov 4;4(11):e006278. **A50808334**	Method; For storage and DNA extract on a single colony was purified from the primary culture plate. When different colony morphologies were observed, a single colony from each type was purified. Additionally, for a randomly selected water sample, 24 colonies were individually picked from one waterfilter primary microbiological plate for sequencing. Results; A total of 86 genome sequences were generated from the 71 positives, as in some cases multiple colony picks were sequenced. Seventyeight patient samples were screened for P. aeruginosa of which 39 (50%) were positive. A total of 55genome sequences
	were generated, as in some cases multiple colony picks were sequenced.
Environment agency – Methods for the examination of waters and associated materials Archived 2018 **A50808335**	Sec on 8.3.3 and 9.7.1

I believe that the facts stated in this witness statement are true. I understand that proceedings for contempt of court may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief in its truth.

The witness was provided access to the following Scottish Hospital Inquiry bundles/documents for reference when they completed their questionnaire/ statement (Appendix A)

The witness verbally introduced or provided the following documents to the Scottish Hospital Inquiry for reference when they completed their questionnaire statement (Appendix B)

Appendix A

A50071192 - Bacteraemia rates and Resistance Paediatric Haemato-oncology 20142018 **(Bundle 27, Volume 6, page 107)**

A50071192 - Environmental Organisms, Antibiotic use and Antibiotic Resistance – **(Bundle 27, Volume 6, page 121)**

A42401483 Report- Application of Whole Genome Sequencing Alastair Leanord and Derek Brown **(Bundle 6 page 1195)**

Appendix B

A50808335 Cupriavidus CoE WGS proposal 221220 Final v3 Al edits (**Bundle 27 Volume 17 document 35)**

A50808337 Email chain between M Weinbren and A Leanord regarding WGS protect 17-19 January 2021 **(bundle 27 volume 17 document 36)**

A50808336 Patterns of colonisation of Pseudomonas aeruginosa: a 3-year prospective study Intensive Care Medicine **(Bundle 27 Volume 17 document 37** Multiple types of Legionella pneumophila serogroup 6 in a hospital heated-water system associated with sporadic infections **(Bundle 27 Volume 17 document 34)**

A50808339 Bacterial genomic epidemiology with mixed samples. Microb Genom. 2021 (**Bundle 27 Volume17 document 38)**

A50808334 Genomic epidemiology and longitudinal sampling of ward wastewater environments and patients reveals complexity of the transmission dynamics of blaKPC-carbapenemase-producing Enterobacterales in a hospital se□ng. JAC Antimicrob Resist. **2024 (Bundle 27 Volume 17 document 39)**

A50808342 Infection control in the new age of genomic epidemiology. Am J Infect

Control. (**Bundle 27 Volume 17 document 40)**

A58088341 Using major outer membrane protein typing as an epidemiological tool to investigate outbreaks caused by milk-borne Campylobacter jejuni isolates in California. J Clin Microbiol. (**Bundle 27 Volume17 document 41)**

A50808343 Clonal or not clonal? Investigating hospital outbreaks of KPCproducing Klebsiella pneumoniae with whole-genome sequencing. Clin Microbiol Infect. **(Bundle 27 Volume 17 document 42)**

A5088344 Seeking the source of Pseudomonas aeruginosa infections in a recently opened hospital: an observational study using whole-genome sequencing. (**bundle 27 Volume 17 document 43)**

A50883345 Environment agency – Methods for the examination of waters and associated materials (**Bundle 27 Volume 17 document 44)**

Scottish Hospitals Inquiry
Dr Christine Peters - Post Oral Evidence Statement - Glasgow 3 Hearing - 22 October 2024

1. The Inquiry Team has previously obtained a witness statement from you, and you gave evidence to the Inquiry on 11 and 12 September 2024.

2. After you gave evidence to the Inquiry, the Inquiry took evidence from Professor Alistair Leanord on 9 October 2024. During the course of his evidence, Professor Leanord discussed the use of the antibiotic, Meropenem. Reference was made to a presentation entitled 'Bacteraemia rates and Resistance Paediatric Haematoncology 2014-2018' which you gave along with Kathleen Harvey-Wood to haemato-oncology clinicians in 2018. Specifically, Professor Leanord referred to graph 12, which can be found at **Bundle 27, Volume 6, page 121.**

3. In addition, Professor Leanord also gave evidence to the Inquiry in relation to 'picks' during discussion of a sequencing report prepared by Professor Leanord and Derek Brown dated 18 January 2023, which can be found at **Bundle 6, page 1195.**

4. The Inquiry Team would be obliged if you would answer the questions in this supplementary questionnaire by 5pm Tuesday 22nd October 2024 at the latest.

5. Those responses will be issued to Core Participants.

Supplementary Questions for Dr Christine Peters

In 2018, you were a joint presenter of a PowerPoint presentation to haematooncology clinicians entitled 'Bacteraemia rates and Resistance Paediatric Haemat-oncology 2014-2018' (**Bundle 27, Volume 6, page 107).**

At **Bundle 27, Volume 6, page 121** there is a graph entitled 'Environmental Organisms, Antibiotic use and Antibiotic Resistance'.

In that regard:

Q1. Please briefly explain the purpose of preparing this graph.

A I prepared this graph as part of a piece of work I undertook as Clinical Lead for Microbiology for the RHC and QEUH in order to inform the Microbiology and clinical teams about the types of infection and resistance patterns we were seeing in the Haemato-oncology patient cohort. Emails surrounding these discussions have been submitted to the inquiry. This would be best practice for Microbiology input into specialist units and is not done often enough due to time resource limitations. The need arose to complement the work of Alison Balfour for the IMT on meropenem use, and the AMT committee which was looking at antibiotic use on

the unit. I also carried out a look back exercise for each of the patients involved in the early 2018 IMT as requested by the IMT looking at meropenem use in these specific patients. The concept of antimicrobial selection pressure is a very basic one in microbiology and was of course considered in the IMT. I decided to ask for the antibiotic use data from Pharmacy colleagues and put it together with the resistance data to understand the trends more fully. I aimed to chart the use of specific antibiotics and resistance patterns over time. I had previously done a similar extensive piece of work in Crosshouse as part of my AMR responsibilities there. Antimicrobial stewardship has been a core component of my practice and interest since early in my Microbiology training. I presented this graph and the following graphs to the ID and Haematology- Oncology Clinical teams and we discussed the information together as an MDT and agreed that the issue seemed to be a drive towards the use of broader spectrum antibiotics due to the organisms causing infections, rather than a simple inappropriate use of meropenem which resulted in selection of more resistant organisms. Infection Control is a key component of antimicrobial stewardship – the fewer infections the less the antibiotic needed and so key to reducing antibiotic use is excellence in infection prevention. I attach a full explanation of this work.

Q2. With reference to the graph, please provide a brief explanation of what it shows?

A In order to understand the graph it is important to understand the data that underlies it and how it was processed as well as the complementary graphs that were not included in the presentation but informed the discussions. Please see attached appendix on the work I did. Overall this graph demonstrates a complex of interactions of different antibiotic use on the back ground of a clear epi curve of rising environmental infections. The meropenem use is for all patients on 2A/2B, and not specific to those patients with the environmental organisms.

Q3. Please explain whether the graph supports the proposition that the prescription of Meropenem is a cause of the spikes in infections?

A I do not think the graph and the underlying data support the proposition that Meropenem prescription was causal for the spikes in infection for the time frame included. Firstly there is an increase in overall antibiotic use which increased in line with the number of positive cultures (previous graphs). This is expected – the more infections, the more antibiotics. Secondly, overall resistance of organisms increases at the same time as the increases in infections with the environmental organisms matched with increases in antibiotics – not after a time lag. Thirdly, it is important to note that the graph that Prof Leanord alluded to does not include Klebsiella as I had not included them in the environmental group (they are classed here as enteric, but I had run the analysis for all the groups separately) Fourthly, in charts of the meropenem use, the increase in Tazocin and Ciprofloxacin antibiotic resistance occurs contemporaneously with meropenem use. There are spikes in

meropenem use in 2015 and 2016 which are unrelated to increases in environmental cases and occurred prior to the QEUH team integrating into the paediatric microbiology service. The signal for increased meropenem use in 2018 was explored by an assessment of each case with an environmental bacteraemia and was not found to be associated with meropenem use in the time frame.

Q4. Are you aware of any published material which discusses this issue? If so, please identify it and if possible, attach copies or links to your reply.

A There is a vast and ever growing literature on the subject of antimicrobial stewardship and impact on HAI rates of infection. Infection prevention and antimicrobial stewardship are two sides of the same coin. Failures to prevent spread and transmission boost infection rates of resistant organisms and drive antibiotic use. Antibiotic use selects for resistance. see: *Llor and Bjerrum, 'Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem', Ther Adv Drug Saf, Vol. 5(6) 229–241 – 2014* **A50790514 (Bundle 27 Volume 17 Document 11**). There are many examples of this, however antibiotic restriction is not always associated with reduction in resistant infections see *Schuts et al, 'The Effect of Antibiotic Restriction Programs on Prevalence of Antimicrobial Resistance: A Systematic Review and Meta-Analysis', Open Forum Infectious Diseases - 2021**A50790512*** **(Bundle 27 Volume 17 Document 10)** Rises in HAI infections usually require a multipronged approach to prevention: *Balkhy et al, 'The epidemiology of the first described carbapenem-resistant Klebsiella pneumoniae outbreak in a tertiary care hospital in Saudi Arabia: how far do we go?', Eur J Clin Microbiol Infect Dis, Vol 31 901-909 - 13 January 2012* **A50790510 (Bundle 27 Volume 17 Document 3**) and *Modie et al, 'Outbreak of cephalosporin resistant Enterobacter cloacae infection in a neonatal intensive care unit', Archives of Disease in Childhood, Vol 62 148-151 – 1987* **A50790511 (Bundle 27 Volume 17 Document 8.** Multiclonal outbreaks of Stenotrophomonas can occur in the context of no meropenem selection pressure if there is a viable source delivering a high bio-burden: *Kazak et al, 'An evaluation of a Stenotrophomonas maltophilia outbreak due to commercial arterial blood gas collection kit', Antimicrobial Resistance & Infection Control, 13:53 - 20 May 2024* **A50790513 (Bundle 27 Volume 17 Document 7)**

Meropenem selection pressure is also complex with interesting studies demonstrating translocation from gut to lung for example of Pseudomonas, with the conclusion being prevention of colonisation being important to prevent translocation infection and resistance when on meropenem: *Wheatley et al, 'Gut to lung translocation and antibiotic mediated selection shape the dynamics of Pseudomonas aeruginosa in an ICU patient', Nature Communications, 13:6523 - 22 November 2022* **A50790515 (Bundle 27 Volume 17 Document 6)**

While antibiotic use is frequently identified as a risk factor for cases of infection in an HAI outbreak, this is never described as a lone factor, and in this patient cohort is basically a descriptor of the infected patient irrespective of cause. Notwithstanding this literature and theoretical basis for the contribution of antibiotic use in a given outbreak, I have not seen a published outbreak of a mixture of water borne organisms in a hospital location that has been concluded as being caused by Meropenem use, rather than the water as a source being the primary cause needing rectified.

In relation to 'picks' and the sequencing report prepared by Professor Leanord and Derek Brown dated 18 January 2023, which can be found at Bundle 6, page 1195, in the course of carrying out a DNA analysis, particularly by whole genome sequencing, one or more colonies or 'picks' will be selected for that process.

Q5. Are you aware of any published material which discusses the number of such 'picks' which should be used to ensure reliable results or conclusions? If so, please identify any such publications, and if possible, attach copies or links to your reply.

A I am aware that the number of picks from a plate is very important for analysing the genetic diversity of a species isolated from any clinical sample. This is particularly true for chronic infections such as the CF lung where a single sample can contain a number of strains, as well as varying SNP (single Nucleotide polymorphisms) differences eg regarding Pseudomonas see *Diaz Caballero, Julio et al. Selective Sweeps and Parallel Pathoadaptation Drive Pseudomonas aeruginosa Evolution in the Cystic Fibrosis Lung. mBio vol. 6,5 e00981-15. 01 September 2015* **A50804148 (Bundle 27 Volume 17 Document 32)** where 20 picks from a plate were taken – just to look at the diversity within one patient lung, or re Stemnotrophomonas used 24 colonies per sample of lung or sputa *Chung, Hattie et al. Global and local selection acting on the pathogen Stenotrophomonas maltophilia in the human lung. Nature communications vol. 8 14078. 19 Jan. 2017* **A5081028 (Bundle 27 Volume 17 Document 30**) and for Burkholderia cenocepacia – 40 colony picks per sputa is suggested to find the range of antimicrobial sensitivity alone – *Moore, John E et al. Case Report: The Conundrum of What to Pick? Antibiotic Susceptibility Variability in Burkholderia cenocepacia in Cystic Fibrosis: Implications for Antibiotic Susceptibility Testing and Treatment. Br J Biomed Sci, vol. 81 12749. 4.6.24* **A50804147 (Bundle 27 Volume 17 Document 31** In terms of environmental sampling this is even more important as it is likely that there are multiple lineages competing in different niches, and the numerical possibilities are many orders of magnitude greater than in the clinical setting. The water sampling pick numbers has been referenced in Dr Inkster's work: **Bundle 19, Page 1232.**

Declaration

I believe that the facts stated in this witness statement are true. I understand that proceedings for contempt of court may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief in its truth.

The witness was provided access to the following Scottish Hospital Inquiry bundles/documents for reference when they completed their questionnaire/ statement (Appendix A)

The witness verbally introduced or provided the following documents to the Scottish Hospital Inquiry for reference when they completed their questionnaire statement (Appendix B)

Appendix A

A50071192 - Bacteraemia rates and Resistance Paediatric Haemato-oncology 2014-2018 - Bundle 27, Volume 6, page 107

A50071192 - Environmental Organisms, Antibiotic use and Antibiotic Resistance - Bundle 27, Volume 6, page 121

A42401483 Report- Application of Whole Genome Sequencing Alastair Leanord and Derek Brown **Bundle 6 pg 1195**

Appendix B

Llor and Bjerrum, 'Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem', Ther Adv Drug Saf, Vol. 5(6) 229–241 – 2014 **A50790514 (Bundle 27 Volume 17 document 11**).

*Schuts et al, 'The Effect of Antibiotic Restriction Programs on Prevalence of Antimicrobial Resistance: A Systematic Review and Meta-Analysis', Open Forum Infectious Diseases - 2021****A50790512*** **(Bundle 27 Volume 17 Document 10**).

Balkhy et al, 'The epidemiology of the first described carbapenem-resistant Klebsiella pneumoniae outbreak in a tertiary care hospital in Saudi Arabia: how far do we go?',

Eur J Clin Microbiol Infect Dis, Vol 31 901-909 - 13 January 2012 **A50790510 (Bundle 27 Volume 17 Document 3**)

Modie et al, 'Outbreak of cephalosporin resistant Enterobacter cloacae infection in a neonatal intensive care unit', Archives of Disease in Childhood, Vol 62 148-151 – 1987 **A50790511 (Bundle 27 Volume 17 Document 8**).

Kazak et al, 'An evaluation of a Stenotrophomonas maltophilia outbreak due to commercial arterial blood gas collection kit', Antimicrobial Resistance & Infection Control, 13:53 - 20 May 2024 **A50790513 (Bundle 27 Volume 17 Document 7**)

Wheatley et al, 'Gut to lung translocation and antibiotic mediated selection shape the dynamics of Pseudomonas aeruginosa in an ICU patient', Nature Communications, 13:6523 - 22 November 2022 **A50790515 (Bundle 27 Volume 17 Document 6)**

Diaz Caballero, Julio et al. Selective Sweeps and Parallel Pathoadaptation Drive Pseudomonas aeruginosa Evolution in the Cystic Fibrosis Lung. mBio vol. 6,5 e00981-15. 01 September 2015 **A50804148 (Bundle 27 Volume 17 Document 32)**

Chung, Hattie et al. Global and local selection acting on the pathogen Stenotrophomonas maltophilia in the human lung. Nature communications vol. 8 14078. 19 Jan. 2017 **A50810282 (Bundle 27 Volume 17 Document 30**)

Moore, John E et al. Case Report: The Conundrum of What to Pick? Antibiotic Susceptibility Variability in Burkholderia cenocepacia in Cystic Fibrosis: Implications for Antibiotic Susceptibility Testing and Treatment. Br J Biomed Sci, vol. 81 12749. 4.6.24 **A50804147 (Bundle 27 Volume 17 Document 31)**

Scottish Hospitals Inquiry

Post Oral Evidence Statement

Susanne Lee

This statement was produced by the process of sending the witness a questionnaire with an introduction followed by a series of questions and spaces for answers. The introduction, questions and answers are produced within the statement.

In relation to 'picks' and the sequencing report prepared by Professor Leanord and Derek Brown dated 18 January 2023, which can be found at Bundle 6, page 1195, in the course of carrying out a DNA analysis, particularly by whole genome sequencing, one or more colonies or 'picks' will be selected for that process.

1. Are you aware of any published material which discusses the number of such 'picks' which should be used to ensure reliable results or conclusions? If so, please identify any such publications, and if possible, attach copies or links to your reply.

A. I cannot access the original work that was done in the Public Health Laboratory Service (which became the Health Protection Agency and now is part of the UKHSA. The Standing Committee of Analysts document , I hope you will find useful is currently being updated and I have received a copy form the Committee chair, you can see the proposed changes as tracked. I will send as an attachment in the email with this document. Whilst the document is labelled as archived on the gov.uk website this is because the funding and status of the SCA has changed and it has not become a charitable organisation.

I will also send some supplementary information and papers which support the need to take multiple picks, including where there have been multiple species

involved in causing patient infection. The point is that to confirm a source, if you have multiple colonies on a plate, you should continue to pick until you have a match or picked them all if there are low numbers, the one you don't pick may well be the match, or at least 30 to have a 95% probability that the isolate is not present. My statistical ability is rusty but a statistician with an understanding of water microbiology would be better able to explain Poisson distribution and overdispersion of microorganisms in water. there is a very good statistician at the UKHSA (Andre Charlett) with expertise in water microbiology statistics (this is necessary to understand the issues of overdispersal of pathogens in water i.e. unlike chemical hazards they are not evenly distributed and may only be present intermittently depending on water usage, pressure etc. causing release from biofilms).

In outbreak situations determining whether a source is the cause of infection is fraught with difficulties. Water Microbiology as stated above is not an exact science as evidence should be taken in conjunction with epidemiology including opportunity and extent of exposure. A failure to isolate the target organism does not mean that the organism is not or was not present at the time of exposure. For several reasons inlcduding:- .

1. Sampling introduces the largest error in any water sampling event, the timing of the sample is critical, to be able to represent the worst case scenario, i.e. the time at which a patient is most likely to be infected directly or indirectly, is after the outlet has not been used for several hours. Even a short flush (period of usage) can remove biofilm from the outlet which means samples taken after even a very short period of use may give a false negative.
2. The conditions and timing of transport to the laboratory and the time between sampling and analysis can also adversely affect the ability to detect a target organism they may go into a viable but not culturable state or die if the conditions are not appropriate

3. In treated water systems the target organism may be in a viable but non cultural form and so would not be detected on laboratory media , (there is still debate about whether VBNC organisms can recover and become virulent).
4. Processing the sample is also likely to reduce the number of target organisms as some will attach to the equipment, and / or be damaged by concentration methods.
5. Bacteria in samples are not evenly distributed, and
6. Samples mixing, whilst intended to break up clumps , may still release bacteria attached to particulate surfaces
7. Depending on the media used, high nutrient media can result in nutrient shock and affect recovery, or the organism may just not be able to grow in the selected media.
8. Background flora may compete with and mask the target organism on the culture plate
9. Flow dynamics have an influence on the sheer stresses within the pipework which can impact on when and if microorganisms are released from biofilms, pressure and flow changes are dynamic in a water system, depending on whether a number of outlets are being flushed, used, or parts of systems drained for remedial work as examples.

A further consideration is that the strain isolated from the patient for typing may not match the strains from the samples is that it is possible that the infection was caused by multiple strains.

Declaration

I believe that the facts stated in this witness statement are true. I understand that proceedings for contempt of court may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief in its truth.

The witness was provided access to the following Scottish Hospital Inquiry bundles/documents for reference when they completed their questionnaire/ statement. (Appendix A)

The witness verbally introduced or provided the following documents to the Scottish Hospital Inquiry for reference when they completed their questionnaire statement (Appendix B)

Appendix A

A50071192 - Bacteraemia rates and Resistance Paediatric Haemato-oncology 2014-2018 - Bundle 27, Volume 6, page 107

A50071192 - Environmental Organisms, Antibiotic use and Antibiotic Resistance – (**Bundle 27, Volume 6, page 121)**

A42401483 Report- Application of Whole Genome Sequencing Alastair Leanord and Derek Brown **(Bundle 6 page 1195)**

Appendix B

A53734014 Multiple Types of Legionella Pneumophilia - Journal of Clinical Microbiology
(**Bundle 27 Volume 16 document 8)**

A53734016 The Microbiology of Waters and Associated Materials (2017) - Practices and procedures for laboratories **(bundle 27 Volume 16 document 9)**

Scottish Hospitals Inquiry
Post Oral Evidence Statement
Kathleen Harvey-wood

1. The Inquiry Team has previously obtained a witness statement from you, and you gave evidence to the Inquiry on 18 September 2024.

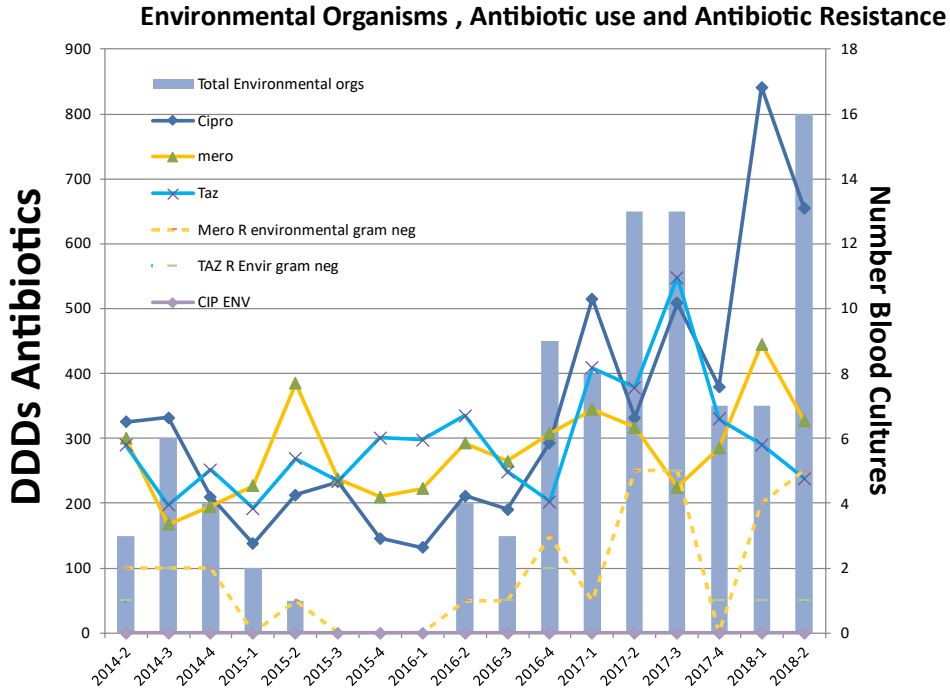
2. After you gave evidence to the Inquiry, the Inquiry took evidence from Professor Alistair Leanord on 9 October 2024. During the course of his evidence, Professor Leanord discussed the use of the antibiotic, Meropenem. Reference was made to a presentation entitled '*Bacteraemia rates and Resistance Paediatric Haemat-oncology 2014-2018*' which you gave along with Dr Christine Peters to haemato-oncology clinicians in 2018. Specifically, Professor Leanord referred to graph 12, which can be found at Bundle 27, Volume 6, page 121.

3. The Inquiry Team would be obliged if you would answer the questions in this supplementary questionnaire by 5pm Tuesday 22 October 2024 at the latest.

4. Those responses will be issued to Core Participants.

Supplementary Questions for Kathleen Harvey-Wood

1. In 2018, you were a joint presenter of a PowerPoint presentation to haemato-oncology clinicians entitled 'Bacteraemia rates and Resistance Paediatric Haemato-oncology 2014-2018' (Bundle 27, Volume 6, page 107). At Bundle 27, Volume 6, page 121 there is a graph entitled 'Environmental Organisms, Antibiotic use and Antibiotic Resistance'. In that regard: Please briefly explain the purpose of preparing this graph.



A. This graph titled "Environmental Organisms, Antibiotic Use and Antibiotic Resistance" in the power point presentation was prepared by Dr Christine Peters, Consultant Microbiologist.

I provided the data for the blood culture results and antibiotic resistance which was obtained from the laboratory telepath system. The DDD data was obtained from Isobel Gourley, Lead Antimicrobial Pharmacist, QEUH.

The graph covers a 4 year period from 2014 Q2 to 2018 Q2. It is prented as quarterly data. The period of 2014 Q2 to 2015 Q2 shows the results for a

year from Yorkhill Hospital before the move to RHC in June 2015.

The left hand axis shows the DDD's (Daily Defined Dose) this is the average standard dose of a drug (antibiotic) to treat an infection. The dotted yellow and blue lines show Meropenem and Tazocin resistant environmental gram negative organisms respectfully.

Right axis shows the number of environmental positive blood cultures which are represented as bar columns.

The aim of this graph was to examine trends of the usage of the antibiotics Meropenem, Tazocin and Ciprofloxacin and the development of antibiotic resistance.

The Meropenem data is for all Haem/Oncol patients and the positive blood cultures are only environmental organisms.

2. With reference to the graph, please provide a brief explanation of what it shows

A. I did not prepare this graph and do not have access to the "raw "data used to produce the graph. However, in answering the question, I have provided my interpretation with information that I have available and an explanation of what the graph shows.

The graph shows that there was a small spike of 6 environmental positive blood cultures in 2014 Q3. This coincided with a low level of Tazocin resistance and a switch to Ciprofloxacin seen as an increase in the DDD's. Of note this increase in environmental blood cultures was a spike which was controlled.

Meropenem and Ciprofloxacin usage was lowest when no infections as seen during the period 2015 Q3 (post move to RHC in June 2015) to 2016 Q1 as there were no environmental positive blood cultures.

During the period 2016 Q2 to 2017 Q2 &3 shows when infections started to rise, note this is an upward trend as noted in my witness statement (Paragraphs 112 and 113).
Tazocin resistance increased in 2017Q3 at the same time as the rise in the number of environmental positive blood cultures, so this meant a move to using Meropenem to treat the bacteraemia's.
The Haemo/Oncology antibiotic policy to treat infection first line antibiotics are Tazocin +/- Gentamicin (1).
If there is no clinical response, patient allergic to Tazocin, antibiogram of infecting organism/s are resistant to Tazocin, then Tazocin is switched to second line therapy antibiotic Meropenem. In some cases where patient is allergic to Tazocin then Meropenem is started as first line therapy.
Tazocin resistance is seen to fall 2017 Q4 and remains static at a low level.

Ciprofloxacin is used to treat environmental infections resistant to both Tazocin and Meropenem and also as a prophylactic antibiotic. Ciprofloxacin DDD increased due to prophylaxis usage related to the 2017 infections peak with a further increase in Ciprofloxacin DDD in 2018 Q1. However, there was no Ciprofloxacin resistance seen in the environmental organisms as shown in the flat line on the graph.

Meropenem DDD related to environmental infection decreased after the move to RHC and remained static, with a peak in 2018 Q1.
Meropenem resistant gram negative (yellow dotted line) highest during the period 2017 Q2 & Q3 and 2018 Q2.
The graph shows that in the period 2018 Q1 = 7 environmental positive blood cultures, 2018 Q2 = 16 environmental positive blood cultures.

In a previous graph from the PowerPoint presentation on page 120: "Total Blood Cultures, total resistant, total antibiotic use" shows the total number of positive blood cultures (Bundle 27, Volume 6, page 120, see also ref 2).
This graph shows that in 2018-Q2 there was a fall in resistance to all the antibiotics and total antibiotic DDD and the total number of positive blood

cultures were also reduced**.**
2018 Q1 = 42 which includes the March 2018 water incident correlating with the increase DDD use of Meropenem during 2018 Q1 (Jan - March 2018). The total number of positive blood cultures then falls in 2018 Q2 = 32.

3. Please explain whether the graph supports the proposition that the prescription of Meropenem is a cause of the spikes in infections?

A. My interpretation of the graph is that the prescription of Meropenem does not support the proposition that it is a cause of the spikes in infections.

Meropenem usage increased as a second line antibiotic in response to infections. Meropenem DDD use did fluctuate and was not on a continuous upward trend.

Meropenem was prescribed on a case by case basis and following antibiotic policy (1). If you look at Meropenem use 2018 Q1 DDD is 420, which falls during 2018 Q2 to 320.

Of interest in period 2018 Q1- 3 patients isolated Stenotrophomonas (all in March) from blood cultures and in period 2018 Q2 there was 3 patients isolated Stenotrophomonas maltophilia from blood cultures.
So, there is no increase in the incidence of Stenotophononas maltophilia infections due to Meropenem in 2018 Q2.

The spikes in infections were due to diverse environmental organisms and the infections were mixed ie polymicrobial which cannot be attributed to Meropenem alone.

Not all the environmental infections were Meropenem resistant organisms. Resistance can be influenced by other factors eg bacteria acquiring plasmids eg genetic – resistance genes, mutations. The high burden of environmental organisms increases the risk of infection and there was an

overall increase in environmental infections independent of the use of Meropenem.

2018 Q1 shows a peak of both Cipro DDD and Mero DDD so the usage of both antibiotics increased. This shows that the spike in infections is not due to the over prescribing of one antibiotic.

4. Are you aware of any published material which discusses this issue? If so, please identify it and if possible, attach copies or links to your reply.

A.

i. Management of Neutropenia and fever: antibiotic policy. (HAEM-ONC-003) **(Bundle 8, supplementary documents Hearing commencing 12th June 2023 document 4)**

ii. Bacteraemia rates and Resistance, Paediatric Haemat-Oncology, 2014- 2018 Report. Dr Christine Peters, Kathleen Harvey-Wood. (**Bundle 27 Volume 6 page 107)**

iii. Audit of Meropenem usage Haematology/Oncology patients RHC produced by Dr Alison Balfour, Consultant Microbiologist.

Declaration

5. I believe that the facts stated in this witness statement are true. I understand that proceedings for contempt of court may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief in its truth.

Appendix A

6. The witness was provided access to the following Scottish Hospital Inquiry bundles/documents for reference when they completed their questionnaire/ statement (Appendix A)

A43808275 – Management of Neutropenia and Fever ; antibiotic policy Bundle 8 Document 4

A50071192 - Bacteraemia rates and Resistance Paediatric Haemato-oncology 2014-2018 - Bundle 27, Volume 6, page 107

A50071192 - Environmental Organisms, Antibiotic use and Antibiotic Resistance - Bundle 27, Volume 6, page 121

Bundle of documents for Oral hearings commencing from 19 August 2024 in relation to the Queen Elizabeth University Hospital and the Royal Hospital for Children, Glasgow

Witness Statements – Volume 12

A50843863