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)**