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

Bundle 24 - Documents referred to in the Expert Report by Allan Bennett regarding Cryptococcus, and Supporting Documentation

Volume 3

SCOTTISH HOSPITALS INQUIRY

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SCOTTISH HOSPITALS INQUIRY

E: Brandon.Nolan[redacted]

Sent by email: Allan Bennett[redacted]

19th June 2024

Dear Mr. Bennett,

The Scottish Hospitals Inquiry - QEUH/RHC – Cryptococcus investigation Instructions to Mr. Allan Bennett

1. The Scottish Hospitals Inquiry would like you to produce a supplementary report following your main report of 5 May 2024 to address the question of whether the ventilation system in the QEUH/RHC in general and particular Wards 2A (before rebuilding), 4C, 4B and 6A contributed in any way to what appears to be an anonymous number of Cryptococcus neoformans that had connection to the hospital. It is hoped this can be produced promptly and issued to CPs of the Inquiry in mid July. Mr Bennett would speak to it when he gives evidence in November.

2. Mr Bennett is aware from his previous instruction that the Inquiry is interested in three key questions, these being:

1) From the point at which there were patients within the QEUH/RHC was the ventilation in an unsafe condition, in the sense that it presented an additional risk of avoidable infection to patients?
2) Are the water and ventilation systems no longer in an unsafe condition in the sense that they now present no additional avoidable risk of infection?
3) Is there a link, and if so in what way and to what extent, between patient infections and identified unsafe features of the water and ventilation systems?

3. In the past nine months the Inquiry Team has been investigating the extent of Cryptococcus cases and this note now sets out the extent of the current understanding of the Scope of this issue.

Scope

4. On 20th December 2018 an IMT chaired by Dr Teresa Inkster was *'called to discuss two cases of Cryptococcus neoformans in blood cultures from haematology patients'.*[1] Sandra Devine completed the HIORT, HIIAT was scored red. As described

[1] 20.12.2018 IMT Cryptococcus (A36605178)

below two patients in the QEUH/RHC (Patients A and B) died having contracted Cryptococcus neoformans on [redacted] 2019 and [redacted] 2018 respectively.

5. **Fifteen IMTs regarding Cryptococcus** took place between 20.12.2018 and 08.02.2019 inclusive. Dr Inkster chaired all 15 IMTs. Several actions were proposed in the IMTs, air samples take, with discussions taking place between Dr Inkster and Peter Hoffman of Public Health England (with Mr Hoffman agreeing regarding cleaning and wondering if there is potential structural issues which has allowed the ingress of pigeon faeces into the ventilation system[2]) and consideration of various hypothesis, with the only obvious source being identified as pigeons[3]. Key points from the IMTs:

(1) The potential for Cryptococcus to enter the hospital via the ventilation system was put forward in the IMT of 07.01.20219[4].
(2) Portable HEPA filers put in place in ward 6A between IMTs of 7th and 16th January 2019. Dr Inkster advised that *Cryptococcus Albidus* has been isolate in Wards 4C and 6A, and although a different strain also comes from pigeon droppings. Dr Elizabeth Johnston in Bristol suggesting that the most likely breach in the ventilation system and suggested this hypothesis be considered with duct work and HPV cleaning[5].
(3) The use of prophylaxis medication was introduced in 6A and subsequently in 4C[6].
(4) The issues of mould in 6A (shower seals broken – bases) contributed to higher particle counts in 6A even following HEPA being installed IMT 17.01.2019. Pigeons in plant room being considered here.
(5) Hypotheses were considered from the outset of the IMTs, with it being identified in the IMT of 20.12.2018 that the two patients did not have contact to each other[7].

6. A paper entitled **Review of *cryptococcocus* spp cases diagnosed in NHS Greater Glasgow and Clyde laboratories** was prepared by Dr Iain Kennedy on 10 January 2019.[8] It considered both Hospital Acquired Infections and Health Care Associated Infections. In considered a similar, but different mix of patients from the later report of the IMT Expert Advisory Sub Group.

7. The IMT was stood down by the Infection Control Doctor, Dr Inkster (Chair of the IMT) on 8th February 2024[9], with the final HIIORT taking place on 15th February 2019[10]. The IMT commissioned a review to investigate the hypotheses and any subsequent hypotheses, this review was conducted by the **IMT Expert Advisory Sub-Group** (the 'Sub-Group').

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[2] IMT meeting minute - Cryptococcus - 17 January 2019 - Part 2 PM (A36690599)
[3] 27.12.2018 IMT Cryptococcus (A36605180)
[4] 07.01.2019 IMT Cryptococcus (A36690566)
[5] IMT Meeting Minutes - Cryptococcus - 16 January 2019 (A36605168)
[6] Scottish Hospitals Inquiry - Bundle of documents for the Oral hearing commencing 12 June 2023 - Bundle 1 - Incident Management Team Meeting Minutes (IMT Minutes) alias (zA2177720)
[7] 20.12.2018 IMT Cryptococcus (A36605178)
[8] Review of cryptococcocus spp cases diagnosed in NHS Greater Glasgow and Clyde laboratories details - Objective ECM (scotland.gov.uk)
[9] [redacted]
[10] HIIORT 15.02.2019 (A37750823)

8. Prior to the Sub-Group beginning work on 19 January 2019 Scottish Government publicly announced that NHS GGC had revealed that two patients being treated in the QEUH/ RHC had died after contracting Cryptococcus, a fungal infection "caused by pigeon droppings" at the QEUH. That proposition has attracted considerable media attention.

9. GGC convened a Cryptococcus IMT Expert Advisory Sub-Group chaired by Dr John Hood to investigate on the current and any further hypothesis relating to the Cryptococcus incident within QEUH/RHC[11]. Members are named in TOR of the Sub-Group, with representatives from Health Facilities Scotland (HFS), Health Protection Scotland (HPS)[12], Public Health England, NHSGGC Estates and Facilities, Infection Control.

10. The meetings of the Sub-Group were recorded in the IMT Expert Advisory Sub-Group Minutes[13]. With the group sitting between 14th February 2019 and 14th January 2021 inclusive. The seven main hypotheses, as highlighted in of the Cryptococcus IMT Expert Advisory Sub-Group as developed throughout the course of the meetings can be summarised as follows:

1) Plantroom Air
2) Outside air source
3) Lack of 'Protective Isolation'
4) Cylinder Room in PICU
5) Helipad
6) Specimen Transport System (POD)/Pneumatic Tube System
7) Dormancy/ Reactivation

With other areas of concern being the roof vegetation and garden; pressure differentials between Ward 4B and 4C, and the proximity to sewage and refuge works (but this was dropped from discussion relatively early on). A member of the Inquiry Staff has produced a comprehensive summary of the sub-group and its the hypotheses which is offered for further consideration.

11. A report of the sub-group's findings was requested by the Chief Executive[14], with the final report being produced 5th April 2022[15]. This report was not a report of the sub-group but rather a report of NHS GGC, with NSS not endorsing the report[16], as will be discussed later.

12. The Sub-Group report is also summarised in PPP5 at para 7.15[17].

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[11] IMT Expert Advisory Sub Group - Draft Terms of Reference (A39234207)
[12] It is understood that HPS and HFS come under the umbrella of NHS National Service Scotland (NSS), and their involvement will hereinafter be referred to as NSS.
[13] Scottish Hospitals Inquiry - Hearing Commencing 19 August 2024 - Bundle 9 - QEUH Cryptococcus Sub-Group Minutes (External Version) (A47175206)
[14] IMT Expert Advisory Sub-Group Minutes - Cryptococcus - 9 August 2019 (A39233902)
[15] Report prepared by Cryptococcus IMT Expert Advisory Sub-Group dated 5 April 2022 (A39235063)
[16] https://erdm.scotland.gov.uk/documents/A43637755/details
[17] PPP 5 - QEUH Campus - History of Infection Concerns (HOIC) NHS Greater Glasgow and Clyde Response - 21 April 2023 (A45285823)

13. The Sub-Group report concludes that it is unlikely that the case-patients contracted Cryptococcus neoformans infection while in the QEUH/ RHC.

14. The Inquiry Team understands that Cryptococcus neoformans is a species of fungus; an encapsulated yeast that can live in both plants and animals. It is often found in bird excrement, and it can cause disease in apparently immunocompetent as well as immunocompromised human hosts. While it is associated with pigeons and their droppings, it can be found elsewhere. Infection with Cryptococcus neoformans is rare (perhaps 19 cases in a ten-year period over all of GGC Health Board[18] or 20 cases in Scotland in a ten-year period in Scotland[19]). There are other species of cryptococcus. Cryptococcus neoformans has not been isolated in the hospital environment but apparently the organism is difficult to culture.

15. At the time when the sub-group convened there were two cases from QEUH/RHC which were the focus of the sub-group following the IMT of 20th December 2018. Two cases of Cryptococcus neoformans were reported in December 2018 in patients with [redacted] cancers, [redacted] (Patient A) and [redacted] (Patient B). In each case the patient died, [redacted] Patient A was cared for in Ward 4C Patient B was cared for in Ward 6A.

16. Patient A was an adult patient, '*admitted to Ward 4C,* [redacted] *had a positive blood culture after 3 weeks admission. Patient was* [redacted] *cancer treatment*'[20].

17. Patient B was a paediatric patient, [redacted]. Patient B was admitted to Ward 2A on [redacted].2018 and remained there in [redacted] room until moved to Ward 6A on [redacted] 2018 as part of the Ward 2A decant. Patient B transferred to PICU on [redacted].2018[21]. Patient B died [redacted] 2018. '*A* [redacted] *postmortem was carried out as the cause of death was not clear, postmortem tests found that the patient was positive with Cryptococcus neoformans which had spread all over the body with positive CSF, splenic aspirate and lung fluid. Samples from the postmortem match the blood culture samples taken from the patient prior to death*'[22].

18. [redacted]

19. At the time of the first meeting of the sub-group on 14th February 2019, Dr Hood commented that both cases were linked in time and place, there are clear issues of pigeons around the hospital, he acknowledged that 'we are growing Cryptococcus albidus (a surrogate for Cryptococcus neoformans) in the air in different wards of the

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[18] Review of *cryptococcocus* spp cases diagnosed in NHS Greater Glasgow and Clyde laboratories, 10 January 2019
[19] A36605180, IMT 27 December 2018, Bundle 1, page 251
[20] 20.12.2018 IMT Cryptococcus (A36605178)
[21] 20.12.2018 IMT Cryptococcus (A36605178)
[22] 20.12.2018 IMT Cryptococcus (A36605178)
[23] Scottish Hospitals Inquiry - Hearing Commencing 19 August 2024 - Bundle 9 - QEUH Cryptococcus Sub-Group Minutes (A45379981) p5

hospital, including the wards'[24] patients A and B were in and the plant rooms serving the wards, risk present to both patients, no HEPA or positive pressure rooms, neither had optimal anti-fungal prophylaxis for cryptococcus. Dr Hood considered that Patient A might be a re-activation, due to being [redacted]

20. NHSGGC contend that these are the only two confirmed cases/infections in patients at QEUH/RHC between 26.01.2015 and 12th April 2024[25].

21. The Inquiry's investigations provide the following understanding of Cryptococcal infections from 2015 to 2020 at QEUH/RHC. The Inquiry considers that there may be seven potential cases with 5 potentially being epidemiologically linked to QEUH/RHC:

1) Patient A
2) Patient B
3) H1 – QEUH for 5 days Ward 8D from [redacted]11.2017 to [redacted].12.2017 – tested positive for Cryptococcus Neoformans on at [redacted] on [redacted]08.2018[2627]. [redacted].
4) H2 - [redacted]/08/2018 – [redacted] patient presented in [redacted] QEUH admission in April 2018 for 2 nights 11A[2829]
5) Patient C – paediatric patient – [redacted] Admitted to RHC/QEUH from [redacted]/1/20[redacted]. In a variety of wards (6). Culminated on [redacted] July 2020 [redacted] Issue was positive serum CrAg (1:5) late June to late August 2020. NB CSF CrAg always negative. At least one paper suggested that any level <1:8 would count as negative.

22. It seems possible that Patients H1 and H2 are the [redacted] cases referred to at the foot of page 2 of the 'Review of *cryptococcocus* spp cases diagnosed in NHS Greater Glasgow and Clyde laboratories' prepared by Dr Kennedy on 10 January 2019 and also appear in the righthand 2018 column in Figure 1 in the Sub Group Report[30] albeit that in Dr Kennedy's report he does not appear to be aware that H1 and H2 had previous admissions to QEUH.

23. Further discussion will take place with CLO (who represent NHS GGC) and a further RFI regarding epidemiologically linked cases will be issued to CLO in early course.

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[24] Scottish Hospitals Inquiry - Hearing Commencing 19 August 2024 - Bundle 9 - QEUH Cryptococcus Sub-Group Minutes (A45379981) p6
[25] SHI RFI 26 Cryptococcus RESPONSE 2024-05-01
[26] Scottish Hospitals Inquiry - Hearing Commencing 19 August 2024 - Bundle 9 - QEUH Cryptococcus Sub-Group Minutes (A45379981) – Sub-group IMT 26.11.2020 p286
[27] Spreadsheet provided to Inquiry by Dr C Peters
[28] Scottish Hospitals Inquiry - Hearing Commencing 19 August 2024 - Bundle 9 - QEUH Cryptococcus Sub-Group Minutes (A45379981) – Sub-group IMT 26.11.2020 p286
[29] Spreadsheet provided to Inquiry by Dr C Peters
[30] Bundle 6: Page 1124

24. In respect of patient C's case it was the subject of the IMT of 2nd July 2020[31], this sets out [redacted] admitted to RHC for [redacted] discharged on [redacted]03.2020 and then was in and out for treatment, on around [redacted]6.2020 routine screening picking up the Cryptococcus (it was a faint positive and there was discussion with regards to false positives – it did in fact turn out to be positive). Child was treated for Cryptococcus and subsequently discharged. An IMT took on 02.07.2020 detailing the incident, Professor Leanord chaired the meeting, with the hypothesis being Environmental – community or hospital; Testing – false positive; Activation of previous latent infection. A HIIORT (02.07.2020) followed in line with Annette Rankin's guidance[32]. The IMT was closed by email dated 9th July 2020[33] [34] The Inquiry understands that [redacted] case is referenced in the HCAI of 10.07.2020 marked as being dealt with and closed[35]. It should be noted that Christine Peters disputed the accuracy of the IMT minutes and the closing the IMT appears to sit contrary to this despite Dr Peters raising the matter on 3rd July 2020, 6 days prior to IMT being closed[36]. Further, matters were raised regarding the suggestion of the testing being a false positive[37]With Dr Elizabeth Johnston from the Lab in Bristol emailing on 7th July 2020 to advise:

> *'I cannot be definitive that these represent false positives, although it is likely and they are less than proof of infection. If the patient does deteriorate and reveals further evidence of cryptococcosis then as you know the first-line treatment would be an initial course of amphotericin B plus flucytosine, followed by long-term fluconazole.*

25. [redacted] responded advising the recipients that the CRAG was repeated on 13.07.2020, and the results were positive in the QEUH lab. This is supported by Dr Sastry's statement that the case was positive and subsequent emails within QEUH regarding the case[38].

26. The Inquiry understands that no further escalation was made in respect of the changing position regarding results for patient C.

27. NHSGGC has not acknowledged this as being a potential case for the purposes of the recent RFI response[39].

28. With regards Patients H1, H2 and Patient C Dr Peters emailed Dr Hood on 23rd September 2020 raising the issue of there being 5/6 case with epidemiological links to QEUH/RHC[40] There is further email correspondence from Dr Inkster to Dr Hood

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[31] IMT 02.07.2020
[32] HIIORT 02.07.2020
[33] Email from Gillian Bowskill to HPS Infection Control NSS team and others providing HIIORT 09 July 2020 - Cryptococcus - HIIORT Ward 6A incident closed - dated 9 July 2020
[34] HIIORT 09.07.2020
[35]HCAI 10.07.2020
[36] Email from A Wallace to C Peters re IPC Sector Reports - 03.07.2020 - 06 July 2020
[37] Email chain - Christine Peters, Kathleen Harvey-Wood, Elizabeth Johnson and [redacted] - Cryptococcal lab results - 6 July to 13 July 2020 (A48304896)
[38] Email chain - Tom Steele, Jennifer Rodgers, Angela Wallace and other NHS GGC staff - IMT Ward 6A Draft Notes of Meeting - 2 July 2020 - Cryptococcus - [redacted] 8 July to 13 August 2020 - Original NHS GGC name - Acrobat Document 35
[39] SHI RFI 26 Cryptococcus RESPONSE 2024-05-01
[40] Email from C Peters to J Hood and others re Cryptococcal cases in Glasgow - 23 September 2020

regarding her concerns surrounding the Cryptococcus case in patient C and patient A[41]. With Dr Peters subsequently carrying out her own investigations and reporting her concerns to Dr Inkster[42] [43]. In doing this Dr Peters raises concerns regarding the air quality in ward 4C being inferior to the equivalent accommodation at the Beatson.

29. The concerns of Dr Peters and Dr Inkster were discussed at the sub-group meeting of 26 November 2020[44]. At which Dr Hood reports that Drs Inkster and Peters believe that two of the cases (H1 & H2) that were believed to be community-acquired are in fact two further QEUH acquired cases. This is on the basis that H1 was in the QEUH for 5 days, in Ward 8D from [redacted]11/17 to [redacted]12/17. H2 was in QEUH for 2.5 days, in Ward 11A from [redacted]/4/18 [redacted] H1 had a positive blood culture with C. neoformans on [redacted]8/18, i.e. 9 months and 1 week later. H2 had a positive blood culture on [redacted]/8/18, i.e. 4 months and 3 weeks later. The IMT further narrates that CP and colleagues also believe there is another child case (C2). [redacted] Admitted to RHC/QEUH from [redacted]/1/20 [redacted] In a variety of wards (6). Culminated in [redacted] July 2020 with [redacted] Issue was positive serum CrAg (1:5) late June to late August 2020. NB CSF CrAg always negative. At least one paper suggested that any level <1:8 would count as negative[45]. The second last sentence sits contrary to the statement of [redacted] referred to in paragraph 18.

30. Of the five potential cases, patient A and patient B are referred to in the final report, as are possibly H1 and H2, being described as community acquired.[46] The case of patient C is not referred to or considered despite being discussed in meetings of the sub-group.

NSS did not endorse the final report of the sub-group

31. NSS has provided an RFI response to the Inquiry[47]. Through the response are various email links and chains of emails detailing the discussion which took place between NSS members of the Cryptococcus sub-group and NHSGGC members between 16.08.2019 and 10.05.2022. NSS reasoning for not approving the final report can be summarised as follows:

(1) NSS had a number of concerns about how the work of the group was documented and recorded[48].
(2) Version control for minutes was confusing and there were examples of when minutes did not reflect discussion at the group meetings[49].

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[41] Email from C Peters to T Inkster re Cryptococcus - 01 October 2020 (A46157888) *not put to EG.
[42] RE_ Emailing_ CryptococcusInBCs.eml
[43] Email from C Peters to T Inkster re Cryptococcus - 01 October 2020 (A46157888) *not put to EG.
[44] Scottish Hospitals Inquiry - Hearing Commencing 19 August 2024 - Bundle 9 - QEUH Cryptococcus Sub-Group Minutes (A45379981) – Sub-group IMT 26.11.2020 p286
[45] Scottish Hospitals Inquiry - Hearing Commencing 19 August 2024 - Bundle 9 - QEUH Cryptococcus Sub-Group Minutes (A45379981) – Sub-group IMT 26.11.2020 p286
[46] Report prepared by Cryptococcus IMT Expert Advisory Sub-Group dated 5 April 2022 (A39235063)
[47] NSS response to Q2 RFI Cryptococcus
[48] Email 4 - 9.03.21 RE URGENT - Notes of Cryptococcus IMT Expert Advisory Sub-Group for return comments by 19th March
[49] Email 4 - 9.03.21 RE URGENT - Notes of Cryptococcus IMT Expert Advisory Sub-Group for return comments by 19th March

(3) A position paper had been developed for presentation to HSE which NSS were concerned did not reflect conclusions by the group[50].
(4) Papers then submitted to the NHSGGC board were found to contain incorrect statements about the work of the group and the conclusions associated with the hypotheses[51].
(5) No version control of the draft reports or documentation of Sub-Group members' comments and whether they had been accepted or declined, and the basis for the decisions[52].
(6) Within the report NHSGGC included data on cases that NSS had no knowledge of and actions that NHSGGC had taken outwith the Sub-Group[53].

32. In a final email exchange between NHSGGC and NSS dated 8th April 2022 NSS advised that the title of the report 'Report from the Cryptococcus Incident Management Team Expert Advisory Sub-Group" is not a true reflection of the authors, and we had previous assurance that this was a NHSGGC report on the finding of the sub group."[54]

33. Points 1,3,4 and 6 are concerning insofar as there appeared to be confusion regarding recording of the meetings, accuracy and agreement on information and conclusions reached. This should be a matter for further consideration by Mr Bennett when considering the Sub-Group.

Previous investigations prior to the Inquiry

34. The Independent Review Group (IRG) concluded there "is not a sound evidential basis on which to make a link between their infection, subsequent deaths, and the presence or proximity of pigeons or their excrement" (see report paras 8.29 and 8.30)[55]. The Review referenced a study commissioned by the QEUH Estates team and carried out by specialists at Quesada Solutions Ltd which used computer simulations to analyse airflow around the rooftop helipad, beneath which pigeons had roosted. That conclusion is challenged by Dr Peters.

35. The Oversight Board final report[56] notes at para 149 that, following reporting of the Cryptococcus incident in January 2019, the Board requested regular updates on air sampling at subsequent meetings but neither the OB nor the CNR further investigated these cases.

Infection Link Report – Dr Mumford and Dr Dempster

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[50] Email 15 SD15
[51] Email from Anne Rankin - Cryptococcus updates within NHS GGC board papers
[52] Email from Anette Rankin - re Patient Sensitive Information Draft 15 Crypto Report
[53] Email 6 04-11-2021 (LI to SD) Cryptococcus Report
[54] Open A48189662
[55] Queen Elizabeth University Hospital Independent Review Report - June 2020 (A32385767)
[56] QEUH Oversight Board - The Queen Elizabeth University Hospital Oversight Board Final Report - final copy from APS (A43572369)

36. Dr Mumford and Dr Dempster prepared the Expert Report 'Review of the Link Between Patient Infections and Identified Unsafe Features of the Water and Ventilation Systems at QEUH/RHC' date of submission 24 May 2024[57].

Confidentiality

37. The Sub-Group report is described as "Confidential Not for Onward Distribution Final Draft 05/04/2022". It contains detailed patient information. However, a redacted version has been made available to Core Participants in Bundle 6, page 1115.

38. The Sub-Group's report is relied on by GGC in its response to PPP5 and is cited at footnote 7. It is also referred to in Sandra Devine's Summary of Patient Safety Indicators which is appended to the GGC Positioning Paper 2. Obviously patient confidentiality must be observed, at least in respect of clinical details, [redacted]

39. The second child patient has not been published in the media, but redactions have been made to IMT previously published and efforts are being made to find the child's family. It is relevant that this is a child case though given the rarity of cryptococcus in general, but in particular in children.

Proposed report

40. Mr Bennett is asked to prepare a short report that addresses the following specific questions and also gives his opinion in respect of the three key questions identified at paragraph 2 of this Note.

1) **Risk Assessment and Infection Link.** The Inquiry Team appreciates that it may not be possible to provide a complete answer to these questions, but a partial answer that addresses the scale of any risk to patient safety in this context or the probability (however expressed) in an infection link would be of assistance. Such an expression of associations, connection or causation should, of course, be accompanied by a discussion of the issues that arise when a retrospective answer to these questions is sought many years after the event and when the possibility of further investigation has passed.

2) **Whether these cases were remarkable in any way**. The Inquiry Team understands that having even one Cryptococcus neoformans case in a hospital in a period of a few years is unusual. If Mr Bennett can provide information about the frequency in which the infection occurs in the population, in hospitals or even in particular patient groups, like HIV patients that would be of great assistance.

3) **Methodology.** In addition to the issues raised by NSS we would welcome Mr Bennett's comment on the methodology of the Sub-Group report in of itself and in contrast to that of Dr Kennedy's January 2019 review. What are the advantages and disadvantages in considering only confirmed infections in the

[57] Qualitative Infection Link Expert Report by Sara Mumford and Linda Dempster - 24 May 2024 - External version (A48460335)

hospital (or HAIs in a pure sense) or widening considering to include HCAIs or unconfirmed infections when trying to understand whether there is a link between the hospital environment and any particular infections? In addition, does any issue arise from what appears to be an ignorance by the Sub-Group of the Patient C case from 2020 or a decision not to consider it for some reason (perhaps because it was ultimately considered to be a 'false positive'). Does Mr Bennett have any other comment on the methodology adopted by any of the groups or individuals who have considered these cases and their connection with the environment.

41. In his report Mr Bennett should seek to avoid mentioning patient identifying information or where aspects of any patient's treatment except where they have to be mentioned because they impact his conclusion and, in that case, he should minimise the references so as to reduce the need for his report to be redacted.

42. It is intended that this Note should (after being redacted) be made available to CPs along with his report.

43. Mr Bennet should take care to explain how any views or opinions he expresses in his report lie within the scope of his own experience and expertise and the extent to which his opinion is based on reliable body of evidence or experience.

Expert report – structure and contents

The expert report should identify historic concerns; assessment of risk in relation to those; and assessment of whether such risk has been successfully remedied and should address the following:

Legal

44. Your CV should be appended to the report or narrated within the report (knowledge, qualifications, experience etc).

45. Any assumptions made in the report should be set out at the beginning of the report. It should also be stated how reasonable or likely it is that the assumption is correct.

46. If you have been provided with any documentation by inquiry team then that should be set out in the report and also appended to the report.

47. Any publications or material used by you to reach a conclusion should be listed at the beginning of the report and also appended to the report.

48. You should make clear which facts stated are within your knowledge. Where there are material facts in dispute, you should express an opinion on each version of the facts. No preference should be expressed for one version over another unless due to experience you consider one version to be less probable. In such circumstances a view should be expressed, and reasons given for it.

49. You should explain if the report is provisional, qualified and whether any additional information is required.

50. Your report should include a glossary of significant technical terms.

51. Where any tests of a scientific or technical nature have been carried out, the methodology used should be stated in the report.

52. If a particular issue or question falls outwith your expertise, then that should be made clear in the report.

53. If there is insufficient data to reach a concluded view then that should be stated in the report.

54. Your report should acknowledge that primary duty of expert is to the Inquiry to enable informed findings to be made. The expert should also acknowledge that they have prepared their report consistent with any applicable professional code of conduct.

55. The duties of an independent expert are as set out in ***National Justice Compania Naviera SA v Prudential Assurance Company Limited*** [1993] 2 Lloyds Rep 68 – (The Ikarian Reefer) which are set out in Appendix 1. In this case the duty is owed to the Inquiry as opposed to a court.

Yours sincerely

[redacted]

Assistant Solicitor to the Scottish Hospitals Inquiry for
and on behalf of,
The Rt Hon Lord Brodie KC PC,
Chair of the Scottish Hospitals Inquiry

Scottish Hospitals Inquiry

UKHSA Rule 8 response

In respect of the following information from the National Infection Services regarding the positive test results for Cryptococcal infections for all or any hospitals within the United Kingdom between 26th January 2015 to date:

Rule 8 Information request
1. Confirmation of the total number of positive test results for *Cryptococcus neoformans* cryptococcal infection(s) from hospitals within the UK between 26th January 2015 to date, to include both CRAG positives and culture positives;
UKHSA response
UKHSA does not collate standardised data related to Cryptococcal infection episodes from hospital laboratory reports as this is not a notifiable disease. However, what we can provide as a guide is the numbers of isolates of Cryptococcal species neoformans and previously designated Cryptococcal species received by the UKHSA Mycology Reference Laboratory (MRL). The MRL provides diagnostic, surveillance, and consulting services for the management of fungal infections to UK hospitals. It manages the National Collection of Pathogenic Fungi and provides fungal identification and susceptibility testing, full range of fungal biomarkers, microscopy and histological slide analysis and culture. There are a number of caveats to this data: 1. The UKHSA Mycology Reference Laboratory will not receive isolates from all patients with cryptococcal infection; for some patients there will be no isolates obtained and for others the local and regional mycology/microbiology laboratories will be able to deal with the samples without involving the reference laboratory. In some cases there may be multiple specimens received by the laboratory related to sequential sampling of the same patient with the same infection. Furthermore, the data within each dataset has been de-duplicated as far as possible, but not between data sets. 2. Cryptococcal antigen testing is a simple test that can often be conducted locally by non-specialised laboratories so positive results with this test reported by or known to UKHSA will be an underestimate of total cases in the UK. A positive result is highly suggestive of an infection with *Cryptococcus neoformans* or *Cryptococcus gattii* but cannot distinguish between them. It will not detect infection with *Naganishia* species. This test is frequently repeated on patients over time to monitor the response to treatment. 3. This means that the data sets cannot be used to provide a comparative test rate by region because different hospitals will use and report tests in different ways.

4. The *Naganishia* species isolate results have been included as these were previously classified as *Cryptococcus* species and were the only species found in the extensive environmental sampling carried out by [redacted] in 2019 and 2020. The substantial numbers of environmental isolates have been noted in Table 1 b; all the other isolates from this genus were from possible superficial infection sites, but unlike the true cryptococcal species they would very rarely cause deep infection. The *Cryptococcus neoformans* and *Cryptococcus gattii* isolates are almost exclusively from blood or cerebrospinal fluid (CSF) samples so represent deep infection.

The number of isolates sent for identification and susceptibility testing is outlined in Table 1 below:

Table 1: Isolates of *Cryptococcal* species and previously designated *Cryptococcal* species received by the UKHSA Mycology Reference Laboratory from 04 October 2016 to 11 June 2024.

Year	*Cryptococcus neoformans*	[redacted]	*Naganishia diffluens*	*Naganishia albida*
2016 (Oct–Dec)	12		<5#	
2017	35		8	
2018	37	<5#	7	
2019	38		81*	5**
2020	30	<5#	14***	<5#
2021	30	<5#	5	
2022	28		8	
2023	29		14	
2024 (Jan–June)	8	<5#	9	

#to reduce deductive disclosure all numbers less than 5 are presented as <5 in alignment to public reporting of surveillance data for rare infections
***** Including 66 environmental isolates from [redacted]
** all environmental isolates from [redacted]
*** including 4 environmental isolates from [redacted]

The numbers of serum and CSF samples that test positive for cryptococcal antigen is outlined in Table 2 (below):

Table 2: Positive cryptococcal antigen tests conducted by the UKHSA Mycology Reference Laboratory from October 2016 to June 2024

Year	Serum	CSF	TOTAL
2016 (Oct–Dec)	15	9	24
2017	29	10	39
2018	27	13	40
2019	34	19	53
2020	39	16	54
2021	34	8	42
2022	39	13	52
2023	39	15	54
2024 (Jan–Jun)	32	5	37

These are different and probably overlapping data sets as in some cases cultures may be sent subsequently from patients who have positive antigen test results, and antigen test results may be used to monitor response to therapy. Results are only available from the current UKHSA Laboratory Information Management System (LIMS) which was introduced in October 2016.

2. Confirmation of the hospital from which each positive test results is from

UKHSA response

Disclosing that a particular hospital sent a sample on a particular date could identify the patient (and in doing so, the nature of their infection) given that these are rare infections. Whilst UKHSA wishes to support the inquiry in their investigations, following formal legal advice, UKHSA considers that the information requested is sensitive and should we disclose, may lead to a risk of deductive disclosure of Confidential Patient Information. For disclosures of CPI to be lawful it is necessary to comply with both UK GDPR and the common law duty of confidentiality and apply the Caldicott Principles where any sharing of CPI is intended.

3. Confirmation of which strain of cryptococcal infection is present in each culture result
UKHSA response
Information on strain type is not routinely collected.

Review of *cryptococcocus* spp cases diagnosed in NHS Greater Glasgow and Clyde laboratories

Background

Two cases of *Cryptococcus neoformans* were detected in inpatients at Queen Elizabeth University Hospital within 17 days in late [redacted] 2018. Given the unusual nature of the pathogen, and time, place, person links between the cases, the public health protection unit undertook to review case of *Cryptococcus* in the Greater Glasgow and Clyde area.

In the absence of specific criteria for fungal infection, in this document hospital acquired (HAI) and healthcare associated (HCAI) infections definitions used are from the Health Protection Scotland SAB guidance.

Due to small numbers and inclusion of clinical details, there is a possibility of deductive disclosure, and therefore this document should not be shared outwith the IMT

Search Strategy

ECOSS, the national laboratory data system, was interrogated for all positive results for *Cryptococcus* spp. for all specimen types, detected in GRI, SGH or RAH microbiology labs, for the 10 year period between January 2009 and December 2018

Results

Unless otherwise stated, results are for *Cryptococcus neoformans.* Due to the small numbers, data should be interpreted with caution.

A total of 37 unique patients were identified.

The following exclusions were applied:

- 11 faecal samples, where patient had diagnosis of cryptosporidiosis (an unrelated parasitic gastrointestinal infection)
- 6 cases where the sample was referred from another Board area
- 1 case where the diagnosis of *Cryptococcus albidus* was later changed to *Candida albicans* following reference lab testing.

Limited additional information available in the electronic case record for some patients.

Summary (n=19)

Cases were predominantly male (14/19, 74%), and median age was 53 (range 1 year to 80 years)

Specimens were predominantly from normally sterile sites – blood and/or CSF (some cases had positive results from more than 1 sample type) – with one case having positive sample from peritoneal dialysis fluid (described further below). Two cases had samples from non sterile site – mouth swab, wound tissue.

Mortality in this patient group was 32% at 30 days and 47% at 60 days, though only a proportion of these deaths are attributable to *Cryptococcus* infection.

Epicurve

The chart below demonstrates that distribution of cases over time.

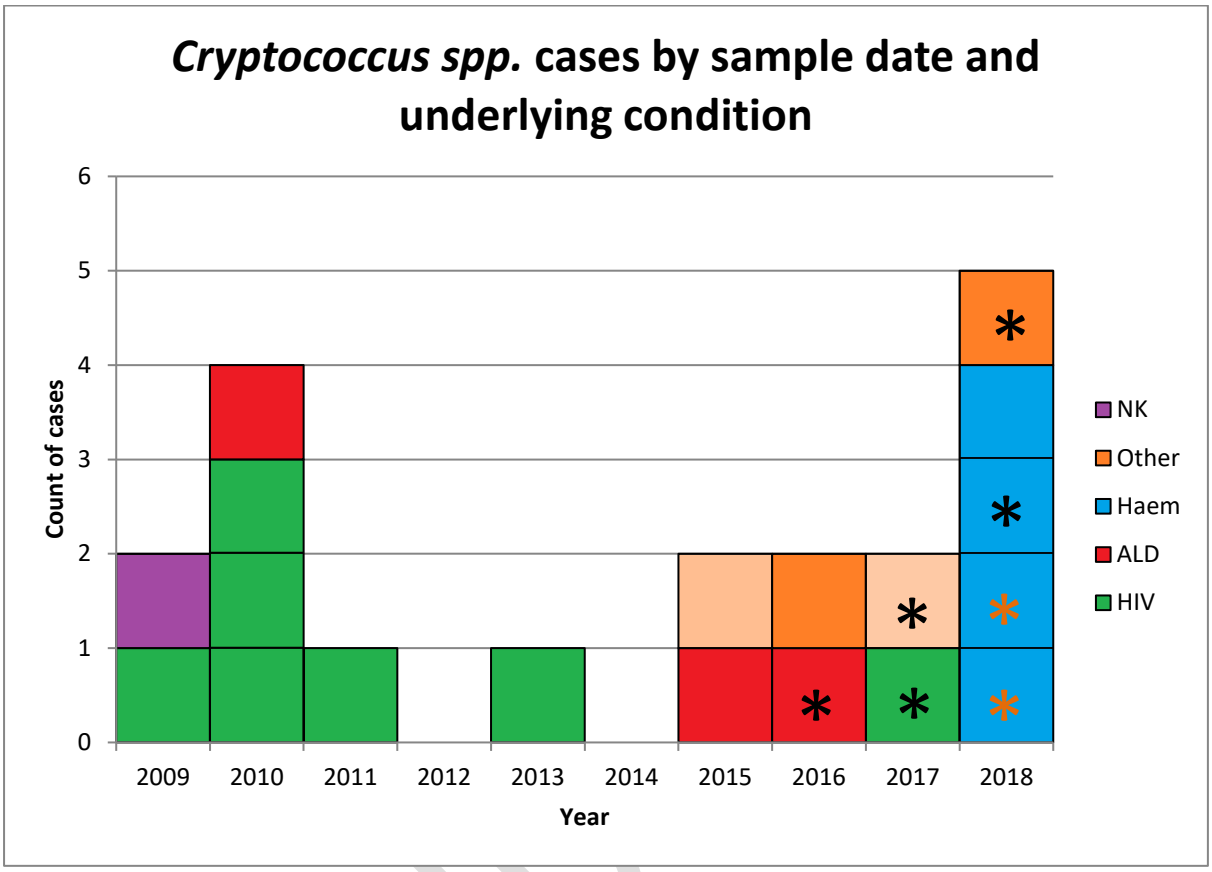


Figure 1. Each box=1 case. Lighter shaded boxes indicate species other than *C. neoformans*. Cases marked '*' meet definition for hospital acquired or healthcare associated infections. See Text for details

Case details

Two patients met criteria for HAI. Five patients meet criteria for HCAI: 3 had outpatient/community venepuncture; 2 had more significant invasive interventions.

HIV

Cryptococcus infection is a well documented infection in patients with HIV. One patient had venepuncture within 30 days of sample date, meeting the HCAI definition.

Haematology

The two HAI cases with underlying [redacted] are well known to the IMT and are not further described here. They are the only two cases with recent inpatient management in QEUH/RHC.

The other two [redacted] cases both had [redacted]. Both had recently ceased treatment [redacted]. The regular care of both patients was at GGC sites other than QEUH

The first of these patients had gone on to develop [redacted] shortly prior to their *Cryptococcus* diagnosis, and had a [redacted] 24 days prior to sample date, meeting the HCAI definition.

The other patient had a [redacted]) at QEUH approximately four months prior to sample date.

Alcoholic liver disease

One patient meets HCAI criteria due to venepuncture within 30 days prior to sample date. No other relevant information for these patients in electronic record.

Other

- Paediatric [redacted]. *C. Curvatis* one of four organisms isolated from peritoneal fluid during one of the admissions for peritonitis. Meets HCAI definition.
- Patient referred for [redacted] Respiratory sample positive for enterovirus. Mouth swab had light growth of *C. Lauretti* along with two candida species. Clinical significance likely to be limited.
- Adult patient, fit and well. Soft tissue from infected wound following accidental penetrating injury (hand tool driven into finger) positive for *C. neoformans*
- Patient with multiple [redacted] but no obvious significant immunosupression. Approximately 6 weeks prior to sample date had been prescribed [redacted] Both have possible immunsuppresive effects. Meets HCAI criteria due to venepuncture within 30 days prior to sample date

Summary

- Disease caused by *Cryptococcus* spp. are rare, with only 19 cases over ten years.
- In the earlier part of the study period cases are dominated by patients with HIV
- In recent years the picture is mixed.
- 2018 had the highest number of cases (5), with cases clustered in the second half of the year. Second highest incidence was 2010 (4)
- In 2018 the cases were predominantly in patients with underlying haematological conditions
- As well as the two previously identified HAI cases, there were five cases attributable as HCAI. 3 of these cases meet HCAI definition due to venepuncture within 30 days of sample date.
- The limited information available to PHPU does not support a link between the current incident and any additional cases.

Mandatory - Healthcare Infection, Incident and Outbreak Reporting Template (HIIORT)

Complete within 24 hours for all HIIAT Red and Amber;
for HIIAT Green complete only if HPS Support requested.

Section 1 :Contact Details	
NHS Board/Care organisation	NHS Greater Glasgow and Clyde
Date and time of reporting	20.12.18
Person Reporting and designation	Dr T Inkster Lead Infection Control Doctor Sandra Devine Associate Director of Nursing IPC Lynn Pritchard LNIPC Susie Dodd LNIPC
Telephone number and email	Sandra.devine[redacted]
Section 2: Infection Incident/outbreak Details	
Care facility/hospital	Queen Elizabeth University Hospital
Clinical area/ward and speciality	[redacted]
Total number of beds	N/A
Total number of beds occupied	N/A
Section 3: Initial assessment	
Type: Incident/outbreak/ data exceedance e.g. Gastrointestinal, decontamination failure	Two cases of Cryptococcus neoformans in the past week. Considered an exceptional infection
Infectious agent known or suspected	Cryptococcus neoformans
Case definition	Any patient diagnosed for clinical samples with Cryptococcus neoformans
Date of first case (if applicable)	[redacted].11.18

Total number of confirmed patient cases 2	Total number of probable patient cases 0	Total number of possible patient cases: 0	Total number of staff cases: 0

Number of patients giving clinical cause for concern as a consequence of this incident/outbreak	none
Number of deaths as a consequence of this incident/outbreak	1
Was the infectious agent cited as a cause of death on a **death certificate* (**if yes, state which part of the certificate**)**	[redacted]

Additional information:

Cryptococcus neoformans is an encapsulated yeast that can live in both humans and animals and is largely found in soil and pigeon excrement

Summary

2 clinical isolates within 17 days on the same hospital site. Both were[redacted] patients – one adult and one paediatric. Summary of the two cases is as follows:

[redacted] admitted to Ward 2A of the Royal Hospital for Children (RHC) on[redacted] 2018. The patient was too unwell to mobiulise out of[redacted] room or anywhere in the hospital. Ward 2A was decanted to ward 6A, Queen Elizabeth University Hospital (QEUH) on[redacted] 2018 to allow for upgrade works to take place. The patient was transferred to paediatric intensive care unit (ward 1D) on[redacted]/18.[redacted] tested positive for Cryptococcus neoformans from blood cultures obtained on[redacted] Post mortem samples reveal Cryptococcus neoformans from multiple sites

The adult case in still in hospital and is[redacted] is currently on treatment. The infection is not thought to be significantly contributing to[redacted] condition at this time.

Control Measures

Review of cases (PAG) on the 18.12.18 and immediate actions as follows:

- Review of drugs given to patients by the aseptic pharmacy (in progress).
- Review of PICU to review possible contamination with pigeon excrement on window ledges etc. Findings – excessive volumes of pigeon droppings have been noted outside of PICU in enclosed external atriums. There is no window or door access to the external atrium for staff or patients. Pigeons have been reported to be nesting on the sills of the external atrium throughout the summer months and as a result nets were placed overhead and spikes applied to window sills. The extensive pigeon excrement is no longer visible although some pigeon droppings do remain on the external windows and sills. The same was also visualised on overhead canopies at entrance way to the Royal Hospital for Children.
- Review of plant room on the roof of the adult hospital – evidence of pigeon droppings and feathers in the plant room. Microbiology will sample droppings from this areas and also the air with settle plates and active air sampling After this estates will decontaminate the areas as per instructions from the IMT.
- Samples of faeces will be sent for further analysis – Bristol
- Air sampling of ward areas will take place

IMT convened on the 21.12.18 actions from this;

- All high risk patients will receive prophylaxis.
- Establish if both patients received drugs from the aseptic pharmacy
- Place spikes on all areas where birds might nest in both buildings
- Review plant room daily and put measures in place to prevent further access to the areas by birds. Investigate for access points
- Vet Consultant at HPS has been contacted by Consultant Public Health Medicine to establish incidence/epidemiology.
- Epidemiology of cases will be reviewed by CPHM
- Bristol mycology – typing not routinely available but they will attempt sequencing. Advice sought re epidemiology – they have not seen hospital acquired cases before, usually sporadic community cases
- Ongoing surveillance – clinicians and microbiologists will consider as part of differential diagnosis and send serum antigen and blood cultures.

Lab contamination has been ruled out

Section 4: Healthcare Infection Incident Assessment Tool (HIIAT) (link to tool)		
Severity of illness	Minor/Moderate/Major	Major
Impact on services	Minor/Moderate/Major	Minor
Risk of transmission	Minor/Moderate/Major	Moderate
Public anxiety	Minor/Moderate/Major	Major (among this group of patients)
HIIAT Assessment	Red Amber Green	RED
Section 5: Organisational Arrangements		
PAG/IMT meeting held	Both Y /Y	Date: 18.12.18 & 20.12.18 Chair: Dr Inkster
Next planned IMT	Yes (sooner if is another case)	Date:27.12.18
Press statement (send with HIIORT or provide date for receipt)	Holding, Release Date:20.12.18	
HPS support requested	Y Vet consultant	Date..20.12.18
Other information: e.g. decisions from IMT		

Complete this update section weekly as a minimum if red or amber or as agreed with IMT and HPS for onward reporting to SGHSCD.

Section 6: Update						
On this date:	27.12.18	7.1.19	9.1.18	17.1.19	18.1.19	22.1.19
Cumulative total of confirmed patient cases	2	2	2	2	2	2
Cumulative total of probable patient cases	0	0	0	0	0	0
Cumulative total of possible patient cases	0	0	0	0	0	0
Cumulative total of staff cases	0	0	0	0	0	0
Total number of symptomatic patients today	1	0	0	0	0	0
Number of patients giving cause for concern	0	0	0	0	0	0
Total number of deaths as a consequence of the incident since last HIIORT report	1	1	1	1	1	1
Is the ward/services closed	no	No	No	No	No	No
Is a service restricted	no	No	No	Yes	Yes	Yes
HIIAT assessment	AMBER	Green	GREEN	GREEN	AMBER	

Organisation update certification information)	*Comments (including changes to any control measures, case definition or death)*
Date:	IMT 27.12.18 – Actions and Update Update Adult patient responding to treatment. No new cases. Actions update: • GP Environmental Ltd carried out Pest Control and Housekeeping Inspection of Various Plant rooms (31, 32, 33, 21, 22, 41 and 41A at QEUH, Glasgow. Deep clean completed in response to recommendations within the report. • Additional bird proofing implemented in an area identified within their report “Pigeons had gained access through what appears to be weather damaged cladding and have been using the pipes and high beams as a roosting point. The roosting areas were mainly at the roof access point below the large roof overhang”. • Unable to speak to family of the paediatric patient at this time. To be arranged as soon as possible. • Provisional report from samples of bird faeces is negative, however, there may have been some issues with sampling. • Air sampling results are not available yet.

	• Plant room D (1, 2, 3) pigeons in situ now removed. • Public health epidemiology confirms and general increase in cases although numbers are very low. 5 cases since June 2018. Update from HPS Consultant Vet still awaited. • Typing by Bristol lab still awaited. • All high risk patients will continue to receive prophylaxis. Additional agreed actions: • Plant rooms will now be inspected every two weeks for evidence of pest, infestations. • Water tanks reviewed and they are covered so unlikely to be a source. • Estates will check window seals for any obvious gaps. • Public health to update HPS Consultant Vet re findings of epidemiology. • Occupational health will consider any issues for staff who would normally work in the plant room in respect of PPE. • Confirmed that specialist contractors wear appropriate PPE. • Estates will plan for cleaning of window ledges in PICU. • Continue to review epidemiology. • Estates to look at removing vegetation from level 4 QEUH rooftop and place spikes on patients windows • Review carts taking patient supplies to ward to ensure clean
Date: [redacted] January 2019	HIIAT remains Green. No new suspected cases. [redacted]. Cryptococcus is not associated with [redacted] death. IMT held to update clinicians with available air sampling results. Fungal counts identified in plant room 12 including Cryptococcus. Isolate being sent to Bristol to confirm species and compare with patient isolates. Fungal growth on plates from wards 6A and 4C (these are not hepa filtered wards). Plates left to incubate for longer than specified which may account for some overgrowth. Air sampling being repeated. Prophylaxis continues in adults without any issues. Paediatric prophylaxis has been challenging – paediatrics do not tolerate long term prophylaxis and there have been 2 episodes of anaphylaxis. Actions from the meeting; • Repeat air sampling as well as await results still outstanding from initial sampling. • Plant rooms will be inspected every two weeks for evidence of pest infestations • Estates to Clean window ledges visible from PICU • Report awaited from GP environmental detailing options for reducing pigeon infestations in and around the QEUH site • Review of portable filter options for use in ward 6A • Await feedback from HPS re. national picture relating to Cryptococcus

	cases amongst humans
Date[redacted] January 2019	Adult patient [redacted]. Not recorded on either part of patients death certificate so not considered either a cause or contributor to the patients death.
Date:9 January 2019	Confirmed that samples from the wards grew Cryptococcus. Significant concern among clinical staff. Agreed to resample and install portable hepa filter units into all rooms, adjacencies and corridors. Re- sample pre and post installation. No new cases. NB this was written retrospectively and in error. The plates were unable to be assessed with any degree of reliability as they had been left to incubate longer than normal. Cryptococcus was not identified in ward samples until the 16th January S Devine.
Date: 16 January 2019	IMT Results from air sampling from 9/1/10 now available. This was before portable HEPA filters were in place but after the plant rooms had been decontaminated. Cryptococcus has been isolated, however it was a different type from the one isolated from the patients. After discussion with expert from Bristol it was proposed that the most likely source is a breach of the ventilation system and that GGC should consider HPV cleaning of the system. Cryptococcus was not found in samples from PICU. In the absence of post filter insertion sampling ICD was asked if there were any other indicators that could be used to reassure clinical staff that filters were working. Lead ICD agreed to carry out repeat air sampling and particulate counts on the evening of 16th January. Actions Obtain additional units for the 6A corridor and deploy additional units to complete coverage in corridor of 6A and ward 4C inpatient rooms. Ascertain risk in adult renal unit and requirement for hepa filter units in 4C/additional prophylaxis. PM Particulate sampling results although lower than previously reported remained higher than expected. LICD conducted through examination of the built environment and identified areas of mould/damp in some joins in the shower rooms e.g. skirting board joins. The hypothesis is that this could account for the higher than expected particulate count although it should also be noted that these room and not occupied solely by the patient but at least one parent. These rooms also have toys, parents possessions etc so not a typical clinical environment.
Date:17 January 2019	IMT to discuss results and actions from particulate counts and findings from the review of the environment. HIIAT GREEN?? Actions/Summary: • Lead Infection Control Doctor has contact Public Health England to ascertain if this problem has occurred in other hospitals and if so what action was taken to resolve it. Advice from a National Expert is that over time the system will through dilution clear itself. As an additional control measure Estates have contacted a specialist contractor to assess the feasibility of decontamination of the system using hydrogen peroxide vapour. In addition the system will be assessed to establish if there is any other source of contamination. • Portable Hepafilter units have been deployed to ward 6a with additional units being delivered into the adult general haematology ward today. • All high risk patients are receiving antifungal prophylaxis.

	• Air sampling has confirmed that wards in the 7th floor have Cryptococcus in samples, however, patients in this area are at extremely low risk of developing this type of infection • Very high risk patients will be relocated to the adult bone marrow transplant unit as an additional precaution until estates issues have been rectified. • Facilities have engaged contractors to check with thermal imaging on the windows within the wards to see if there are any possible leaks. • SCRIBs will be completed 18/1/19 to enable estates colleagues to commence work to rectify issue in showers over the next couple of days. Next IMT 18/1/19 at 3pm.
18th January 2018	HIIAT assessed as AMBER Severity of illness - minor Impact on services- moderate Risk of transmission - moderate Public anxiety - moderate Summary No new cases have been identified. All at risk groups remain on profalaxis. Actions • Air sampling complete as requested at IMT 17/01/19. • Hepa filters in all key areas with more being delivered tomorrow for renal transplant areas. • HAI SCRIBE complete for works which will progress over weekend. • Teleconference with Peter Hoffman and microbiology – results of which will be communicated at next IMT. • High risk patients moved to adult BMTU. • Other patients on ward risk assessed to ensure highest risk are in rooms with no issued with showers. • **Proactive press statement to be released – we will forward on as soon as this is available**. • Comms prepared for patient and parents. Members of IPCT and SMT Women's and Children's continue to make themselves available to address specific concerns of patients, parents and staff. • No report on thermal imaging action re windows. • Review of filtration within ventilation system is ongoing with estates colleagues.

21st January 2018	**HIIAT AMBER** Severity of illness - minor Impact on services- moderate Risk of transmission - moderate Public anxiety - moderate **<u>Situation Update</u>** No new cases. Water ingress in shower areas was more significant than thought (6A). There was visible mould evident when flooring was lifted and as a consequence all patients were risk assessed and four patients were moved to PPVL rooms in Clinical Decisions Unit in RHC. The rest of the patients (4) were relocated to the beginning of the ward were the showers appeared to be in the best condition. A operational group will meet this afternoon to consider options in terms of relocating patients in RHC. HSE have indicated this morning that they will make visit to the site on Thursday 24th January. **RHC Air sampling** Air sampling done in RHC (PICU, Renal Unit) all negative. 6a & 4c 4c results not available as yet. Ward 6A results show a single colony of yeast in one bedroom and some in a corridor but several rooms are negative for Cryptococcus. Full fungal cultures will be available mid week. **Update on Actions** **New:** Communication via other forms of social media will be put in place today to reach the wider population of NHSGGC. All families who are inpatients or who are due to come in have been spoken to by clinical staff – this has been ongoing. They also received hard copy information on Friday18th. Further communication to parents by member of NHS Board to be considered. Draft letter to be developed by directorate and issued. Nursing staff in both 6a and 4c have raised concerns and have been spoken to. Review showers in 4c and rectify any issues noted. Haematology consultants (paeds) briefed today. Continue with air sampling on site twice weekly. **Update**: Work is ongoing to repair shower rooms. 8 should be repaired by Wednesday. Directorate review of options to move patients from adult back to children's hospital.

	Thermal work on windows complete. Some minor issues identified but no major concerns noted. NB Please note update from 9th January Next IMT tomorrow 22/01/19 location and time to be confirmed.
22/01/18	**HIIAT AMBER** Severity of illness - minor Impact on services- moderate Risk of transmission - moderate Public anxiety - moderate **Update** All patients from 6a now in CDU. BMT patients remain in ward 4b No new cases. Plan in place for new admissions. **Review of Actions/New Actions** • Work still ongoing in rooms used by low risk patient, one room with some issues in shower will be used as an OPD room for low risk patients. • On target to complete works on at least 6 rooms by 23/01/19. A further 8 rooms should be complete by next week at the earliest. Air testing will take place once the rooms are all complete, they have had a HPV clean and before HEPA filters are put back in place. Once this is complete the rooms will be tested with the HEPA filters in place. • Some repair work also scheduled for ward 4c. • Letter for patients/parents will be approved by CEO and will be issued to all in-patients and out patients. • Core briefs have been issued to staff to update them on the situation. Going forward social media will be used to also send this message out.
24 January 2019	**HIIAT RED** Severity of illness - minor Impact on services- moderate Risk of transmission - minor Public anxiety - major **No new cases** **Additional Hypothesis** In radiology there is a door which smoke testing has confirmed in not sealed when closed. Outside this door is a courtyard and within this area there is a heat exchanger. Bird dropping were evident in this area and the hypothesis is that the heat exchanger may be causing spore dispersion close to an air inlet.

	Update • Haematology/Oncology now located in CDU. Day cases on first floor. • 6A scribes complete. Repairs and HPV cleaning should be complete by Monday 28.01.19. Air sampling will commence after this has been completed – probably Wednesday 30.01.19. Sampling will be done pre and post HEPA filter placement. • Ongoing investigations in plant room. • Courtyard near radiology being reviewed. • Letter to patients/parents developed. Both in patient and outpatients will be issued with same. • Supplies boxes reviewed – procurement confirm no problem in Hillington with pigeons. • Roof top garden assessed (QEUH) no signs of nesting. Will need to be assessed to develop solutions to remove garden material. Pest control in attendance. Guidance will be sought re mid term solutions. • Twice weekly air sampling in level 7 (QEUH) as a control.
25/01/19	IMT HIIAT assessed as AMBER Severity of illness - minor Impact on services- moderate Risk of transmission - minor Public anxiety - moderate No new cases **Update** Shower repairs and cleaning of chilled beams (6a) will be complete by Monday, Air sampling will commence on Wednesday. Action • Review of types of filters to be added to ventilation system to prevent ingress of Cryptococcus. • Haematology/oncology paediatrics patients now in CDU. BMT patients in ward 4b adult BMTU. • Vet lab Ayrshire – results, crypto albidus in bird faeces these will now be sent to Bristol. • Air sampling – results not available as yet. • Peter Hoffman has asked for some information re ventilation, the answers are currently being developed. • Review of helipad. Downdraft airflow and patient transport equipment. • 6a will be reviewed by LICD and LIPCN on Monday after repairs are complete. Next meeting 29TH January

28 January	**IMT** HIIAT assessed as RED due to public anxiety Severity of illness - Minor Impact on services- Moderate Risk of transmission - Minor Public anxiety - Major Update • Vet lab Ayrshire – results, crypto albidus in bird faeces these will now be sent to Bristol – post meeting – these samples were discarded. New samples will be obtained. • One patient transferred to [redacted] • 13 patients in CDU. • Letter issued to all inpatient parents – no issues raised. Letters being sent to outpatient cohort. • Adult BMT (4B) three patients remain on ward. • 2a functioning as acute admission – no issues identified in haematology/oncology in this area – **only in extremis** and four BMT rooms would be used. • Micro – air sampling - Level 7(indicator ward) most recent results all negative therefore may be able to lift some control measures. Lead ICD to review • Work on 6a should be complete today. • Additional HEPA filters purchased. • Hepa filters will be left in wards 6A and 4C long term,pending works to upgrade them. Maintenance programme to be put in place. **Hypothesis Update** Visit to helipad – obvious birds and faeces. Trolleys will have bird faeces on wheels cannot be transferred onto new trolleys as they are trauma patients. Other centres with helipad being contacted re what they have put in place to address this. Not likely to affect haematology patients as not admitted via this route **New Actions** • After discussion recommendation is that HEPA filters remain in situ in high risk areas • SLWG to further develop hypotheses , and explore further future preventative methods we can put in place . **Communications** • Letter issued to all inpatient parents – no issues raised. Letters being sent to outpatient cohort. • Families will be advised that they can contact GGC comms if reporters appear at their home. Formal communication with numbers etc will be developed. • W & C senior management team have briefed clinical directors for each specialty or their equivalent regarding incident. This will be followed up with some formal written communication. • Family of adult family has asked for additional information this will be actioned by clinical team and LICD. Next IMT 30 January 2019

30 January 2018	**IMT** HIIAT assessed as RED due to public anxiety Severity of illness - Minor Impact on services- Moderate Risk of transmission - Minor Public anxiety - Major Update • New bird faeces samples have been obtained and further samples to be obtained from the helipad and these will now be tested. • Adult BMT (4B) 4 paediatric patients remain on ward. • Micro – air sampling - PICU – initial air samples obtained on 21st December 2018 showed no growth of Cryptococcus however the chair of the IMT has now been informed that that further sample taken on this date have grown cryptococcus albicus. Discussion with expert in Bristol suggests that the counts of Cryptococcus in the air may have now reduced due to natural dispersion. • Work on Ward 6a is now complete and HPV cleaning has been undertaken prior to air sampling and heap filters being installed • Additional HEPA filters purchased. • Prophylaxis and heap filters remain in place for all high risk patients. **Hypothesis Update** Due to updated air sampling results from PICU the hypothesis generated at the last IMT has now changed. PICU is served by Plant Room 41 on Level 4 and this area was previously inspected and found to be contaminated with pigeon faeces but no sign of infestation. A separate subgroup will now be convened to review all possible hypotheses. Air sampling of plant room 41 will take place **New Actions** • Jamie Redfern will review all patients who was admitted to the PICU via the helipad in December. • Guidelines for hepafilter changes is being developed. • Dr T Inkster has requested a review of all samples related to the incident. • SLWG to further develop hypotheses , and explore further future preventative methods we can put in place. • Facilities to review down drafts created by helicopter landings and any potential dispersal of pigeon faeces. . **Communications** • Dr T Inkster will speak to the family of the adult patient who have requested update of all development. • Facebook page to be set up by comms dept with 2 members of Paediatric SMT as administrators to allow parents to raise any concerns and GGC the opportunity to respond. • Letters being sent to outpatient cohort. • Media enquiry from BBC regarding the cause of death of the adult patient and a response has been prepared. Next IMT to be agreed.

4 February 19	**IMT** HIIAT assessed as AMBER Severity of illness – minor Impact on services- moderate Risk of transmission - minor Public anxiety - moderate **Update** • SLWG will meet this week for the first time. • One case with a positive Aspergillus PCR but normal CT scan – to be reviewed by lead ICD • Air sampling of ward 6a is still outstanding but the plates are negative so far (final results should be available this week). • Plant room samples associated with PICU not available. • Other samples from RHC not available as yet. • Filters arrived and now in place • Pigeon faeces samples sent to Ayrshire lab. • Maintenance guidance for HEPA filters sent to group. This will be put into place. • TAC mats for trolleys in helipad– samples being sent to facilities colleagues for review. **New Actions** • Filters are being sources that will improve filtration associated with general ventilation. **Communications** • Board supported facebook page is being set up to support parents of this patient group**.** • Letters to parents will be sent to LICD. LICD will forward to HPS/SGHD as requested when received. • NSD will be updated re press releases as requested. • Public Health Protection Unit have developed information for the general public. This will be sent to LICD for comment. • Occupational health update for staff to be sent out. Next IMT Friday 8th 12md.
8 February 19	**HIIAT AMBER** Severity of illness - minor Impact on services- moderate Risk of transmission - minor Public anxiety - moderate **Update** • Air sampling ward 6a (QEUH). Results are that most room are free of fungal spores. Minimal positive samples with Penicillium which is not significant. Particulate counts are also much improved. • IMT decision is that we can now move patients back into the ward. BMT patient will continue to be looked after in ward 4B (Adult BMT). • Tac mats ordered for helipad. • Interim report from Ayr lab – yeast but final results are not available. **New Actions** • LN IPCT will check ward and feedback to estates/facilities any final issues before children move back. • HEPA filters will remain on 6A long term. • Prophylaxis guideline will be developed for paediatric haem-oncology with micro and ID consultant and pharacy. • LICD will initiate fortnightly air sampling in 6a.

	• Maintenance programme will be put in place for HEPA filters. These are cleaned between patients with actichlor. • Draft water damage policy has been prepared but is still to be ratified. Possibility for named estates colleague allocated to each high risk area is being explored. • Vent cleaning frequency being increased to three monthly. **Communications** • Face book page in development, should be available soon. • Occupational advice to go out to staff as soon as possible. • W & C senior management team will develop a briefing with communications to give to parents regarding the move back. LICD, consultants and SMT W & C will be available if anyone has any questions or concerns.
15 February 19	HIIAT GREEN Children have moved back to ward 6A and we have had no new cases of Cryptococcus. The expert advisory group met for the first time on the 14 February 19 and minutes will be shared with the IMT once available. No further meetings planned.

Section 6: Update						
On this date:	24.01.19	25.01.19	28.01.19	30.01.19	04.02.19	08.02.19
Cumulative total of confirmed patient cases	2	2	2	2	2	2
Cumulative total of probable patient cases	0	0	0	0	0	0
Cumulative total of possible patient cases	0	0	0	0	0	0
Cumulative total of staff cases	0	0	0	0	0	0
Total number of symptomatic patients today	0	0	0	0	0	0
Number of patients giving cause for concern	0	0	0	0	0	0
Total number of deaths as a consequence of the incident since last HIIORT report	0	0	0	0	0	0
Is the ward/services closed	No	No	No	No	No	No
Is a service restricted	No	No	No	No	N0	No
HIIAT assessment	RED	AMBER	RED	RED	AMBER	AMBER

ONCE COMPLETED, EMAIL TO: [redacted]

Report from the Cryptococcus Incident Management Team Expert Advisory Sub-Group

CONFIDENTIAL NOT FOR ONWARD DISTRUBUTION

Final Draft 05/04/2022

Full: NOT redacted

Contents

Summary of Findings

Hypothesis number 1: Plantroom (PR) air (particularly on Level 12, QEUH).

The Hypothesis was that *Cryptococcus neoformans* spores, (and those of *Cryptococcus* species) if present, could get into the Air Handling Unit (AHU) during a Final Filter change with the belief that without the presence of the Final Filter (to protect and remove), the air from the Plant room (presumed to have spores of *C. neoformans* in it) would gain entrance to the duct work and thence to the patients. Importantly, it was discovered that during a Final Filter change the air from the duct work comes forcefully BACK UP the duct and pushes out INTO the Plant room. This is thought to be a 'thermal effect'.

1. There have been more than 3000 air samples taken and *Cryptococcus neoformans* has never been found in any room, ward or in any of the samples taken from the air circulating inside or outside the Hospitals.
2. Non-neoformans Cryptococci have been found in air samples not only in areas served by AHUs on Level 12 but also in different levels of the QEUH and RHC, AND also found in air in the Laboratory Building. It should be noted that the Laboratory building and their associated Plant rooms are completely separate from those in QEUH/RHC. It is also important to note that these Plant rooms in the Lab building showed absolutely no evidence of either ingress of pigeons or pigeon guano.
3. The above is highly suggestive of the presence of the Cryptococci in the 'outside air' as it was also still present after months of active pest control, inspection and cleaning of the QEUH/RHC Plant rooms.

This Hypothesis was therefore deemed UNFEASIBLE

Please, also note, that in this part of the Report a discussion concerning the issues of damp/wet pigeon guano takes place, i.e., spores less easily aerosolised and larger spore size.

Hypothesis number 2: Outside Air Source

1. Wards 4C and 6A had F7 standard air filters but did not have HEPA filters therefore would allow through a percentage of *C. neoformans* spores if present in the outside air.
2. The investigations and finding detailed above in hypothesis 1 informed the consideration of hypothesis 2.

Thus Hypothesis 2 was therefore deemed 'POSSIBLE'.

Hypothesis number 3: Lack of 'Protective Isolation'

'Protective Isolation' requires 3 things:

- Air should be HEPA filtered.
- Patient's room must be positively pressurised to its surroundings.
- Air in room must uniformly leak outwards.

This is to prevent ingress of non-HEPA filtered air – 'dirty air' that may carry, e.g., fungal spores including *C. neoformans*.

Following extensive air sampling, pressure and flow testing, the following was concluded:

- 4B is only ward with HEPA filtered air, but lacks control of the air particularly around one of its entrances. It should however be noted that the rooms in 4B are HEPA filtered but not in the corridor and this would in turn make control less effective.
- 4C does not have HEPA filtered air, but surprisingly has best control of the air around it.
- 6A does not have HEPA filtered air and has poor control of the air around it.

List of mitigations taken to address some of these issues is contained in each section of the report.

In all these wards the above is related to the air sampling results.

The Bone Marrow Transplant Unit (BMTU) is situated within 4B, even though one might think that this patient population are likely to be the most 'at risk' of *C. neoformans* infections, in fact, the literature would suggest otherwise, with very few cases reported in BMT patients. No one has yet elucidated why this is the case.

Ward 4C also houses the Renal Transplant patients. Air sampling showed that air movement around/within this ward is controlled best, but it is not HEPA-filtered. This ward carries out 140 Renal Transplants per year. These patients are among those identified in the literature as 'at risk' of getting infections with *C. neoformans* however following review of this patient cohort, no cases have ever been identified. Case A spent all of their stay in QEUH in this ward.

Ward 6A, Case B spent a proportion of their time in this Ward. Please also note, that again, there is no HEPA filtration in this area and real issues with control of the air around both of its entrances, particularly the main entrance. This is fully explained and discussed in the report.

Hypothesis – number 3: 'lack of protective isolation' deemed POSSIBLE, particularly in Case B, but less likely for Case A.

Hypothesis number 4: Cylinder Room in PICU (Paediatric Intensive Care Unit)

Inexplicable route for Patient A (adult) and unlikely route for Patient B (child)

Hypothesis Number 4 is possible but very unlikely for patient B and inexplicable for patient A.

Hypothesis number 5: Helipad

'In the Computational Fluid Dynamics simulations undertaken, they demonstrate that the air arriving at the AHU intake locations does not originate in the region beneath the Helipad for any of the scenarios considered. As a result of this conclusion, it is therefore *unlikely* that debris from the Helipad area is being carried into the hospital ventilation system(s), so anything drawn into the AHU's intakes is coming from the wider environment and not affected by the shape of the building or the presence of a helicopter'

Hypothesis Number 5 is rejected as an unlikely route.

a) See report from Experts
b) REJECTED as cause, by Group

Hypothesis number 6: Specimen Transport System (POD)

POD system AKA 'pneumatic tube system'

This system is used to move specimens from a ward to the labs (and back the other way) via compressed air drawn from either the Plant room (PR 31 – not a PR on Level 12) or the ward area. This is via an enclosed tube system. These PODS then discharge the air into the ceiling void above the Ward Treatment Rooms on their return to them.

The worry was that unfiltered air, particularly from the Plant room might get into the prep/ treatment rooms on the ward.

Deemed by Group as an UNLIKELY route

Hypothesis number 7: Dormancy/Reactivation (complex)

That the cases acquired the *Cryptococcus neoformans* prior to their admission to the QEUH/RHC. The infection lay dormant until their immune system was sufficiently compromised by their co-existing conditions.

The literature review supports this hypothesis. However as reported in many other cases within the literature, due to the length of time that may have elapsed since first exposed and the complexity of how reactivation occurs, this is very difficult to prove.

VERY POSSIBLE for BOTH cases but likely to be VERY DIFFICULT TO PROVE.

IMPORTANT FINDINGS OF OTHERS AND SOME QUESTIONS TO CONSIDER

1. **Marr, KA et al, (2020)[0].** Important to note that Haemato-oncology patients with particularly [redacted] are not the only patients at risk of infections with *C. neoformans.* See above paper, there are a wide variety of other diseases that predispose to this infection noting that the QEUH/RHC is the biggest acute hospital in Scotland and will contain many patients who are/were at risk.

2. Note that children very rarely contract infections with *C. neoformans* (this is already a rare disease in adults with only the 17 cases in GGC area in 10 years, 2009-2018) with only 1 of 18 in a child.

   Again, no one understands why this is so much rarer in children.

3. Note that very few cases, of what is believed to have been, 'hospital-acquired' see Farrer, RA *et al*. (2021)[1] – who quote only one: **Vallabhaneni, S *et al*. (2015)[2]** in Arkansas, USA. There are only, perhaps, a few more cases of hospital-acquired cases in the literature.

4. Note that the literature also suggests that adult males have *C. neoformans* infection about twice as frequently as adult females – this was observed over 50 years. See **Guess, TE et al. (2018)[3]**. Also see cases in GGC, 2009-2018 – 18 cases: 6 Female and 12 Male. [redacted]

5. Other question regards 4C and Renal Transplants – who are 'at risk' but so far, no cases with approximately 140 transplants per annum (in QEUH). Only case in 4C was Case A, a [redacted] patient.

6. Genomics. These were carried out in Boston (USA) on the isolates from the two patient cases in QEUH and also two 'community- acquired' cases from 2018. This was published by Farrar, RA et al. (2021) [1].

The findings were that all four were completely different, but no environmental *C. neoformans* isolates had (so far) been isolated (by us) in Glasgow. The only guano specimen from the QEUH/RHC site had grown *Cryptococcus uniguttulatus* (from the Helipad).

All of the above will be discussed further in the main report.

Introduction

In November and December 2018, the microbiology laboratory in the Queen Elizabeth University Hospital campus confirmed that they had identified *C. neoformans* from the blood cultures of two patients. Both were [redacted], one adult and one paediatric. Patient A (adult patient) had a blood culture (BC) taken on [redacted] November 2018 and this was positive for C. *neoformans*. Patient B (paediatric patient) had blood culture on the [redacted] 2018 from the [redacted] line which was positive for C. *neoformans*, not reported until the [redacted] 2018. It should be noted that patient B was also admitted to the Paediatric Intensive Care Unit (PICU) Royal Hospital for Children during [redacted] admission (site map appendix 1).

This was considered an exceptional infection episode and was therefore reported to Health Protection Scotland (HPS) as per Chapter 3 of the National Infection Prevention and Control Manual. This incident was first reported to HPS on the 20th December 2018 and incident updates continued until the incident was declared over on the 15th February 2019.

There was an initial Problem Assessment Group meeting held on the 18th December 2018. This was followed by 12 Incident Management Team (IMT) Meetings, the first of which was held on the 20th December 2018 and the last one on 15th February 2019. At this time the main hypothesis was, that cryptococcal spores (from pigeon guano) were being aerosolised into the Plant room air, then getting into the Air Handling Units (AHUs) during routine maintenance, i.e. during shut down, opening and final filter change, then onwards to the patients down the duct.

On 20th February 2019 the IMT was stood down by the Infection Control Doctor (IMT Chair). There had been no additional cases since and control measures had been put in place.

One of the actions from the IMT was to commission a review from a group of experts to investigate all possible hypotheses suggested by the IMT and any subsequent hypothesis developed by the Cryptoccocal IMT Expert Advisory Sub Group to determine, if possible, the route(s) of transmission of these rare but significant infections with findings presented in a report format. Membership included representatives from Health Protection Scotland (HPS), Health Facilities Scotland, National Infection Service Reference Laboratory (Public Health England - Colindale) and clinical experts and engineers from NHS Greater Glasgow and Clyde.

The Cryptoccocal IMT Expert Advisory Sub Group chaired by Dr J. Hood was established in February 2019. By 18th November 2019, over 3300 air tests had been conducted since 5th December 2018, air sampling continued until February 2020. The report will be submitted to the Chair of the IMT and the relevant governance groups within GGC including the Board Infection Control Committee, Acute Clinical Governance and Board Clinical Governance Forums and the NHS Board.

Background

C. neoformans is a fungus that lives in the environment (including soil, some trees including decaying wood) throughout the world. It has a known, although complex, association with the guts of pigeons and other birds. Although most people who are exposed to the fungus do not get sick from it, a small number of people can become infected after breathing in the spores. Only one outbreak associated with a hospital has ever been previously reported in the literature Vallabhaneni, S *et al* (2015)[2].

C. neoformans infections are very rare in people who are otherwise healthy; most people affected are immunocompromised (weakened immune system). Classically it occurs in patients with advanced HIV/AIDS, however the incidence in this group depends on where you are in the world and the access to antiviral medication. There are large numbers of cases reported in sub-Saharan Africa where HIV therapies are not readily available.

Please, also, refer to the work of Goldman *et al* (2001)[4] and Kao & Goldman, (2016)[5], on Children and *C. neoformans* infections. 'According to this model, infection is acquired early in life, but remains latent only to be re-activated in the context of immunosuppression. Primary progressive infection also appears to occur as indicated by 'outbreak' reports and the demonstration of recent acquisition of infection from the local environment.'

This is the concept of latency or dormancy. This adds to the complexity of investigating the source of the infection. *C. neoformans* has a known, although complex association with the gut of pigeons and other birds.

The issues of latency and dormancy are fully explored in the hypothesis section of this report, i.e. it is, usually, not possible to determine exactly when patients have been exposed to the *Cryptococcus neoformans*.

Introduction to *C. neoformans* and pigeons plus a little on the exposure to *C. neoformans* and the immune response to it.

Lin, X & Heitman, J (2006)[6] The Biology of *C. neoformans* Species Complex, *Annu. Rev. Microbiol*. 60: 69-105.

This is a useful introduction even if from 2006 but as you will see much more has been learnt since. Page 76: '*Pigeons*. *C. neoformans* serotypes A and D have been isolated from various sources in nature. Their association with pigeon guano is well established, and the fungus has also been less commonly isolated from droppings of other avian species such as chicken, goose, duck, eagle, owl, peacock and parrot. Although cryptococcosis has been associated with birds for almost 50 years, pigeons, however, do not acquire cryptococcosis and point sources for infection have not been identified'.

'Substantial evidence establishes a link between the worldwide distribution of *C. neoformans* and pigeons. However, whether pigeons are infected or serve as carriers for *C. neoformans* is debatable. Most evidence thus far does not support the hypothesis that pigeons themselves are infected; rather they are likely carriers of the fungus.'

'First, although there is an established association between pigeon guano and *C. neoformans* strains, few studies have found *C. neoformans* within the body of birds. The pathogen, however has been cultured from the surface of birds including beaks, feathers and legs, possibly because their habitats (with their guano) are contaminated and enriched for the fungus'.

'Second, aged pigeon guano and the dirt and dust surrounding the guano are more likely to be positive for *C. neoformans* than are fresh droppings, suggesting either that the fungus could originate in the soil and flourish in this particular environment after the soil is contaminated with bird guano, or that the few cells originally in the guano could amplify better in the exposed environment. Because airborne *C. neoformans* cells have been collected from the air above bird guano collected from soil, but not from air above guano deposited on a large adjacent asphalt area, it is less likely that the fungus was originally present in the guano. Population densities of *C. neoformans* in excreta samples are usually significantly higher than those from other sources, such as plant samples, suggesting that avian droppings offer suitable conditions and possibly less competition for the growth of the fungus. It has been documented experimentally that the fungus multiplies well in sterilized pigeon or chicken guano. Dry excrement is a more favourable substratum because it has fewer bacteria and therefore less competition for growth, which could help explain the higher population density found in this substratum.'

'Third, the host environmental conditions in birds are not suitable for the growth of *C. neoformans*. The internal temperature of pigeons is as high as 42 degrees C, and most *C. neoformans* strains cannot survive at this elevated temperature. When a large number of *C. neoformans* cells were fed to birds, viable cells could be recovered shortly after the feeding but no viable cells of *C. neoformans* were detected in the droppings after longer incubation, suggesting that birds can effectively clear fungal cells from their body. In addition, bacterial flora isolated from the intestinal contents of apparently healthy pigeons inhibits the growth of *C. neoformans in vitro*.'

'These lines of evidence indicate that the environment in the gastrointestinal tract of pigeons does not favour multiplication of the fungus, and pigeons are not likely to be systemic carriers of *C. neoformans* in nature. Isolation of *C. neoformans* from avian environments may reflect colonization by enrichment due to the favourable conditions of guano-contaminated soil. However, this does not necessarily mean that birds do not play an active role in dissemination of *C. neoformans* in nature, since they could either pass the fungus through their body or carry the fungus on their surface and could readily transport the cells for a long distance. Birds, most notably pigeons, still remain the most probable vector for worldwide dissemination of this fungus.'

As well as the above paper there are several Review articles which are very informative and are contained, mostly, in the Bibliography section of this report.

Important quote from Maziarz & Perfect (2016)[7] 'The many factors in the immunologic responses to *C. neoformans* cannot be covered completely in this review, but several observations can be made:'

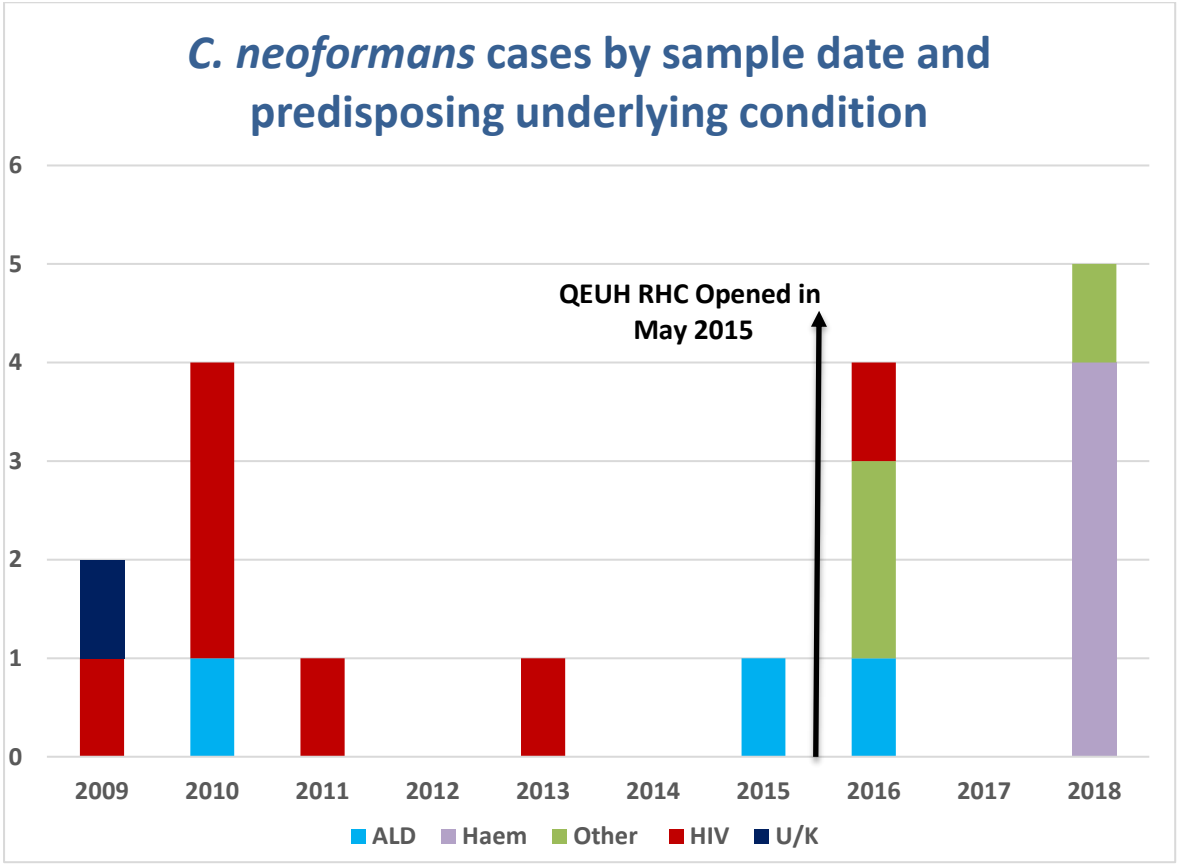
'First: exposure is frequent, and the healthy immunocompetent individual is generally resistant to cryptococcal disease. In fact, even in this group, some apparently normal hosts with cryptococcosis have been found to possess anti-granulocyte macrophage colony stimulating factor antibodies as a potential immune defect.'

'Second: the effective immune response is through a helper T cell-supported reaction and anything that weakens it may let cryptococci survive and thrive. This includes destruction of CD4 + cells by HIV, reduction of TNF activity by anti-TNF inhibitors, or the multifaceted immune suppressant effect of corticosteroids. From activated macrophages to the development of protective antibodies over non-protective antibodies, immunity changes over the course of cryptococcal infections. In fact, even some of our protective host mechanisms might be used against us, as surfactant D may be co-opted by Cryptococcus to gain entry into the lung. Clearly, cryptococcosis emphasizes the Goldilocks paradigm of immunity. It produces disease when immunity is too little or too much, but when the human host immunity is just right, disease does not appear.'

Local Epidemiology

The numbers below represent all cases of *C.neoformans* that have occurred in the Greater Glasgow and Clyde Health Board (GGCHB) area between 2009 and 2018.

Figure 1



The distribution of cases over time across all of Greater Glasgow and Clyde Health Board. This includes cases in other hospitals and the community. (U/K is unknown)

In summary:

- Disease caused by *C. neoformans* is rare, with only 18 cases over ten years in the GGCHB area (see Figure 1).
- In the earlier part of Figure 1, the cases are dominated by patients with HIV.
- In recent years the picture is mixed.
- 2018 had the highest number of cases (5) with cases clustered in the second half of the year. The second highest incidences were in 2010 (4) and 2016 (4).
- In 2018 the cases were predominantly in patients with underlying [redacted]
- Cases were identified in both, other hospitals and in the community, but only two cases believed to be possibly hospital-acquired.

Table 1

Underlying Condition	Number
HIV	7
Alcoholic Liver Disease (ALD)	3
[redacted]	2 1 1
Others • Soft tissue infection • Steroid treatment secondary to respiratory infection • Malignancy (GI) • Unknown	 1 1 1 1
Total	18

Therefore, we can see the wide variety of illnesses (within the GGC area) that may predispose patients to infections with *C. neoformans* (not just [redacted] or HIV).

Note that only one of the above was a child – Case B (1 of 18).

Hypotheses

Of the seven hypothesis which were considered by the IMT five were excluded after investigation. Two were taken forward by the sub group (highlighted in bold below):

- Ingress of pigeons into the Plant room (s) with contamination of the Plant room (s) (PR) with their guano (? containing spores of *C. neoformans*). These spores then gained entry to the air of the PR and then into the Air Handling Units serving specifically the case-patients and others.
- Ingress of cryptococcal spores (if present) with the outside air, a small proportion of which would not be removed by the F7 filters, to all areas of the hospital (s), including the Laboratory Block etc. Except where the ventilation system was specialised, e.g. with HEPA filtered air such as the Bone Marrow Transplant Unit (please refer to hypothesis 2) or ultraclean operating theatres.
- Patient to patient contact – excluded – no links identified.
- Aseptic pharmacy – excluded – no links identified.
- Lab contamination – processes reviewed and hypothesis excluded.
- Stores becoming contaminated outside prior to delivery – process reviewed and no evidence found. Excluded.
- Windows not sealed – after review – Excluded.

The C. *neoformans* IMT Expert Advisory Sub Group reviewed the two hypotheses considered by the IMT in addition to a further five generated by this group following evidence review and investigations undertaken as described in this report.

Hypothesis – Number 1 – Plant Rooms

Pigeon ingress and then fouling in Plant rooms leading to cryptococcal spores (if present) entering the Plant Room air (on for example, Plant rooms on Level 12 QEUH) and then gaining access to the Air Handling Units (AHU's) ventilating the rooms/wards where the case - patients were.

The theory was that when the AHU was shut down, opened, with the final filter removed and changed, there was - believed at that time - the opportunity for *C. neoformans* spores (if present in Plant room air) to be 'sucked' into the open AHU, then into the duct and then down it to the 'at risk' patients.

This would need to have happened when the AHU was shut down, in order to carry out routine maintenance such as removal and or changing, of the final F7 filter, thus possibly allowing spores (if present) from the Plant Room air to get into the duct and then to the patient.

Firstly

AHUs in Plant rooms related to case patient rooms/wards were not opened when the case patients were in these rooms/wards. This was true for the whole patient journeys (in both cases).

Secondly

Initial Plant room air samples were taken on the 21st December 2018. These were sent to the laboratory at [redacted] and were reported as *C. albidus* (8*/32). When these samples were sent to the National Reference Laboratory (NRL for Fungi, Bristol) it was subsequently found that 7/8* were in fact *C. diffluens* and only one was confirmed to be *C. albidus.* This is important, in that the initial advice from the NRL in Bristol was that *C. albidus* could be employed as a surrogate marker for *C. neoformans,* advice that was later altered after review by NRL. Their experience was also that *C. neoformans* appears to be very difficult to grow from air samples.

On reflection we may have failed to grow C. *neoformans* from outside air (if it was present) due to the presence of significant numbers of other fungi, especially *Aspergillus* spp. This is likely to make spotting it difficult. Perhaps we should have employed Staib's Medium (Bird Seed Agar). However, since we had success in isolating 96 times, 5 different *Cryptococcus* spp., in 12 months of indoor ward sampling, it may have been that *C. neoformans* was simply not present in these air samples.

Thirdly

The Finding of Pigeon Ingress and Fouling on Level 12, QUEH in Late November/Early December 2018.

In late November / early December 2018, pigeon ingress and fouling were found in Plant Room number 123D (Level 12, QEUH). The AHUs in this Plant room serves wards ending in D e.g., 4D, 5D, 6D, 7D etc. This Plant room therefore, did not supply air to any of the wards the case patients had been in, i.e., 2A, 6A, PICU or 4C. It is also worth noting that the time at which you would expect spores to be at their highest level (in the above Plant room air scenario) would be when the cleaning up of the pigeon fouling, was in progress – with the possible risk of aerosolisation into the surrounding air. These areas, in PR 123, were cleaned on the 6th & 7th December 2018.

Fourthly

Note that AHU 123-07 was opened in PR123 on 29th November 2018. Please also note that Patient A had a positive blood culture (BC) (with *C. neoformans)* on the [redacted] November 2018, which was [redacted] days prior to the opening of AHU 123-07 in PR123 on 29th November 2018. AHU - 07 had last been opened on 11th April 2018. It should also be noted that Patient A was in Ward 4C (which was served by AHUs in PR124C, NOT PR123D) for their entire stay in the QEUH (which is from [redacted] November 2018 to [redacted] January 2019).

Patient B had been transferred from 6A to the Paediatric Intensive Care Unit (PICU) on [redacted] 2018 served by air from a Level 3 Plant room, not any of those from Level 12. Importantly, and in any case, this was [redacted] days prior to the opening of AHU 123-07 [redacted] 2018).

It is, also, important to point out our interest in PR 123 AHU – 07, while it did not serve directly any of the case-patient Wards, it did serve the right-hand side of the Facilities Corridor on Levels 4, 5, 6 and 7. This corridor (Facilities) on the right-hand side of Level 6 ends with an interface with itself, 6A and 6D.

It was therefore also important to show that Patient B was not present in 6A when AHU 123-07 was opened on [redacted] 2018.

The above should give the reader a hint of the complexities of the possible air movements within this hospital. Please see Hypothesis 3, Lack of 'Protective Isolation'.

Fifthly

The Hypothesis was that air from a Plant Room (postulated to contain aerosolised spores of *Cryptococcus neoformans*, from the postulated presence of pigeon guano) could possibly gain access to the patients via the Air Handling Units (AHUs) when they were shut down and opened to replace the Final Filter – thus allowing aerosolised spores (if present in the Plant Room air) down the then 'filter-less' duct. The theory was that the air would be 'pulled' into the AHU through its open door and proceed down the duct to the patients.

In reality the OPPOSITE happens. When the AHU is shut down and the door opened – and the Final Filter removed - air is driven, at some force, OUT of the duct and INTO the Plant Room – a presumed thermal effect – NOT down the duct to the patients.

Perhaps more importantly, in terms of the two case-patients: NO AHUs that served any of the Wards/individual PICU room(s) were shut down and opened, during the time that either of the two patient cases were present in these Wards/individual room(s) in PICU.

Sixthly

It is also important to point out that when the ventilation system is operational (i.e., when the AHU is ON) that the part of the AHU from the fan onwards (about half way down the unit) is all under positive pressure i.e., the air within the unit can leak OUT but air (i.e., Plant room air) CANNOT leak IN. Next, the air goes through the fine filter (Final Filter) prior to entering the duct work which takes the air to the wards and rooms that it serves.

It is also important to realise, that from that fine filter (Final Filter) in the AHU to the Ward/Rooms themselves - that the duct work is also under positive pressure. Therefore, as above, filtered air can leak OUT of the duct, BUT air (including unfiltered air) cannot leak INTO the duct.

Therefore: both the outside air via the air intakes and any ingress of Plant Room air gaining access prior to the fan in the AHU (as this part of the AHU is under negative pressure, so air can leak IN) – air from *BOTH the above* will be met by the same Final Filter. Air, after passing the Final Filter and entering the duct work, is under positive pressure, so that air will always leak OUT not IN and therefore this gives the protection of preventing ingress of unfiltered air into all of that duct work.

We also continued to find the intermittent presence of *Cryptococcus* spp., mainly *C. diffluens*, in room/corridor air samples (but never *Cryptococcus neoformans*). We have found these (non-*C. neoformans* cryptococci) in air samples not only from rooms in QEUH/RHC but also in rooms/areas of the Lab Block (which is in a completely separate building, which also contains its own separate Plant rooms from those serving the QEUH or RHC).

These (Lab block) positive air samples were NOT related to obvious pigeon ingress / faecal contamination of any of the supplying Plant Rooms, all of which have had routine inspection and routine cleaning since late December 2018 / early January 2019.

CONCLUSIONS

We can, therefore, say that the presence of non-*C.neoformans* cryptococci in Ward areas of the QEUH, RHC and Lab Block is highly unlikely to be related to pigeon fouling in the Plant rooms/AHUs for the following reasons:

Firstly, we have never found *C. neoformans* either from samples of Plant room air or from any room/ward air at any time, but it should also be noted that *C. neoformans* has never been isolated from any air sample in this study (>3000 samples). *Cryptococcus* spp. (*not C.neoformans*) have been found in Plant Room air but only once from outside air (QUEH roof, with a *Cryptococcus curvatus* in December 2018). We have also found in ward/room air samples in QEUH/RHC between late 2018 to December 2019 some 96 isolates of a varying *Cryptococcus* spp., but again not *C. neoformans* (Table 2).

Secondly, we continued to find these non-*C. neoformans* cryptococci, not only in areas served by AHUs on Level 12 but also on different levels of QEUH/RHC and also in areas in the LABORATORY BUILDING, served by Plant rooms/AHUs which are in a completely separate building from those in the QEUH/RHC and they also had NO evidence of pigeon ingress/guano.

Thirdly, it should also be noted that these non-*C. neoformans* cryptococci were still present in air samples taken after months of active pest control inspection, cleaning and prevention.

This all suggests that these *Cryptococcus* species are/were present in the outside air and some were coming in through the F7 filters and/or due to ingress of unfiltered outside air (due to, lack of 'protective isolation', see later) and not related to any pigeon ingress and pigeon guano contamination of any Plant room.

Table 2*: Cryptococcal* species isolates from air sampling 21 Dec 2018 to end Dec 2019

	C.diffluens *(N. diffluens)*	*C.albidus* *(N.albida)*	*C.albido-similis* *(N.albido- similis)*	*C.uniguttulatus* *(F.uniguttulata)*	*Crypto.curvatus* *(Cutan.curvatus)*	TOTAL
Dec 21st2018 N=53	14	0	1	0	1 Roof	**16**
Jan 2019 N=422	24	3	0	0	0	**27**
Feb 2019 N= 440	0	0	0	1	0	**1**
March 2019 N= 320	4	0	0	1	0	**5**
April 2019 N= 334	2	0	0	0	0	**2**
May 2019 N=420	7	3	0	3	0	**13**
June 2019 N=448	8	0	0	0	0	**8**
July 2019 N=419	3	0	0	2	0	**5**
August 2019 N=150	3	0	0	1	9	**13**
Sept 2019 N=98	2	0	0	0	0	**2**
Oct 2019	0	0	0	0	0	**0**
Nov 2019	0	0	0	2	0	**2**
Dec 2019	2	0	0	0	0	**2**
Total so far	**69**	**6**	**1**	**10**	**10**	**96**

Summarising: the hypothesis was that cryptococcal spores, if present in the Plant Room air, could get into the AHU during a filter change when the AHU door was open and the final filter removed. The spores would then get into the AHU and then down the duct, to the patients. In reality this is/was clearly, NOT the case.

When the AHU was shut down and the Final Filter was removed, air was, in fact, forcefully pushed OUT of the duct BACK INTO the AHU and then OUT OF THE AHU INTO the Plant Room. This was believed to be, a thermal effect.

Therefore, the air of the Plant Rooms on Level 12 (or any other Plant Room) is an unfeasible source/route for *Cryptococcus neoformans* spores (from pigeon guano, if present) via the AHU(s) during shut down and change of the Final filter.

OTHER REASONS WHY PIGEON GUANO IN PLANT ROOM 123 IN LATE NOVEMBER, EARLY DECEMBER 2018 WAS NOT LIKELY TO BE RELATED TO THE TWO CASE PATIENTS.

Implications of Wet Pigeon Guano

From the pictures of PR 123D, it is clear that the guano and the area containing it have been wet and possibly were still damp/wet.




Firstly, damp or wet pigeon guano will make aerosolisation of the cryptococcal spores much more difficult. Aerosolisation is more likely only to take place easily from dry pigeon guano/soil mixture.

Secondly, the size of the cryptococcal spores is critical, we are looking at sizes of probably 1 to 3 microns in diameter to get deep lung deposition i.e., into the alveoli of humans and then cause infection. Much of this work was carried out in the 1970s and 1980's by a Group working in Oklahoma., Ruiz, Bulmer, Fromtling, Neilson[8,9,10,11,12] and others who studied *C.neoformans* in natural habitats i.e., soil, which is believed to be a significant habitat of *C. neoformans*.

In 1981, these workers looked at large piles of pigeon guano compared to loosely scattered dry guano on the floor of a pigeon infested tower. They found that large piles of guano contained <0.3% of the number of viable *C.neoformans* cells compared to the *C.neoformans* cells grown from the average samples of floor material. They concluded that 'These findings may be important in the epidemiology of cryptococcosis because the finer, looser and drier material would be more easily aerosolised and therefore, may represent a greater potential health hazard.' Ruiz *et al* (1981) [8]

Thirdly, the same group, Neilson *et al* (1977)[12] also noted the importance of the size of the capsule of the *C. neoformans* cells in the environment. They found that the capsule size was 'intimately' linked to the amount of water present. They felt it was logical that capsule production may be an 'on/off affair' depending on the environmental conditions, e.g., after rain the amount of moisture and transported nutrients in the soil would increase dramatically with perhaps capsule production being 'turned on' with a subsequent increase in size of the cell, making it less likely of deposition in the alveoli.

They also found the opposite happened when *C. neoformans* cells were grown in dry soil; the longer the incubation period the smaller the cells, so the more likely they could be aerosolised and the more likely their deposition in the alveoli.

They also noted in this paper that 'this further substantiated their earlier observations that in nature many cells (of *C. neoformans*) may exist in a relatively small non-encapsulated state. Such particles may be the true infectious particles in cryptococcosis'

Fourthly, Bacterial decomposition, the effect on *C. neoformans* in fresh or wet pigeon droppings:

Staib, F (1963)[13] commented on the growth *of C. neoformans* in either fresh or wet pigeon guano. 'I stated that solutions of fresh bird manure offer favourable conditions for only about 24hrs. The bacterial decomposition of bird-manure substances can cause a strong alkalinization within 3-4 or 5 days '.

The growth of *C. neoformans* can be stopped and even isolation of *C. neoformans* is not then possible. This alkalinisation depends on the proportion of faeces and urine and the degree of *moistening*. After saving dry *C. neoformans* – containing canary-bird and pigeon manure for one year *C. neoformans* remained able to grow in this dry hard manure. Ruiz *et al* (1982).[11]

Abou-Gabal, & Atia (1978)[14] they noted that: Under: 'Effect of pigeon intestinal bacterial flora on *C. neoformans* – seven different species of bacteria were recovered from the intestinal contents of pigeons. They were: *Staphylococcus albus, Streptococcus faecalis, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis and Klebsiella aerogenes*.

The suspension comprising these isolates exhibited a complete inhibitory effect on the growth of *C. neoformans* and no viable cells of any of the tested strains were detected after one week's incubation period. In the control bacteria-free tubes, the average numbers of viable *C. neoformans* counted reached 96 x 10^4 per gram.'

They concluded that: 'It seems a greater likelihood that initial inoculum for colonization of pigeon droppings by *C. neoformans* may originate from other sources, most probably the soil. Isolation of the fungus from soil, free of pigeon guano, is well documented (quoting 8 papers). The coincidence of accumulated pigeon droppings in nature besides other favourable environmental conditions may support the increased prevalence of *C. neoformans* in such locations.'

Kwong-Chung, KJ & Bennett, JE (1992)[15] quote Staib above – and go on to say: '*C. neoformans* cells are highly resistant to desiccation. When the weathered droppings are diluted and plated on agar media as many as 5 x 10^7 viable *C. neoformans* cells may be found per gram of faecal material. Fresh pigeon droppings or wet droppings on the other hand, infrequently contain *C. neoformans*. The bacterial decomposition of wet bird droppings causes a strong alkalinisation, and *C. neoformans* stops growth on the substrate with alkaline pH.'

Therefore, the four points above suggest that the damp pigeon guano in PR 123 did not result in as a significant risk as was originally postulated, therefore another reason for ruling out this hypothesis.

The role of water (e.g., rain) and its effect on the pathogenesis of infection with *C. neoformans*, specifically on aerosolization and size of capsule etc, should also be viewed on its likely effect on *C. neoformans* in its environmental sources (soil and guano).

This is, perhaps, one of the reasons that there are significantly fewer cases in the West of Scotland than say in the Southern States of the USA, likely to be due to the different weather/climatic conditions here and perhaps, particularly the frequency of rain fall, humidity etc.

Quote from Bratton, EW *et al* (2012)[16].

In this paper: 'Under Limitations': 'this review was limited to a single tertiary care centre and teaching hospital. Our medical centre averaged nearly 15 cases of cryptococcosis per year and this likely reflects both an endemic exposure to this yeast in the environment within the Southeastern USA and an enriched population of immunosuppressed individuals due to our hospital's care patterns. The actual number of cases seen in a particular medical centre certainly varies within the U.S.'

Therefore, Duke University Medical Centre (between 1996 and 2009) saw an average of 15 cases of *C. neoformans* per year compared with the Greater Glasgow and Clyde Health Board Area (between 2009 and 2018 – a 10-year period) who saw an average of only 1.8 cases per year.

Fifthly, where is the soil? On reflection of the presence of pigeon guano on the floor on PR123 and also e.g., guano on the helipad – there is NO actual 'soil' present as there would be in the natural environment (but admittedly, there may have been some dust, but I would think that the Plant room floors were more like an 'asphalt area' noted below).

See quote from: Lin, X and Heitman (2006)[6], Page 76: 'Second, aged pigeon guano and the dirt and dust surrounding the guano are more likely to be positive for *C. neoformans* than are fresh droppings, suggesting either that the fungus could originate in the soil and flourish in this particular environment after the soil is contaminated with bird guano, or that the few cells originally in the guano could amplify better in the exposed environment. Because airborne *C. neoformans* cells have been collected from the air above bird guano collected from soil, but not from air above guano deposited on a large adjacent asphalt area, it is less likely that the fungus was originally present in the guano. Population densities of *C. neoformans* in excreta samples are usually significantly higher than those from other sources, such as plant samples, suggesting that avian droppings offer suitable conditions and possibly less competition for the growth of the fungus. It has been documented experimentally that the fungus multiplies well in sterilized pigeon or chicken guano. Dry excrement is a more favourable substratum because it has fewer bacteria and therefore less competition for growth, which could help explain the higher population density found in this substratum.' NB more of this paper is quoted on Pages 8 & 9 of this report.

Therefore, the Plant room floor or the helipad platform are not mimicking what is going on in the natural environment, i.e., it is likely that it is the 'soil' itself that may contain the *C. neoformans* (? less likely to be present in the pigeon guano) see paragraph entitled 'Third' in Lin & Heitman (2006)[6].

Therefore, the above gives another reason (in addition to the evidence of water on the Plant room floor) that the Plant room was a very unlikely source of, functioning and aerosolized, *C. neoformans* spores.

It should be noted (again) that what pigeon guano samples were taken from the QEUH site did not grow *C. neoformans,* these were from the Helipad and sent to the Veterinary microbiologists. They grew *Cryptococcus uniguttulatus*. Interestingly, this finding was the same as that of the Swedish workers - Matteson, R *et al.* (1999).[17]

Action taken by NHSGGC to mitigate this potential risk:

- Regular cleaning and inspection plant rooms.
- Pest control measures implemented to reduce the numbers of birds throughout the campus.
- Paediatric Radiology Courtyard. The area has been netted across the top of the courtyard to prevent any birds roosting in this area.
- F7 filters on AHUs were changed to F9 in all AHUs serving Ward 6A and 4C.
- Tackmats were installed at helipad lift to remove any contamination brought in on trolley wheels. These Tackmats are monitored by the security and portering team and changed as required.

- Quarterly inspections are carried out to ascertain if filters on AHU(s) need to be changed.

Therefore, the Plant Rooms on Level 12 (or any other Plant Rooms) are unfeasible to have been the source of *C. neoformans* spores (from pigeon guano) in a Plant room - by this postulated route, over the timeframes noted above.

Hypothesis Number 1 – Unfeasible.

Hypothesis Number 2 - Outside Air Source (External Air)

C. neoformans present in the outside air entered the AHU ventilating the rooms/wards where the case - patients were.

Cryptococci (including *C. neoformans*) are most likely to be periodically present in the outside air (but impossible to prove definitively as we have not been able to grow *C. neoformans* from extensive air sampling either external or internal) and so may enter the AHU's and then subsequently may still be present in the filtered air delivered to the ward areas.

But note, testing only a few times monthly and a relatively small sample size (volume: 500L and time: 3 minutes). Filtration of air destined for 'general wards' (including 6A and 4C) is of F7 standard (?80% filtered), i.e. NOT of the standard required for patients needing 'protective isolation' (which is HEPA filtered air). Please note however, that many hospitals will not even have filters of F7 standard in general wards as the QEUH/RHC does.

In areas where 'protective isolation' is required e.g. Bone Marrow Transplant Units / Haemato-oncology Wards, filtration should be of a HEPA filter standard, i.e. 99.9%. Please also note that 'protective isolation' not only requires HEPA filtered air but also requires positive pressure within the room and with the air uniformly leaking outwards.

FINDINGS

When sampled (>3000 samples) (21st December 2018 to January 2020) the adult BMT had only 8 isolations of *Cryptococcus* spp. compared to 88 isolations found in the rest of the hospital (not only including 4C and 6A) from non-HEPA filtered environments. *Cryptococcus* spp. continues to be isolated from patient care wards and in other areas on site but never *C. neoformans.*

Therefore, a possible route is that cryptococcal spores are entering through the outside air. The F7 filters are NOT sufficient to, nor intended to, remove all of them, not only all the cryptococcal spores, but also many other fungal spores such as those of *Aspergillus* spp (a much more likely pathogen in these patients). This is clearly seen in the air sampling results (See Tables 3a, 3b, 4 & 5 in Hypothesis 3 below).

It should be noted, again, that in December 2018/January 2019 there were widespread positive air samples with *C. diffluens,* not only in areas served by Plant rooms on level 12 (A, B, C and indeed also D, when checked) but also in 1C, RHC served by a Level 3 Plant room and PICU (RHC) served by PR 41. Subsequently, when air tested, *C. diffluens* was found in many areas of the Laboratory Block which is remote from the Plant Rooms (PRs) in QEUH/RHC. The Lab Block PRs were not known to have/had any issues with pigeon ingress. Also, subsequently, we continued to grow cryptococcal species from both 6A and 4C, despite regular inspection and routine cleaning of these Plant Rooms serving the QEUH/RHC.

The above findings (in the Lab Block) are highly suggestive that cryptococci (and specifically *C. diffluens* and other *Cryptococcus* spp.) are likely to often be present in the outside incoming air and their presence is not likely to be related to the presence of pigeons in these Plant room(s). Note that *C.diffluens* was also grown from two air samples (from 2 bathrooms) recently (late 2019) in Ward B7 of the Beatson Cancer Centre (at Gartnavel General Hospital). Prior to December 2018 these would not have been identified. What this shows is that in another hospital (2 miles away) *C. diffluens* was also present in air samples (and ironically where the adult BMTU and Haemato-oncology Unit had been previously).

Please see Table 3a and 3b below in Hypothesis 3 (note that this was originally in Minute no 27, 26th February 2020) showing *Cryptococcal* species isolates from air sampling: 21st December 2018 to end December, 2019*, note updated to include 6A results from 21st December 2018 to 16 January 2019*. Although the QEUH Bone Marrow Transplant Unit (4B) results are significantly lower than the rest of the hospital it is an indicator (we should be expecting more 0,0 counts here) even in a BMT with HEPA filtered air and positively pressured rooms. Therefore, there are still issues that need to be addressed, however, it should also be noted that the corridors in 4B are not specially ventilated, i.e. the reason for positive samples in this area could be that the BMTU does not have HEPA filtered air in the corridor.

Action taken by NHSGGC to mitigate this potential risk:

- F7 filters on AHUs were changed to F9 in all AHUs serving Ward 6A and 4C.
- Quarterly inspections are carried out to ascertain if filters on AHUs need to be changed.
- Mobile HEPA filters were located in areas throughout ward 6A and 4C.
- As an additional risk reducing measure within ward 4C, recirculation air scrubber fans were installed (Camfil Camcleaner 400 concealed fan units) within the ceiling space of each ensuite on ward 4C and 6A, then each space was validated to quantify the improvements achieved. The Cam cleaner consists of a pre-filter (bag) and a secondary HEPA filter.
- Routine air sampling is undertaken in ward 4B and results are reviewed by ICD/Microbiologist.
- Ongoing surveillance of infections linked to air as per the National Infection Prevention and Control Manual is in place.

The Cryptococal IMT Expert Advisory Sub Group was unable to prove this hypothesis as ***none*** of the extensive air sampling yielded a positive result for *C. neoformans*. The limitations of the

tests and the difficulty in isolating the organism are discussed in the first section and apply to all air sampling results.

Hypothesis Number 2 is possible.

Hypothesis Number 3 – Lack of 'Protective Isolation'

The possibility that unfiltered air from the Plant rooms could, via mechanical or electrical risers and or service voids, get into the rooms/wards where the 'at risk' patients were and an explanation of the varying degrees of the 'lack of control' of air movements around the entrances and exits of 6A, 4C and even 4B.

*There are no 'protective isolation' rooms in the general wards in QEUH (this includes 6A and 4C). One patient was in 4C for their entire hospital stay, while the other was in 6A a proportion of their hospital stay. Rooms in these wards do not have: HEPA filtered air, positive pressure within the room and with the air uniformly leaking outwards. Indeed, there are also a few issues with 'protective isolation' in 4B.

(But please note that there are no Standards or Guidelines for 'Protective Isolation')

**The lack of these 3 crucial controls means that it is possible that unfiltered air may gain access to the patient rooms/areas of these wards, e.g., from mechanical risers, electrical risers and service voids etc and also (importantly) any 'lack of control' of the air movements around the entrances/exits to these wards (please refer to mitigations implemented to address this further on in this report).

FINDINGS

The ward areas where the two case-patients were located, were 'general wards' (4C & 6A) with F7 filtration (? less than 80%). Investigation, of these areas, showed that the ventilation was 'dilution' only. The aim of ventilation, in 'protective isolation', should be dilution and exclusion (of unfiltered/dirtier air). **See paragraph above.
Some may point out that 4C and 6A have portable HEPA filters in both rooms and corridors and indeed some in the toilet areas. It is important to realise that these cannot remotely remedy the lack of proper 'protective isolation' noted. This is borne out by the air sampling results. Again, please note these are general ward areas and not specially ventilated wards.
Air testing has also revealed the presence of other types of fungi, e.g., *Aspergillus* species (see Table 5, below) which are known to affect BMT patients, however it should be noted that, there is limited evidence that *C. neoformans* actually poses a significant risk to this patient group (BMT patients) with only, about, 20 cases reported in the literature, Firacative, C *et al*. 2020[18]. It should be noted, that this is the case, and that neither it has been explained nor understood.

In addition, it should also be noted that both the case patients in the QEUH/RHC were not BMT patients and that the BMT Unit does have HEPA-filtered air in the rooms which also 'uniformly

leaks outwards'. Note however, that there are still issues, as 4B does not have ventilation in the corridor (air pushed out from rooms only) nor does the corridor have a solid ceiling. A major issue (see later) in 4B corridor is that at its interface with 4C corridor, periodically, air moves from this area (4C) into 4B, i.e., there is lack of 'protective isolation' in the corridors.

We will relate the air sampling results in 4B, 4C and 6A and also relate the results to: the voids/risers and the control of the air (or lack of it) in and around these wards.

Table 3a

This compares fungal air samples taken in individual rooms of 6A, 4B and 4C. The corridors of 6A, 4B and 4C and individual rooms of Beatson B8 & B9 (Air samples from time prior to move into QEUH, in years 2016 to 2018).

WARD	Total (paired) AIR samples	Total counts	Mean count (95% CI)	Median count	No (%) of samples with counts of 0,0	No (%) of samples with counts of >0,0
4B rooms	217	238	1.10 (0.80 – 1.40)	0	135 (62%)	82 (38%)
4B corridors	47	153	3.25 (2.73 - 3.77)	2	10 (21%)	37 (79%)
4C rooms	126	325	2.58 (1.54 – 3.62)	1	51 (40%)	75 (60%)
4C corridors	22	112	5.09 (3.44 - 6.74)	2	3 (14%)	19 (86%)
*6A rooms (Outlier removed)	239	1181	4.92 (3.98 – 5.86)	2	48 (20%)	191 (80%)
6A rooms	240	1526	6.33 (3.41 – 9.25)	2	48 (20%)	192 (80%)
*6A corridors	24	345	14.4 (10.95 – 17.87)	13	0%	24 (100%)
Beatson	218	120	0.55 (0.24 - 0.86)	0	172 (79%)	46 (21%)

*Please find in Table 3b below the addition of the total paired fungal air samples for 6A including those between 21st December 2018 and 16th January 2019, in the table 3a above is 6A results that are only between 12th February 2019 and 31st August 2019.

Table 3b

*6A rooms (Outlier removed)	292	1215	-	-	54 (18.5%)	238 (81.5%)
*6A Corridors	28	358	-	-	1 (3.7%)	27 (96.4%)

Table 4

WARD	NO of Paired AIR Samples	Paired samples with *Crypto* spp.	% with *Crypto* spp.
4B	264	4	1.5%
4C	148	11	7.4%
6A	320	36	11.3%

4B & 4C samples taken between 21st December 2018 and 31st August 2019.
6A samples taken between 21st December 2018 and 16th January 2019 and then between 12th February 2019 to 31st August 2019.

Table 5

WARD	No of Paired AIR Samples	Paired samples with *Aspergillus* spp.	% with *Aspergillus* spp.
4B	264	6	2.3%
4C	148	7	4.7%
6A	320	37	11.6%

4B & 4C samples taken between 21st December 2018 and 31st August 2019.
6A samples taken between 21st December 2018 and 16th January 2019 and then between 12th February 2019 to 31 August 2019.

Please note the following:

1. We employed as a reference point for the room air samples with about 3 years air counts taken in the BMTU, at the Beatson Cancer Centre (when still operational), between 2016-2018. This Unit was acknowledged as a Unit that was partly designed, by an expert, Andrew Streifel of Minneapolis, and therefore built to a high US standard in terms of its ventilation and 'protective isolation'.

2. Each Ward; 4B, 4C and 6A were compared to each other (the Beatson BMTU only compared with paired fungal air samples*) in three ways:
   a. Number of paired air samples with fungal counts of 0,0* (Tables: 3a and 3b)
   b. Number of paired air samples with isolation of *Cryptococcus* spp. (nos and %) (Table 4)
   c. Number of paired air samples with isolation of *Aspergillus* spp. (nos and %) (Table 5)

It is quite clear that looking at the results of these 4 wards that there is a consistency between them:

In terms of % of 0,0 counts going from best to worst is: Beatson with 79% of 0,0 counts; 4B with 62% of 0,0 counts; 4C with 40% of 0,0 counts and 6A with 18.5% of 0,0 counts.

Please see Tables 4 & 5 (excluding the Beatson) which both concur, when comparing counts for *Cryptococcus* spp. or *Aspergillus* spp., that the best to the worst is 4B, 4C to 6A.

The questions to be asked are: why is 4B not of the standard of the Beatson (please refer to the section on the decision-making processes/rationale for the move from the Beatson to QEUH), why is 4C worse than 4B and 6A the least effective (not as good as 4C)?

We will now look at why these specific wards have issues with their air quality: in terms of their ventilation, the control (or lack of it) of the air movements around them and the possible role of their voids and risers. i.e., their ability to provide 'protective isolation'.

Ward 4B

It should be noted that in 4B, all the rooms were under positive pressure of between 9 to10 Pascals (Pa) to the corridor with the room door closed. But note that there is no ventilation of the corridor, just 'spill over' from the rooms and the corridor does not have a solid ceiling. Normally a BMTU would have both of these. Consequently, these latter two points have implications in providing 'protective isolation'.

Peter Hoffman noted in Minute no 7 of 10 April 2019 and emphasised the need for solid ceilings in these critical areas 'A false ceiling adds a level of instability to pressure control (positive pressure) of such a room, and such pressure is crucial (along with HEPA filtration of the air).'

Voids
Specifically looking at the IPS (Integrated Plumbing System) panels, which behind them carry the water pipes to the wash hand basins in both the patient rooms and the toilets and to the toilet itself. Importantly, 4B had also all its IPS panels sealed with silicone, therefore no movement of air either in or out of the void was therefore possible (up to a point, as the seal will eventually degrade).

Risers
Ward 4B (unlike 4C and 6A) had the Risers sealed above and below the ward. Therefore, no ingress of e.g., 'dirty air' from a Plant Room possible by this route.

The Mechanical and Electrical Risers (small rooms) in 4B were investigated by JH and IP (Ian Powrie) on 10 May 2019.

Findings:

i. Doors to the Risers are kept locked
ii. Visually they *all* appeared well sealed and smoke testing showed no ingress or egress of air.
iii. All Risers were found to be under *negative pressure* to the Ward with air moving into the Risers, from the Ward, at between 1.7 to 4Pa

Air testing was carried out in the Risers.

Table 6

Riser	Fungal Counts	Isolates
HOW-038 Mech	0,3	1 each of: *Penicillium* spp. *H. hyphomycete* *Cladosporium* spp.
HOW-200 Elect	1,0	*Cladosporium* spp.
HOW-207 Mech	0,1	*Aspergillus fumigatus*
HOW-035 Elect	1,1	*H. hyphomycete* x2

Therefore, air all moving in correct direction and counts low (but note, more an indication of counts in the corridor)

Control of air around Entrances

The important issue in 4B, is the 'lack of control' of the air at the interface of the entrance at Room 76, which is directly opposite to the entrance/exit from 4C. It should be noted that this exit from 4B is purely used as a Fire Escape route, therefore it was neither completely sealed nor locked. On the left is a Room used by 4C Medics and a door from this Room out onto the Roof on Level 4. On the right coming out of 4C exit is a corridor (which becomes the Facilities corridor) and immediately off this (on both the left and right) are Bed/Patient Lift lobby Core C and FM Lift lobby Core C. There is also the complication that on the immediate left before Bed/Patient Lift lobby Core C is an Inter-departmental Corridor that runs straight up to the Controlled (main) Entrance to 4B.

In early May 2019 Ian Powrie (Senior Estates Officer)/John Hood (Chair of the Cryptococcal IMT Expert Advisory Sub Group) measured the pressure differences across the entrance to 4B opposite the entrance to 4C. With both doors shut we found a differential pressure of 4Pa going from 4B out to the Corridor and a differential pressure of 10Pa going out to the Corridor from 4C i.e., towards the 'entrance' to 4B.

On 10th May 2019 we checked these results. Again, with both 4B and 4C doors shut, we found 4Pa going out from 4B and 10Pa going out from 4C. However, if we then ***opened*** the door from 4C this resulted in 4B going from 4Pa out, *to* ***going negative*** and pulling 1.5 Pa INTO the bottom of Ward 4B. Indicating a failure to control the air movements around that entrance of 4B. Therefore, 'dirty' non-HEPA filtered air was intermittently being pulled into the bottom Corridor of 4B.

The air sampling results for 4B for 2019 would support this likely intermittent issue (and 'lack of control' of the air) at the bottom of 4B.

<u>Air sampling results</u>
Ward 4B air sampling results from 21 December 2018 to 17 January 2020 grew in air sampling only a total of 8 isolates of *Cryptoccoccus* spp. The first being in May 2019 and the last in January 2020.

The main entrance to 4B is controlled, so does not allow entry without agreement and therefore the door should not be left open for long periods of time. The beds from this entrance go from 99 to 89 – there was only a single isolation of *Cryptococcus* spp. in Room 90. Going round to the opposite side of the ward from Rooms 85 to 80, again there is only a single isolation of *Cryptococcus* spp. in Room 81. In Rooms 79 to 76 (noting that Room 76 is the last Room prior to the 'closed' exit) there were a total of 6 isolates of *Cryptococcus* spp. in this area; 3 positives in the Corridor near Rooms 77 & 78 with 2 positives from Room 78 and 1 positive from Room 77. Reiterating: this gives a total of 6 isolates at the end of this corridor (with only 2 from the rest of the Ward) where we know that intermittently air (which is not HEPA-filtered) from outside the Ward is almost certainly getting into that part of 4B.

Therefore, the above is the likely explanation of the 'lack of control' of the complex air movements around that entrance to 4B at Room 76.

The reasons for retrofitting the BMTU into the QEUH and the governance approving this move are listed below:

In July 2013 the Quality and Performance Committee in GGC approved a paper outlining the background and clinical reason for transferring BMT services from Beatson Oncology Centre (BOC) to QEUH. The following is a summary of this paper:

In June 2013, there were 52 designated Haematology inpatient beds across NHS Greater Glasgow & Clyde: 38 at Beatson West of Scotland Cancer Centre (BWOSCC) and 14 at the Southern General Hospital. The wards at the Beatson Oncology Centre managed acute and non-acute haematology patients, chronic and acute leukaemia, inpatient chemotherapy, inpatient radiotherapy, and housed both the Scottish Unrelated Donor Bone Marrow Transplant service and the West of Scotland Sibling Donor transplant programme.

Following a series of clinical meetings for the Clinical Service Review, the haematologists expressed the view that the new service model should split acute and non-acute haematology, with preference for maintaining all acute services at the New South Glasgow Hospital, due to the on-site availability of ITU. This would allow future-proofing of the service against changes in patient populations (e.g., paediatric sickle cell patients graduating to adult care) and fluctuations in activity.

The clinical drivers for the move from BWOSCC to QEUH were:

- To ensure 24/7 on-site ITU cover and to meet clinical standards
  For Bone Marrow Transplantation (all forms), services require JACIE accreditation which already stipulates that there must be robust and reliable access to ITU-level care. This is currently available on the Gartnavel site, supported by ITU at the Western Infirmary, but is unlikely to be maintained at existing levels after 2015.

  The Beatson WOSCC is the only UK transplant centre which does not have full ITU access on-site, and it is expected that future iterations of the JACIE standards may make this an explicit requirement.

The existing NICE and British Society of Haematology standards for the management of acute haemato-oncology patients specify on-site access to HDU, ICU, central line insertion facilities, dialysis or haemofiltration and interventional radiology. After 2015, the New South Glasgow Hospital will be the only site which can fulfil these requirements, as all inpatient Renal services will also be on Level 4, NSGH.

- Out-of-hours care
  At present, haematology out-of-hours is covered by multiple high-intensity (1 in 2 to 1 in 4) rotas at consultant level. This model would allow a single specialist rota, based at nSGH (new Southern General Hospital). All out-of-hours admissions would be to that site.

This proposal was approved in July 2013.

Ward 4C

Voids

Early on, 5th February 2019 we checked the Voids related to the IPS panels in Room 68 in 4C where Case A spent her entire hospital stay.

Findings:
As above, unlike 4B, these panels had not yet been sealed with silicone. (See 4B Voids and IPS panels above). However, it was *impossible* to get the pressure probe between the joins in these panels (such was the tight fit) and importantly, smoke was neither sucked into nor blown out of the Void. On removing these panels, smoke testing did show that the Void was, however, under positive pressure to the Room, with smoke moving into the Room. However, it was unlikely that the Voids in 4C, Room 68 were an issue as although not sealed with silicone there was no movement of air from the voids to the Room, until the IPS panels were actually removed.

Risers

The Risers were found not to be sealed above and below as in 4B.

Table 7

No	Riser Name	Direction of flow	Fungal Counts
1	RENW 178 (Elect)	*Riser to Corridor: 0.1 to 0.2 Pa	5,1
2	RENW 212 (Mech)	Corridor to Riser: 18Pa	9,11
3	RENW 220 (Elect)	Corridor to Riser: 0.2Pa	1,1
4	RENW 223 (Mech)	Corridor to Riser: 15 to 16Pa	2,4

Comment: On the face of it 4C Risers are an unlikely issue with only one (no 1) with hardly any positive pressure **out to** the corridor and two risers with >15Pa pushing **into** the Risers.

Control of air around Entrances

As noted above, at 4C/4B interface, 4C is pushing air out of the Ward (by Room 75) at +10Pa therefore this gives very good control of keeping out the air from around this complex area (see 4B control of air around entrances).
Similarly, at the 4C/4D interface (checked on 3rd September 2019): 4C is pushing air out towards 4D at approx. +12Pa, with all doors shut. 4C is pushing out towards 4D at +6Pa, with door to Lift lobby open. 4A is pushing air out towards 4D at approximately + 10 Pa with all doors shut.

Importantly, no configuration of opened doors at the 4C/4B interface or 4C/4D interface, resulted in air being pushed *into* 4C. Therefore, the above suggests that the Control of the Air around both entrances to 4C is reasonable compared to 4B and 6A (just not HEPA–filtered like 4B).

Air sampling results
Please note that 4C has only 10 rooms for Haemato-oncology patients (Rooms 66 to 75 with Room 75 the last in corridor before the intersection opposite 4B). The rest of 4C Rooms 51 to 65 consists of Renal patients, including Renal Transplants (i.e Solid Organ Transplants – SOT).

There were only 12/148 positive *Cryptococcus* spp. air samples from 4C between 21st December 2018 and 31st August 2019. Room 68 (1), Room 69 (2), Room 70 (2) Room 71 (1), Room 73 (2), Nurses station in Corridor – nearest Room 71 (3) and in Mech Riser RENW 223 (1) note that it was pushing 15 to 16 Pa from corridor into the Riser.

These air sampling results do not alter the fact that there is 'Control of the Air' around both entrances to 4C (unlike that around 4B and 6A) - as it is clearly pushing air OUT of both of them – which is good.

Ward 6A

Voids
As noted for Ward 4C early on (5th February 2019) we checked the Voids related to the IPS panels not only in Room 68 in 4C where Case A spent her entire hospital stay, but also in Room 5 in 6A, where Case B spent 49 days.

Findings:
As above, unlike 4B, these panels had not yet been sealed with silicone. (See 4B Voids and IPS panels above). However, it was *impossible* to get the pressure probe between the joins in these panels, such was the tight fit, and importantly, smoke was neither sucked into nor blown out of the Void. On removing these panels, smoke testing did show that the void was, however, under positive pressure to the Room, with smoke moving into the Room.

However, it was unlikely that the Voids in 6A, Room 5 were an issue as although not sealed with silicone there was no movement of air from the voids to the Room, until the IPS panels were actually removed (as was the case with 4C room 68 above where Case A spent all of her stay in QEUH).

Risers
As with 4C, the Risers were **not** sealed above or below the Ward as in 4B.

Table 8

No	Riser Name	Direction of Flow	Fungal Counts
1	GENW1-068 (Mech)	Corridor to Riser: 5Pa	2,0
2	GENW1-054 (Elect)	Corridor to Riser: 0.1Pa	13,7
3	GENW1-082 (Mech)	Riser to Corridor: by smoke only	1,0
4	GENW1-085 (Elect)	Just positive to Just negative	62,30
5	CA6-006 (Mech)	Riser to Corridor: 3Pa	0,0

Comment: Clear issue with consistent movement of air from CA-006 riser, very near to 6A entrance opposite 6B. Note that this Riser is opposite Room 1 in 6A.

Control of air around Entrances
Interface of 6A, 6B and Lifts (Sept 2019)

1. All doors shut: 6A is **negatively** pressurised i.e., pulling air into ward from this area (6B and Lifts) at, – 3.5 Pa
2. Door to lifts open: 6A **still negatively** pressurised but less so at – 1.9Pa
3. Door to 6B open: 6A **more negatively** pressurised at - 9.3Pa
4. Both above doors open: 6A **negatively** pressurised at – 7.4 Pa

Interface of 6A, 6D and Facilities Corridor (Sept 2019)

1. All doors shut: 6A positively pressurised at + 0.3 to +1Pa
2. Door to 6D open: 6A negatively pressurised to -1.9 to -2 Pa
3. Facilities Corridor door open: 6A positively pressurised to + 3Pa, i.e., air being pushed out of 6A.
4. Doors to Facilities Corridor and door to 6D open: 6A positively pressurised at +2.3 to + 4Pa, i.e., air being pushed out of 6A

The important findings here are that, firstly, there is poor control of air movement around the 6A/6B/Lifts interface with air being pulled into 6A between 1.9 to 9.3Pa depending on which of the doors are open. Therefore, we can clearly see the complexity and poor control of air around 6A, particularly at the 6A, 6B & Lifts interface, while it is not so bad at the 6A, 6D & Facilities Corridor interface. At the 6A, 6D & Facilities interface, depending on which doors are open, between +0.3 to +4Pa of air is being pushed out of 6A to about 2Pa being pulled in.

Air Sampling Results
6A had 36 isolations of *Cryptococcus* spp. (from air sampling) between 21st December 2018 and 16th January 2019 and between 12th February 2019 and 31st August 2019, see Tables 3a, 3b and 4. None of these were *Cryptococcus neoformans*.

These cryptococcal isolations support, 'the lack of control' of the movement of air at the 6A/6B/Lifts interface (with air being pulled into 6A between 1.9 to 9.3Pa, depending on the configuration of opened doors) and also Riser CA6-006 pushing air out into the corridor at +3Pa.

Table 9 -The air sampling results for 6A are as follows:

Room No	No of Crypto Isolates
1	4
2	3
3	1
4	1
5	2
6	2
7	0
8	2
9	1
10	1
11	0
12	0
20	1
21	1
22	0
23	1
24	2
25	1
26	2
27	1
Room no/Corridor/Riser	No of Crypto Isolates
Corridor by Nurses Station Opposite Room 5	9
Clean Utility, between Rms 8 & 20	2
GENW1-085 Riser	1
	Total Crypto Isolates 38

We can clearly see that air is being pulled into this end of 6A, perhaps most of the time. This air will be a mixture of unfiltered air due to its 'lack of control', particularly with that from Riser CA6-006 (and note that this Riser is directly opposite Room 1). Room 1 is also the first room in 6A after the entrance to 6A from Core A lobby which has the entrance to 6B opposite and the Lift lobbies on the left.

The results support the theory that there is poor control of the air movement around Ward 6A entrances – *particularly the entrance opposite 6B (see above).* There are 13 positive *Cryptococcus* spp. results in Rooms 1 to 6.
There are also 9 *Cryptococcus* spp. positive results at the Nurses station, in the Corridor opposite Room 5 (Case-patient Room). There are only 9 positive *Cryptococcus* spp. results in Rooms 20 to 27 at the other entrance to 6A. This clearly supports the hypothesis that the problem is due to the pulling in of 'dirty' air into 6A at the Entrance at Room 1 coupled with

the issue of a Riser opposite Room 1 with likely 'dirty' air coming out of this Riser into 6A at +3Pa.

I will finish with my (John Hood) 'Take Home Message' from the Minute of 18th December 2019: 'That now we know how complex the air movements are around these wards (4B, 4C & 6A) we could spend much time collecting more DATA on this, essentially trying to understand the complexities of it (it would be hugely time consuming), but…. the point is that we know this is happening, at least intermittently….and we must mitigate its effect i.e., stopping the ingress of unfiltered or dirtier air getting into these areas'. Noting: 'lack of HEPA filtration in 4C and 6A with only 3 ACH, lack of solid ceilings and no ventilation in 4B corridor (only spill over from the rooms) …to name but a few…'

Therefore, there are clearly failures/lack of 'protective isolation' in all 3 wards including in 4B.

Action taken by NHSGGC to mitigate this potential risk:

- F7 filters on AHUs were changed to F9 in all AHUs serving Ward 6A and 4C.
- Quarterly inspections are carried out to ascertain if filters on AHU need to be changed.
- Plant re-calibration and ventilation system re-balance to change ward 4C Room Differential pressures to corridor to be nominally positive (+ve).
- Deployment of mobile city M HEPA air scrubbers to assist in reducing the existing particulate within the Air in wards 6A, 4C and 4B.
- CVG (Ceiling Ventilation Grilles) removed and replaced with a standard ceiling tile to reduce the risk of particulates moving from the corridor ceiling void into the corridor transfer area and rooms in 4B, 4C and 6A.
- 4C, installation of recirculation air scrubber fans.
- Enhanced supervision in place in 6A where any issues regarding the ward estate is noted, escalated and actions put in place. (Monthly).
- Chilled beams are cleaned every 6 weeks in 6A and the recommendation is that this should be done yearly.
- Ongoing surveillance – clinicians and microbiologists will consider as part of differential diagnosis and send serum antigen and blood cultures.
- All windows in the affected wards were checked to confirm that there is no ingress (directly) of air from the outside.
- As an additional risk reducing measure within ward 4C, recirculation air scrubber fans were installed (Camfil Camcleaner 400 concealed fan units) within the ceiling space of each ensuite on ward 4C and 6A, then each space was validated to quantify the improvements achieved. The Cam cleaner consists of a pre-filter (bag) and a secondary HEPA filter.
- Adjust door seals to Gruffalo corridor light well, door seals adjusted to minimise air passage from outside environment.
- All IPS panels in 4B, 6A and 4C to be sealed with silicone.
- Door risers were sealed in 4B, 6A and 4C.
- Door seals between Ward 4B and 4C were adjusted to reduce the passage of air between the spaces.

- Routine air sampling is undertaken in ward 4B and results are reviewed by ICD/Microbiologist.
- Ongoing surveillance of infections linked to air as per the National Infection Prevention and Control Manual.

NB this list is not exhaustive.

It should however, be noted, that a move from the Top Floor of the Beatson Cancer Centre - which had one of the best built Units in the UK (in terms of ventilation, including HEPA filtration and strict control of air movement etc) - was suddenly required (see page 29). The organisation then had to provide an adult BMT Unit and adult Haemato-oncology Wards on the QEUH site, due to the lack of an ITU on the Gartnavel General Hospital campus (which the Beatson is on). This issue arose sometime after the design stage of the QEUH. Therefore, it was never likely to be possible for them to replicate the Top Floor of the Beatson in the QEUH in the timescale required, *at such short notice*.

Thus, Hypothesis Number 3 is possible, in Case B – a child – (due to the issues in 6A) but much less likely for Case A (as in 4C).

However, important to note that children are much less likely of contracting *C-neoformans* infections than adults.

Hypothesis Number 4 - The Cylinder Room near PICU

Unfiltered (outside air) circulating in the cylinder room (medical gas store) near PICU entered the patient room.

There is a cylinder room (medical gas store) CCW-050 in PICU with unfiltered (outside air) coming straight into this room. It overlooks the 'Sanctuary' (outside) where a pigeon roosting / guano problem was also noted (see PICU floor plan below). Please note that CCW 083 is the case - patient Room, Bed 5. Note that when the case-patient was in this room it was a Positive Pressure Ventilated Lobby Room (PPVL) (but not ventilated with HEPA filtered air) however it was subsequently changed to a Negative Pressure 'isolation room' shortly afterwards. This means that we were not in a position to see what the air movements were in and around this room when it was a PPVL room. A Negative Pressure Isolation Room is completely different, as this room has air being constantly extracted and discharged safely, in order to remove any airborne pathogens. The PPVL room is essentially trying to achieve the best of both worlds i.e., the room is ventilated itself but the lobby is under negative pressure to both the patient room and the ward corridor, with air being pulled in and extracted from the room and the ward corridor itself.

The possible issue with PPVL rooms is that if the doors from the lobby to both the patient room and the corridor are both left open, they then may allow ingress of air from the corridor straight into the patient room.
If both doors are open for a specific length of time, an alarm should sound. See Health Building Note 04-01, Supplement 1, 2013. Isolation Facilities for Infectious Patients in Acute Settings, page 4. Other (duplicate air samples) from PICU grew results shown in Table 10 below:

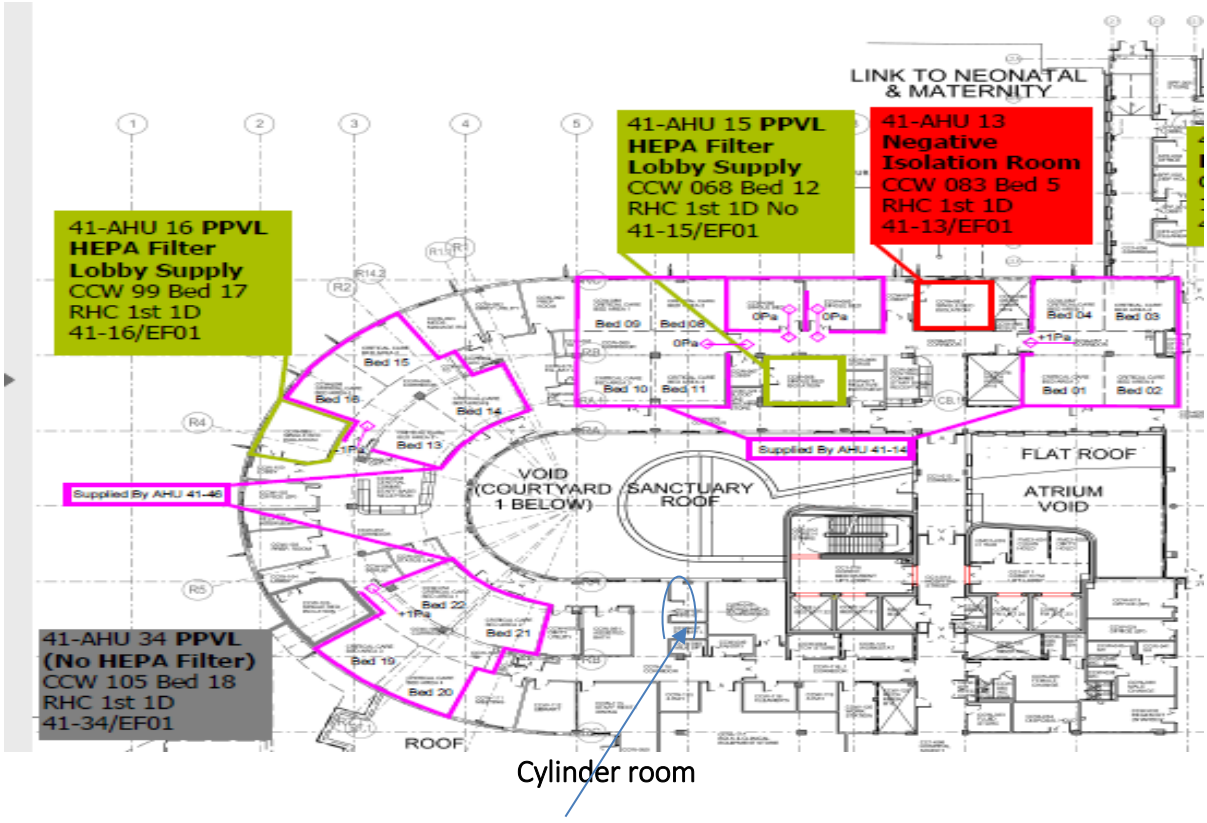
Table 10

Date	Room/Area of PICU	Air testing Results	Organism (s)
080219	Area 14	0,0	Nil
080219	Area 16	0,0	Nil
080219	Room 17	0,1	*Exophiala* spp.
080219	Room 18	0,0	Nil
080219	Room 18 (repeat)	0,0	Nil
080219	Area 21	1,0	*Cladosporium* spp.
080219	Nurses Station	3,2	*Rhodotorula* spp. and *Penicillium* spp.
080219	Cylinder Room	20,2	*Mycelia sterilia* ; *Penicillium* spp.
080219	Outside Cylinder Room	2,2	*Penicillium* spp.
270319	Cylinder Room	6,5	*Exophiala* spp., *Rhodotorula* spp. & Penicillium spp.
270319	Outside Cylinder Room	51,53	*Exophiala* spp., *Rhodotorula* spp., *Yeast* spp., *Aspergillus candidus and Penicillium* spp.
270319	Nurses Station 1	13,10	*Exophiala* spp., *Mycelia sterilia*., & *Yeast* spp.
270319	Nurses Station 2	29,31	*Exophiala* spp., *Rhodotorula* spp., *Yeast* spp. & *Aspergillus fumigatus*
270319	Area 13-16	4,6	*Exophiala* spp., *Yeast* spp. & *Mycelia sterilia*
270319	Area 19-22 Near Cylinder Room	4,7	*Exophiala* spp., *Cladosporium* spp., *Rhodotorula* spp. & *Yeast* spp.
270319	Room 17 Near Nurses Station 2	7,8	*Exophiala* spp. & *Rhodotorula* spp.
270319	Room 18 Near Nurses Station 2	16,14	*Exophiala* spp. & *Rhodotorula* spp.

FINDINGS

Patient B was in a PPVL (Positive Pressured Ventilated Lobby) room in PICU (nearby). This is therefore a possible but less likely route for the Patient B given the enhanced ventilation and pressure regime designed to prevent air circulation from the surrounding areas. This was also considered to be a very very unlikely route for patient A given the geographical distance from this area and the clinical area they were located in (4C).

Please note the Figure 2 below which shows the Floor plan of PICU.



Please note:

1. Not very near Patient Room CCW 083, Bed 5 – see Floor Plan - above. On opposite side of Ward from Beds 1 to 12.

2. The nearest Beds/ Nurses Station from the Cylinder Room are Beds 17 to 20, and Nurses Station 2.

3. It is also important to note that even although Bed 5 is a PPVL room, but not with HEPA filtered air, it is still likely to have provided a significant degree of protection to the ingress of unfiltered air, e.g., from the Cylinder Room. A problem would occur if the room lobby doors were both kept open for a length of time, but this would have resulted in the alarm sounding.

Please note the Room: CCW 083, Bed 5, outlined in red in the map of the Ward above, which is where Case B was looked after between 27 October and 1 November 2019 and then again from 18 November 2019 to 11 December 2019, when it was still a non-HEPA filtered PPVL Room, NOT - as marked above - as a negative pressure isolation room.

Please also note that CCW 083 Bed 5, on 30th October 2019 had a Filter change and verification carried out. It has been confirmed that the case-patient had been transferred to the HEPA filtered PPVL Room: Bed 12, prior to that filter change.

Action taken by NHSGGC to mitigate this potential risk:

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Room CCW/050 - where gas cylinders are stored. Action taken:

- The high-level air vent in the store was blocked off and fire sealed.
- The low-level vent was fitted with an extract fan with a non-return damper to ensure one way air flow.
- The entrance door was fitted with a fire rated door louvre to ensure air supply to the room from the corridor.

These modifications changed the room's ventilation set up from a displacement regime to a negative regime while complying with the buildings fabric specification and not compromising the rooms intended application as a ventilated bottle store. Now the air pulls through the store and out the building with no external air being pulled into the room, mitigating any concern that external air will be drawn into the ward from this area.

CONCLUSION

This is therefore a possible, but very unlikely route of Cryptococcus for patient B and an inexplicable route for patient A.

Hypothesis Number 4 is possible but very unlikely for patient B and an inexplicable route for patient A.

Hypothesis Number 5 – Helipad

That the down draft from Helipad was aerosolising cryptococcal spores from pigeon guano dust into the air intakes and thence the AHUs providing ventilation into the patient areas.

FINDINGS

Computational Fluid Dynamics (CFD) model was commissioned by GGC. The report concluded:

Comments from Minute of 6 June 2019. 'In the CFD simulations undertaken they demonstrate that the air arriving at the AHU intake locations does not originate in the region beneath the helipad for any of the scenarios considered. As a result of this conclusion, it is therefore, *unlikely* that debris from the helipad area is being carried into the hospital ventilation system(s), so anything drawn into the AHU's intakes is coming from the wider environment' and not affected by the shape of the building or presence of a helicopter. 'Whilst it is not possible to determine how far away potential contamination will originate, it should be noted that anything carried in the flow will be lightweight, since heavier matter will fall out due to gravity.' (See Appendix 3 for full report).

'Peter Hoffman asked if there are louvres on the Plant rooms. Althea explained that there are louvres, but are angled, dropping vertically, so that nothing can fall into the vents. Ian Powrie confirmed there are louvres on the external of the building. The AHU is attached to the louvres with a plenum. Peter Hoffman further asked about the louvres, not the AHU, if the downflow from the Helipad could push the air down into the Plant rooms? Ian Powrie stated that this was not impossible, but is unlikely because the louvres are fitted with sealed insulation boards. Peter Hoffman stated that it would therefore be difficult for air to get into the Plant rooms by this route. Ian Powrie stated that the only issue would be if any of the insulation panels were damaged or dislodged or if there was any movement.'

'There was some discussion after the presentation and Peter Hoffman stated it is unlikely to have been a build-up of aerosolisable material e.g., pigeon faeces as it would be regularly scoured by the helicopter.'

<u>Hypothesis Number 5 is rejected as an unlikely route.</u>

Hypothesis Number 6 - Specimen Transport System (POD)

AKA the 'pneumatic tube system'. This system is used to move specimens from wards to labs (and back the other way) via compressed air drawn from either the Plant room (PR 31 – not a PR on Level 12) or the ward area. These PODs then discharge the air into the ceiling void above Ward Treatment Rooms (on return to them).

FINDINGS

Discussed at length in Expert Group the consensus of which was that the 'risk related to the pneumatic tube system is likely to be small'. Peter Hoffman view: 'Felt that a small amount of unfiltered air coming into a Prep/Treatment room would have little effect on the air quality in a patient room.' 'He thought that this was an insignificant source if the *C. neoformans* was getting to patients by the air.'

Susie Dodd: 'stated that if this was a significant ingress of unfiltered air it would occur in all other Treatment/Prep rooms, thinking that we would be seeing infective consequences related to these other Treatment/Prep rooms as well' Minute of 2nd September 2019'

Hypothesis Number 6 is unlikely

Hypothesis Number 7- Dormacy/Latency/ Re-activation, and therefore often an unknown time of Exposure (and therefore an unknown Incubation Period)

This Hypothesis suggests that both patients could have been exposed to *C. neoformans prior* to their QUEH/RHC hospital admission.

One of the key papers on Dormancy/Latency is: Epidemiological Evidence for Dormant *C. neoformans* Infection (1999). Garcia-Hermoso, GJ *et al*. *J. Clin. Microbiol.* 37: 3204-3209[19]. They state: 'Several observations converge towards the hypothesis that the infectious particles can be acquired long before the infections develop and is diagnosed. First: a high percentage of healthy subjects have anti-cryptococcal antibodies which suggests prior contact with the fungus. Second: patients coming from tropical areas can be diagnosed with *C. neoformans var gattii* long after they have left these countries. Finally, unlike French patients, African patients living in France and diagnosed with cryptococcosis are rarely infected with *C. neoformans var neoformans'* (Serotype D). But a common serotype and cause of infection in France.

'In this study, we addressed the question of the time of acquisition of the infecting organism, an issue that had never before been raised. Using control samples of environmental isolates and two typing methods capable of clustering strains based on their geographical origins, we were able to demonstrate that patients diagnosed with cryptococcosis in France but born in Africa, had acquired their infectious strains a long time ago prior to emigrating from their countries of origin.'

In the discussion they went on to say: 'Based on the RAPD profiles obtained, we showed that the distribution of clinical isolates from nine African patients diagnosed with cryptococcosis in France was significantly different from that of the clinical isolates recovered from the 17 European patients ($p < 0.0005$). Furthermore, a second, independent typing method (CNRE-1

RFLP) confirmed the results, showing two clusters that contained the isolates from eight of nine African patients. This finding suggests that the infecting organism can be acquired long before the infection develops, since these patients had been living in France a median of 110 months, and had not been in contact with the African environment for as long as 13 years. That the African patients were infected with African isolates strongly suggests that these isolates had been sequestered and contained somewhere in the body, most likely in the alveolar macrophages. Then as soon as some kind of immune system defect occurred, which in most cases was AIDS, the fungus could multiply, disseminate and cause infection'.

'The clinical histories of these patients and the demonstration of a geographical clustering of isolates based on the generated profiles, are consistent with a dormant phase of *C. neoformans* within all individuals.'

The most recent review article on Dormancy and latency was published in July 2020: Dormancy in *C. neoformans*: 60 years of accumulating evidence. Alanio, A (2020)[20]. *Journal of Clinical Investigation*; 130: 3353-3360. This is another key paper which not only goes into the history but discusses the latest research on the biology of dormancy and reactivation. But it will give you an idea of the complexities.

'In summary *C. neoformans* can adapt fantastically to various environments, even very drastic ones, such as 8 days of complete anaerobiosis (no oxygen) without extracellular nutrients. *C. neoformans* uses strategies to resist these conditions. It is first perfectly able to enter quiescence in nutrient starvation conditions (stationary phase) or to be pushed into dormancy under additional anaerobiosis exposure. In vivo, one can imagine that viable but non-culturable cells (VBNCs)/dormant yeasts are most likely hidden in the innate immune cells for years before being able to reactivate and multiply in the body of immunocompromised patients but also in the environment. This makes *C. neoformans* the first relevant pathogenic organism in which to study fungal dormancy and its role in pathogenesis in humans.'

DIFFICULTY IN DETERMINING THE ACTUAL TIME OF EXPOSURE TO *C. neoformans* AND RELATING THAT TO WHEN THE SYMPTOMS OF THE DISEASE FIRST OCCUR i.e., THE INCUBATION TIMES

HIV/AIDS

Fessel, WJ. (1993)[21]. Two patients, who were, HIV positive had 'unusually intense exposures' to pigeons/old aviary demolition. Both developed cryptococcal meningitis and were asymptomatic until meningitis developed. The first patient helped dismantle an aviary that had been unused for about 10 years. The wooden floor was rotten and removing it produced clouds of dust and removing the rest of the wood with a chainsaw produced more dust. The demolition took about 2 hrs to complete. Seven weeks later he had first symptoms of Cryptococcal meningitis. Second patient was a 38yr old man whose office had no windows. One wall of the office faced an alley infested with pigeons. The bricks on the outside of this wall were loose; pigeons found their way through the wall and nested in the ceiling above the man's desk. Each day the patient had to remove from his desk the debris that had fallen from the pigeons' nest in the ceiling above. Cryptococcal meningitis developed about 10 weeks after this exposure to pigeons began.'

The author concluded that on the basis of the above case histories 'it is possible that the incubation period of cryptococcal disease is between 6 to 10 weeks. But noted 'that other

sources of infection could not be ruled out, because *C. neoformans* is widespread in nature' and they had not any samples from the environment in either case.

Varying Incubation times in Solid Organ Transplants (SOT).

Ooi, *et al*. (1971)[22] Renal transplant with donor discovered to have cryptococcal granulomas in the other (non-transplanted) kidney on day 5. Patient happy for graft to remain. Cryptococcus not found in urine until day 18 (Treated from day 20).

Sun, H-Y *et al*. (2010)[23]. 175 SOT's. Very early onset in 9/175. 5/9 were Liver transplants. Mean of 5.7 days post-transplant. Two early cases of day 1 onset – undetected pre-transplant infections, plus another 5 cases the likely result of donor acquired disease.
They split the cases into those occurring in less than 30 days and those after 30 days. In the group of 'less than 30 days to diagnosis' there were 2 cases on day 1, and 2 cases on day 25 and one case each on days: 3, 10, 21, 26 & 30.

They commented that 'most post-transplant cryptococcosis is considered to represent re-activation of latent or quiescent infection in the recipient. Assessment of pre-transplant serum samples for cryptococcal specific antibodies exhibited serological evidence of infection before transplantation.' Quoting: Saha et al (2007)[24]. 'Although these patients developed cryptococcal disease significantly earlier after transplantation than those without serological evidence of infection, the median time to onset of disease in patients with prior antibody reactivity was still 5.6 months. Development of cryptococcosis 1 month after transplantation is therefore unusual.'

MacEwan, CR *et al*. (2013)[25] Renal transplant secondary to diabetic nephropathy. Donor believed to have presumed bacterial meningitis. Given basiliximab at induction followed by tacrolimus, mycophenolate and reducing prednisolone. Five days later the team was informed that donor had died of *C. neoformans,* grown from CSF and blood. Donor was HIV negative with no known risk factors and no exposure to steroids or other immunosuppressants. Fluconazole prophylaxis 'not recommended' - due to rarity of *C. neoformans* infection in SOT and issues with interaction with tacrolimus – alters its pharmacokinetics. Recipient, discharged home, on tacrolimus and mycophenolate. Nine weeks post-transplant re-admitted with vomiting and severe frontal headache, also admitted to 3 weeks of frontotemporal headache, with no other signs of meningitis, and felt otherwise well. Therefore, the likely incubation period of 6 to 9 weeks

Baddley *et al*, (2013)[26]. 3 Cases: 1 liver transplant and 2 renal transplants. All 3 on tacrolimus.

Liver Transplant: 2 weeks post-transplant, splenectomy and liver biopsy. Both organs showed *C. neoformans* as did the blood culture.
Incubation period <14 days

Renal Transplant 1: IgA nephropathy and previous Renal Tx. Got anti-lymphocyte globulin and steroids at induction, then maintenance with tacrolimus and mycophenolate and prednisolone. Day 17 post-transplant, malaise and fever – Blood cultures positive with *C. neoformans*, CSF normal.
Incubation period 16 days

Renal Transplant 2: Alport's syndrome. End stage renal disease. Had basiliximab and steroids at induction and then onto tacrolimus, mycophenolate and prednisolone. Admitted 24 days post Tx with fever and neck stiffness. Blood culture and CSF both with *C. neoformans.*
Incubation period 24 days

Chang, Chun-Min *et al*, (2014)[27] Described a donor derived cryptococcal disease in a liver transplant patient. Recipient was 63-year-old female with hepatitis C related cirrhosis complicated by massive ascites and hepatocellular carcinoma. Donor was 48-year-old male with a massive haemorrhage in his left thalamus and ventricles. Recipient's post-operative course was uncomplicated and extubated on post-operative day (POD) 2.

Bilirubin gradually going up from POD 1 to POD 6. Temperature 38.5 on POD 6 with dyspnoea, respiratory failure and was re-intubated. She was commenced on fluconazole on POD 9 for a *Candida tropicalis* in her blood cultures. She had a liver biopsy on POD 14 due to her persistently elevated bilirubin (around 171 micromoles/L). This revealed a 'few cryptococcal – like encapsulated yeasts', 'found incidentally'. The blood culture also taken on POD 14 was also positive for *C. neoformans*. 'Nothing was found in her native liver and or pretransplant donor liver biopsy.'

Incubation period – Chang *et al*. (2014)[27] do not themselves give this but Camargo, JF *et al*. (2018)[28] in their review of all 14 cases (Table 1) – have it at <14 days.

Camargo, JF *et al*, (2018)[28] A cluster of donor-derived *C. neoformans* affecting lung, liver and kidney transplant recipients: case report and review of the literature.
These patients, all three, received their organ from the same donor at around the same time. They were done at different centres and the donor was from a different centre also.

The donor centre did not inform the 3 centres that the donor was found to have *C. neoformans* in blood, identified 8 days post transplants. 'Remarkably, the onset of illness in the kidney and liver recipients occurred more than 8 to 12 weeks after transplantation, which is beyond the incubation period previously reported from donor-derived cryptococcosis.

'None of these patients received antifungal prophylaxis that could have influenced the timing of presentation.' The authors also point out that all three recipients were on either tacrolimus or cyclosporine and that 'one possibility is that clinical presentation was delayed because of the anti-cryptococcal activity attributed to calcineurin-inhibitors. However, this is less likely since in the report by Baddley *et al* (2013)[26] – no 4 above – 'all the recipients were receiving tacrolimus at the time of presentation.'

Quotes from the Discussion: *'Thus the time from transplantation to symptomatic disease is variable and the incubation period, in some cases might be longer than previously described.'

*'The clinical presentation of cryptococcosis can also vary significantly depending on the individual patient's immune response which may contribute to variability in the timing and severity of the presentation. Based on the cases reviewed here the incubation period can range from a few days to more than 3 months.'

[redacted]

Therefore, knowing the actual time of exposure (i.e., the date of transplant), the range of Incubation Periods (in days of the 14 cases above) is **wide**. The range is: 3, 5, 10, <14 (2), 16, 18, 21, 24, 25, 30, 60, 63, 102 days. The explanation of this is perhaps that outlined by Camargo *et al*. (2018)[24] and marked with the * above.

While this work is on Solid Organ Transplant patients, it shows how variable and complex the incubation period in *C. neoformans* can be and that this is also likely to be the case with both case-patients in the QEUH/RHC.

Quote from **Kaplan, MH *et al* (1977)[29]**. 'The true duration of infection (of *C. neoformans*) **is unknown because there is no way to determine when the infection was actually acquired**. (Apart from donor-derived in SOT - as above).

<u>Hypothesis Number 7 is therefore possible, in both patients, that they acquired the *Cryptococcus neoformans* prior to their admission to the QUEH/RHC, but: highly likely to be impossible to prove.</u>

Patient Cases

Patient A

HISTORY

[redacted]

Patient A was then reviewed [redacted] the clinic.

On reviewing patient A's [redacted]

[redacted]

Patient A was admitted to the [redacted] October 2018 'feeling generally unwell with fever and sweats. [redacted].' [redacted] Patient A was then [redacted] transferred back to QEUH on [redacted] November 2018.

In patient course in QEUH

[redacted]

Patient A [redacted] November 2018, Microbiology contacted the ward to advise that the first of these were positive for *C. neoformans*. Antifungals were commenced and by [redacted] December 2018, blood cultures were negative.'

'Blood cultures remained negative' [redacted]

[redacted]

[redacted]

Reasons why the adult case could have been exposed to the *C. neoformans* prior to admission to the QEUH

1. Concept of Latency/Dormancy/Reactivation

See: Hypothesis no 7 and the difficulty in determining the actual time of exposure to *C. neoformans* and therefore the incubation period.

2. Significant Lymphopenia

Lymphocytes (particularly T lymphocytes) are crucial to the human host defence against infection by *C. neoformans*.

See: Wozniak, KL & Levitz, SM (2011)[30] quoting '*C. neoformans*, is an opportunistic fungal pathogen that is typically acquired via inhalation of the organism. *C. neoformans* primarily infects individuals who have impaired T-cell function, particularly those with AIDS and lymphoid malignancies and recipients of immunosuppressive therapies.' ([redacted]

'*C.neoformans* is surrounded by a large polysaccharide capsule which is the organism's virulence factor. As discussed elsewhere in this book, the capsule both subverts phagocytic and B cell defenses. This forces the host to rely heavily on T cell defenses.'

'Acquired Immune Response to *C. neoformans* in Human Cryptococcosis' 'the clinical evidence unequivocally demonstrates that CD4+ T cell-mediated immunity is paramount to the control of cryptococcosis'.

'The vast majority of patients with cryptococcosis have impaired T-cell function due to an underlying disease (particularly AIDS, *lymphoma* and idiopathic CD4+ lymphocytopenia) or receipt of immunosuppressive medications (particularly to prevent rejection of solid-organ transplants, SOT)'.

Some of their conclusions: 'T cells also contribute to protection against cryptococcosis. It is presumed that the major function of T cells is to secrete cytokines that recruit and activate phagocytes to inhibit and kill *C. neoformans*. Th1 and Th17-type cytokines are associated with protection against infection, while Th2-type responses are associated with exacerbation of disease.'

[redacted]

Therefore, it is quite possible that patient A could have been exposed to (and been susceptible to) the *C. neoformans* prior to [redacted] admission to the QUEH on [redacted] November 2018, and it remained 'dormant'/'latent' until [redacted] host defences were finally overcome.

3. Pigeon ingress in Plant Room 123

Please see 'Implications of Wet Guano'

Firstly, the reasons why air, in the Plant Rooms, is not sucked down the duct (towards the patients) in the AHU during a final filter change (as it actually blows out).

Secondly, there was no evidence that either of the two case-patients were present in any wards/room at the time the AHUs serving them, had a final filter change.

Thirdly, the implications of wet pigeon guano etc in the Plant Room and the reasons why (in that situation) it was unlikely that the wet guano would have supported the growth of *C. neoformans* – even if this organism was present in the guano – nor would it have been easily aerosolised

4. Outside Air Source from the Environment – either when case patients outside hospital or when patients in hospital.

Note that we already know from Public Health that there were three other cases of *C. neoformans* infections, from different areas, within the GGC in 2018. Therefore, it is more than possible that (particularly Case A, see below) contracted this from breathing air containing *C. neoformans* spores while in the community.

We also know that there had been, between 2009 – 2017, a total of 13 cases of community-acquired *C. neoformans* infections in the same area (GGCHB). Therefore, we know that it is highly likely to be present periodically in the environment and outside air, in certain areas.

PATIENT A: WHERE/HOW POSSIBLY ACQUIRED THE INFECTION

Firstly, as an Inpatient in QEUH

In other words that the *C. neoformans* spores came in with the outside air and the presence of F7 final filters (of ?80% filtration, rather than HEPA filters, 99.9% filtration) allowed a percentage of cryptococcal spores into the air of the rooms that the case-patients were). An important point is that the presence of F7 final filters should significantly reduce the numbers of spores from the outside air – even although not as good as HEPA filters. Please also see the air sampling results for Ward 4C, the Ward in the QEUH, that this patient was admitted to and stayed in until [redacted] death.

Important points are:

a) The actual control of the air around 4C was not bad compared to (certainly) 6A and also in that 4B had issues with control of the air around it.

b) Note that 4C also does around 140 Renal Transplants per annum. These patients (solid organ transplants) are known to be at risk of contracting infections with *Cryptococcus neoformans*. Note that there have been no cases of this infection, so far, in this group of patients, ever at the QEUH. Please see: Marr, KA et al. (2020) [0]

Secondly, [redacted]

[redacted]

[redacted] was admitted to the QUEH [redacted] November 2018 and had a positive blood culture with *C. neoformans* on [redacted] November 2018. This is a matter of only 15 days.

Thirdly, [redacted]

Fourthly, [redacted]

Fifthly, [redacted]

We will look at how likely [redacted] came in contact with *C. neoformans* while in the QEUH, in these 15 days in November 2018.

We have already explained why Plant room 123 was highly unlikely to have been the source of the *C. neoformans* in the Section above: 'Pigeon Ingress in Plant Room 123'. Therefore, looking at the environmental conditions related to the outside air from [redacted] November 2018.

It is highly *unlikely* that the incubation time could be as short as 5 days (not only because of Dormancy/Latency/Reactivation). Therefore, a review of the weather in 'Glasgow' between [redacted] November and [redacted] November 2018 was undertaken:

[redacted] November	Light Rain	6h
[redacted] November	Light Rain	6h
[redacted] November	Light Rain/Drizzle	12h
[redacted] November	Light Rain	6h
[redacted] November	Light Rain	12h
[redacted] November	Light Rain	6h
[redacted] November	Light Rain	12h
[redacted] November	None	0h
[redacted] November	Light Rain	6h
[redacted] November	Light Rain	12h
[redacted] November	Light Rain	6h
[redacted] November	None	0h

On the 12 days between [redacted] November, on only two days was the weather dry (and one was the last day). Therefore, as with so many consecutive days that were variably wet it seems unlikely that during this period that cryptococcal spores would easily (if at all) aerosolise from an environmental source and if they did, they were likely to also have enlarged capsules

– so less likely to reach the alveoli of humans. (See above pages 18 &19*. Pigeon Ingress in Plant Room 123, under Implications of Wet Pigeon Guano, 2nd and 3rd Paragraphs).

Acquired when at home etc /not as a hospital inpatient

Certainly, for the adult patient it is much more likely that they could have become infected from breathing outside, unfiltered air, at home etc, than air from the QEUH. Many more days at risk. [redacted] – both of which could possibly be/have been a likely environmental source. Please note that in 2009 there had been two cases one with unknown underlying disease and one HIV positive, all three living near [redacted] The rationale for these hypotheses is as follows:

- AHUs and Plant Room air source very very unlikely ('unfeasible')
- F7 at ?80% but still not HEPA
- Patient in hospital for 15 days only, prior to positive blood culture
- Outside hospital (QUEH) for months
- Lymphocytes low for months
- Therefore 'at risk' for months.

Patient B

HISTORY

[redacted]

[redacted]

[redacted] transferred to the Royal Hospital for Children, Glasgow for further investigation and management.

On admission to RHC Ward 2A, [redacted]

[redacted]

[redacted]

[redacted]

The patient was transferred from Ward 2A RHC to Ward 6A on [redacted] 2018, as Ward 2A was closed in view of water contamination issues.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] transferred to PICU on [redacted] 2018, [redacted]

[redacted] returned to ward 6A on [redacted] 2018.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] 2018 was raised and *Cryptococcus neoformans* was isolated from the blood cultures taken on the [redacted] 2018. However, these positive results were not available until after [redacted] death.

At the time of preparation of this report, the post mortem findings were unavailable as the autopsy was undertaken under the auspices of the [redacted] however the results of the PM Microbiology, revealed evidence of disseminated Cryptococcal infection in tissue samples from: lung, spleen and CSF.

Cryptococcosis in Children

Cryptococcal Disease in HIV-infected Children, Kao, C & Goldman, DL, (2016)[5] 'Due to the rarity of paediatric cryptococcosis, the precise prevalence is difficult to define and may vary by region. Studies in US children with AIDS in 1990's estimated an incidence of to be about 1%. The basis for this lower incidence of cryptococcosis when compared with adults remains poorly understood but could be related to differences in exposure and/or immune response that allows for progression of disease. Serological studies suggest that in certain urban areas, sub-clinical cryptococcal infection is common among children older than 2 years of age.

Furthermore, these studies suggest ongoing exposure throughout childhood. Nonetheless, it is possible that the type of exposure in children is qualitatively (e.g., different strains) or quantitatively different when compared to adults. Besides AIDS, cryptococcosis has been described in the context of primary and acquired immunodeficiencies as well as apparently healthy children. This includes hyper IgM syndrome, hyper IgE syndrome, Bruton's agammaglobulinemia, SLE, leukaemia and sarcoma. Organ transplantation and the use of biologic agents (e.g., anti-TNF antibodies) are also recognised as important risk factors for cryptococcosis. Recent studies in adults suggest that subtle differences in the immune system including polymorphism in Fc receptors and antibodies to GMCSF may play an unrecognised role in susceptibility to cryptococcal infection in both apparently healthy individuals and those that are immunocompromised.' 'Because of our relatively small number of cases of pediatric cases of cryptococcosis, much of our understanding and recommendations regarding this disease represent extrapolation from adult data.'

'Since 2009, there have been four series from different countries (USA, Brazil, South Africa and Columbia) describing the paediatric experience with cryptococcosis in HIV-infected children. The number of children in these studies varies from 41 to 361.

The percentage of HIV infected children in these studies varies from 16% in a US study (Joshi, NS *et al* (2010)[31] to 91% in a South African study (Meiring, ST *et al* (2012)[32]). Series of paediatric cryptococcosis have also been reported from China and Taiwan. These studies are remarkable for the percentage of children without underlying immunodeficiency and the absence of HIV infection.'

'The largest description of paediatric (age <15 years) cryptococcosis (n=361, 91% HIV infected) comes from South Africa. In this series, paediatric cryptococcosis represented 2% of all cryptococcal cases over a 2-year period with an annual incidence of 47 cases per 100,000 persons for HIV infected children when compared with 120 cases per 100,000 in HIV infected adults. A bimodal peak in the incidence was found with the greatest incidence in children <1 year of age and a second peak among children 5-10 years of age.'

'This peak in incidence in children <1year of age has not been described in other paediatric series with most reports describing a peak incidence in older children (8-12years), including reports from Botswana and Ghana.'

'The most recent paediatric series of cryptococcosis comes from a national survey of Columbian children (<16 years) over an 18-year period in 2014.' From 1993-2010. See the 3 references listed below. 'This series highlights important trends in paediatric cryptococcosis including the emergence of non-AIDS cases of cryptococcosis in regions where ART (Anti-Retroviral Therapy) is available. In this series, the annual incidence of paediatric cryptococcosis was 0.017 to 0.12 cases per 100,000 children depending on the region of the country. Overall, 41 children, 10 (24.4%) were HIV positive, 3 (7.3%) had reported either corticosteroid use, malignancy or autoimmune disease and 19 (46.3%) had no known risk factors. The mean age of affected children in this series was 8.4 years with a slight male predominance, which is similar to what has been described in previous paediatric series'.
Quoting:
Abadi, J & Pirofski, L (1999)[33]
Likasitwattanakul, S *et al*. (2004)[34]
Gonzales, CE *et al*. (1996)[35]

In summary, paediatric cases of *C. neoformans* infection are a very *rare* occurrence of an already *rare* disease and the literature (above) states that in children '*Serological studies suggest that in certain urban areas, sub-clinical cryptococcal infection is common among children older than 2 years of age. Furthermore, these studies suggest ongoing exposure throughout childhood*.' This leads onto the concept of latency, dormancy and reactivation, as previously discussed.

Key Paper: Cryptococcosis in Columbian children and a literature review. Lizarazo, J *et al*. (2014)[36].

PATIENT B: WHERE/HOW POSSIBLY ACQUIRED THE INFECTION

1. Note the Rarity of this Disease in Children:
   Important to understand the whole issue of children and rarity of infection with *C.neoformans*. See, immediately above in Section on 'Cryptococcosis in Children'

2. Concept of Dormancy/ Latency /Re-activation
   See: Hypothesis no 7 and the difficulty in determining the actual time of exposure to C. neoformans and therefore the incubation period. This Hypothesis suggests that the patient could have been exposed to C. neoformans prior to their QUEH/RHC hospital admission or during their stay in QEUH/RHC. Impossible to be certain when.

3. [redacted]
   Please see written report by Consultant Paediatric Haemato-oncologist to patients GP on child's death. [redacted]

4. Admissions to various areas in QEUH/RHC - [redacted] 2018

   [redacted] 2018, 2A RHC [redacted]

   [redacted] 2018, 6A QUEH [redacted]

   [redacted] 2018, PICU RHC [redacted]

   [redacted] 2018, 6A QEUH [redacted]

   [redacted], PICU [redacted]

   Total of 103 days in Hospital.

5. Hospital While in- patient in QEUH/RHC
   See Wards that the patient was in QEUH/RHC in 2018, No 4 'Admissions to various areas in QEUH/RHC...' above. The important issue is the 'lack of protective isolation' in Ward 6A compared to that in Wards 4B and 4C. See? Pages 31-33 of this Report for the results and comparison with 4B and 4C. 6A is the 'less good' of the 3 wards. While patient in PICU, please see Hypothesis 4, in that when patient in a PPVL Room, with both doors shut, this should be protective. Please note, I have no results of any air samples from Ward 2A.

6. [redacted]
   It is possible, but impossible to prove. Clearly, [redacted] we do not know the presence or absence of C.neoformans in that air. Please note there have been 2 cases (both adults) of C.neoformans in the [redacted] one in December 2015 and one in June 2016.

7. Lymphopenia in Child

[redacted]

8. Pigeon Ingress November 2018

Noted on 28th November 2018 the presence (in PR 123) of 3 dead pigeons and presence of pigeon guano at the top of the PR near AHU's 01 and 05. This was noticed by a contractor working there on that day, he took pictures and sent them to Estates colleagues on that day (please refer to pictures on page17). On the 29th November 2018, AHU 123-07 (at the other end of the PR 123 from the guano) was opened and the Final filter changed. Please see Hypothesis 1 in Draft Report dated 31st August 2020, specifically the reasons why Plant Room air was found not to be pulled down the duct (towards the patients in Wards served by that specific AHU) during the time that the final filter was replaced. Indeed, the air was found to do the opposite, pushing air out of the duct rather forcefully. This AHU 123 – 07 that was opened, served the Right-Hand side of the Facilities Corridor on Levels 4,5,6 & 7 of quadrants D & A, so midway between Wards 6D & 6A on Level 6. Please note however: further evidence to refute PR 123 as the source of *C. neoformans* spores (during replacing of a Final filter) in either of the two cases in [redacted] 2018, see Patient A & Patient B Pathways, below. This is significant, in that it was the Plant room with the most significant contamination with pigeon guano on the site and it may have been a logical leap to assume that this was connected to the cases, however, we now know that this Plant room was in no way connected to either of the patients at any point in their admission.

Patient A Pathway

Patient was in 4C – but this Ward was ventilated by AHUs on PR 124C not, PR 123D. But also note that [redacted] had a positive blood culture with *C. neoformans* taken on [redacted] November 2018 – 8 days prior to the opening of AHU 123-07. Also note that the maintenance records of PR 123 show that prior to this opening on [redacted] November 2018, the previous occasion on which AHUs in PR 123 were opened was on 18th April 2018 – of AHU2 and AHU3. Originally, there were no reports of pigeon ingress of Plant rooms at that time, but see below. It was, incidentally, found (in early January 2021 from checking the Plant room AHU records) of some pigeon ingress in PR 123D in 19th March 2018 – the problem noted 'pigeons' and on 28th March 2018, the 'removal of bird (singular) and sanitisation' took place. It was also noted that: Plant Room 31 (that serves 4B [which was not realised to be the case at this time] and contains part of the POD system), on the 19th June 2018 of single pigeon ingress plus fouling was discovered and the action was that the pigeon was humanely dispatched (singular), fouling cleared and treated with biocide. Please note, therefore, that here is clear evidence that Estates officers were, at this time (early 2018), noting and making sure that pigeon ingress and fouling were being quickly dealt with by Pest Control – this is prior to the issues noted in PR 123D, in early December 2018.

Patient B Pathway

This patient had been transferred from 6A to PICU (RHC) on [redacted] 2018, some [redacted] prior to the opening of AHU 123-07. In PICU the air was from a completely different PR on a different floor in RHC. Essentially even though [redacted] was in the QEUH/RHC for [redacted] to the positive blood culture with *C. neoformans*, it is not straight forward to assume that because [redacted] was in the hospital for that length of time, that [redacted] could not have been exposed to the organism at some time before [redacted] admission. I refer to the work done, particularly in children, with respect to childhood exposure and dormancy/latency/reactivation. See the Section on Cryptococcosis in Children (above). Also note that *childhood C. neoformans* is a rare event compared to the disease in adults which in itself is a rare disease. [redacted]

OTHERS AT RISK FROM INFECTION WITH *CRYPTOCOCCUS NEOFORMANS*

Marr, KA *et al*. (2020)[0] 'Cryptococcosis has decreased in incidence in HIV infected patients, but disease and related mortality are increasing in other immunosuppressed populations. We undertook this longitudinal cohort study as an NIH intramural-extramural effort, positioning 25 centres to identify cases and report longitudinal outcomes. Longitudinal assessment enabled depiction of clinical presentations and outcomes over time, incorporating functional assessments that were not clinical practice.' 'Underlying diseases in the cohort generally reflect other population-based analyses quoting George, IA *et al*. (2018)[37] Results reflect an increasing trend in targeted biological therapies (anti TNFa and interleukin 6).'

'Patients with haematological malignancies had frequently received targeted monoclonal antibodies and small-molecule signalling inhibitor, anti CD20 (JH: rituximab – as in our Case B) etc'
'A sizeable proportion of people had decompensated liver disease as a sole risk, consistent with other reports, and potentially indicative of complex immunodeficiency.'

'Prior serologic studies have shown that many in certain geographic areas are infected with *C. neoformans* early in life, and a substantial proportion of cases that are recognised after SOT (solid organ transplant) reflect reactivation of latent infection' (quoting: Saha *et al* (2007)[24] and Davis *et al*[38] (2007) 'Paradoxical worsening in HIV-negative patients is associated with defective alternative (M2) macrophage activation, pro inflammatory cytokine release, and intrathecal T-cell activation, with resultant axonal damage.'

'In this heterogeneous cohort of people without HIV infection, survival rates were, not surprisingly, lowest in people with CNS (Central Nervous System, JH) disease. Low risks of death were noted among SOT recipients and people with haematological malignancy.' But note only 17 cases of haematological malignancy out of 145 patients. They found that patient age of >60yrs was associated with higher risk of death. They also pointed out that 'The cohort design also has limitations. While it enables assessment of long-term outcomes in a limited cohort of people, it cannot generate estimates of prevalence or geographic distribution, because this is also influenced by site selection.' While bearing this in mind I wish to describe, within their cohort, the various underlying diseases that they found in these 145 patients.

Underlying Disease: no (% of 145)

1. Solid Organ Transplant (SOT)

n = 49 (33.8%)

Kidney Tx	24
Liver Tx	10
Heart Tx	8
Kidney/Panc Tx	3
Lung Tx	3
Kidney/Heart Tx	1
Total	49

2. Haematological malignancy (without haematopoietic stem cell transplant, HSCT)

n = 17 (11.7%)

Lymphoma	7
CLL	4
Myelodysplastic Syndrome /AML	3
Myeloma	2
ALL	1
Total	17

3. HSCT

n = 2 (1.3%) One autologous and one allogenic

Total	2

4. Autoimmune syndromes

n =23 (15.9%)

SLE	3
Rheumatoid arthritis	2
Eosinophilic Syndromes	2
Sarcoidosis	2
Myasthenia gravis	2
Inflamm colitis	2
Autoimmune hepatitis	1

5. Autoimmune syndromes (contd)

PBC	1
Multiple sclerosis	1
Idiopathic thrombocytopenia	1
Polyarteritis nodosa	1
Polymyositis	1
Wegener's	1
Polyarthropathy	1
Psoriasis	1
Unknown	1
Total	23

6. Decompensated liver disease

n = 14 (9.7%)

Total	14

7. Solid tumours

n = 8 (5.6%)

Lung	3
Breast	2
Prostate	1
Rectal	1
Liver	1
Total	8

8. Primary Immunodeficiency

n = 3 (2.1%)

Idiopathic lymphocytopenia	2
Amylogenesis Imperfecta	1
Total	3

9. Miscellaneous

n = 4 (2.8%)

Diabetes mellitus	2
Steroid receipt after pneumonia presentation	2
Total	4

10. None

n = 25 (17.2%)

Total	25

11. Grand Total: 145

IMMUNOSUPPRESIVE MEDICATIONS IN THIS COHORT (n = 145)

1. Glucocorticoid therapy
   n = 69 (47.6%)

2. Cytotoxic chemotherapy
   n = 60 (41.4%)

3. Calcineurin/mTOR inhibitors
   n = 42 (29.0%)

4. Antimetabolites
   n = 36 (24.8%)

5. Targeted antibodies
   n = 10 (6.9%)

6. Other
   n = 6 (1.3%)

This essentially shows the wide range of patients that are potentially at risk (e.g., in the QEUH) from *C. neoformans*, not just those with lymphoreticular disorders [redacted]

Genomics

Farrer, RA, Borman, AM, Inkster, T, Fisher, MC, Johnson, EM & Cuomo, CA (2021). Genomic epidemiology of a Cryptococcus neoformans case cluster in Glasgow, Scotland, 2018. *Microbial Genomics*, DOI 10.1099/mgen0.000537

Abstract 'In 2018, a cluster of two cases of cryptococcosis occurred at the Queen Elizabeth University Hospital (QEUH) in Glasgow, Scotland (UK). It was postulated that these cases may have been linked to pigeon droppings found on the hospital site, given there have been previous reports of *Cryptococcus neoformans* associated with pigeon guano. Although some samples of pigeon guano taken from the site yielded culturable yeast from genera related to Cryptococcus, they have since been classified as *Naganishia* or *Papiliotrema* spp., and no isolates of *C. neoformans* were recovered from either the guano or subsequent widespread air sampling. In an attempt to further elucidate any possible shared source of the clinical isolates, we used whole-genome sequencing and phylogenetic analysis to examine the relationship of the two Cryptococcus isolates from the QUEH cases, along with two isolates from sporadic cases treated at two different Glasgow hospitals earlier in 2018. Our work demonstrated that these four clinical isolates were not clonally related; while all isolates were from the VNI global lineage and of the same mating type (MAT alpha), the genotypes of the two QEUH isolates were separated by 1,885 base changes and belonged to different sub-lineages, recently described as the intercontinental sub-clades VNIa-93 and VNIa-5. In contrast, one of the two sporadic 2018 clinical isolates were determined to belong to the VNIb sub-lineage and the other classified as a VNIV/VNI hybrid. Our work demonstrated that the two 2018 QEUH isolates and the two prior *C. neoformans* clinical isolates were all genetically distinct. It was not possible to determine whether the QEUH genotypes stemmed from independent sources or from the same source, i.e., pigeons carrying different genotypes, but it should be noted that whilst members of allied genera within the Tremellomycetes were isolated from the hospital environment, there were no environmental isolations of *C. neoformans*.'

Cryptococcus Incident Management Team Expert Advisory Sub-Group Chair's Comments on the above Paper, (JH)

1.Introduction, Page 2 - 'Proliferation of *C. neoformans* will occur in pigeon guano, particularly in environments protected from sunlight, such as in lofts [7] Quoting *Iowa State University Center for Food Security and Public Health. Cryptococcosis. Center for Food Security and Public Health Tech Factsheets,* 45. Ames, IA: Iowa State University, 2013.
JH : the author of this paper quotes no papers in supporting this statement.
Please see: the work of Ruiz, Bulmer, Fromtling, Neilson[8,9,10,11,12] specifically Ruiz *et al*[8] (1981). Distribution of *Cryptococcus neoformans* in a Natural Site. Quote: 'Pigeon droppings in a vacant tower were assayed for the number and size of viable cells of *Cryptococcus neoformans*'.

'The dry, thinly scattered floor debris contained 2.6 x 10^6 viable cells per g – 300 times more than were cultured from a large, compact pile of pigeon droppings (7.4 x 10^3 cells per g). Aerosols generated from floor debris containing pigeon droppings had an average of 360 viable cells in 31 L of air, 27 of these cells (7.5%) were 1.1- 3.3 um in diameter, and therefore capable of human lung deposition.'

2. Page 2 - Clinical case summaries.

[redacted] patients had a time period with a gap in cryptococcal cover, where the antifungal was either discontinued or they were switched to another agent. This was a risk factor for cryptococcal acquisition or reactivation.'

[redacted]

3. Page 3 – 'Results: Case description and epidemiological evaluation.' 'Both patients (one adult and one child) had underlying [redacted] Prior to blood culture testing, both patients had been in hospital for a prolonged period of time [redacted]

JH: the adult was therefore not that long in hospital (QEUH) but had been significantly [redacted] for several months beforehand (see above).
'Both patients were from the [redacted]

[redacted]

4. Page 3/4 – 'Genomic analysis of QEUH isolates' 'Sequence and phylogenetic analysis revealed that the two isolates from the 2018 QEUH were not clonally related.' 'Importantly, we confirmed that the [redacted] are genetically distinct, and represent discrete ancestral histories, and that the cases at QEUH in Glasgow, UK, were caused by isolates from two separate sub-clades.'

'Two further isolates were identified from two other patients '
JH: NB two patients in two different hospitals in the same Health Board area in 2018.

[redacted] These cases were determined to be sporadic as they were not linked in time, place or person. Neither patient had a history of significant hospital stay prior to their positive result, although one patient spent 48h in the same hospital as the cluster under investigation, in April 2018'.

[redacted] is a *C. neoformans* var. n*eoformans* (VNIV)/*C. neoformans* var *grubii* (VNI) hybrid, and subsequently excluded from the phylogenetic analysis.'

5. Pages 5/6 - Discussion

'The large number of variants that differentiate the two (Comment: patient's) isolates from 2018 supports a model of independent acquisition by each patient, rather than transmission of a clonal isolate.'

They go on to mention the cluster of *C. neoformans* cases (6) in an Arkansas Hospital in 2013 (Vallabhaneni, S *et al* 2015)[2]. They believed that this is 'Only one other cluster of *C. neoformans* infections in hospitalised patients has been reported in the literature'. '...but no definitive source was established, and environmental sampling was negative. Isolates from these clinical cases appeared genetically diverse, as three separate MLST (multilocus sequence typing) were identified.'

'In the 2018 Glasgow incident, it is possible that patients acquired *C. neoformans* from plantroom contamination entering the ventilation system or voids or from ingress of spores into the building from external air'

JH: Please see the various Hypotheses described above.

'Alternatively, cryptococcal reactivation or recent infection prior to hospitalization is a possibility, but would seem less likely in the context of epidemiological links in time, place and person with a feasable source'. JH: See Hypothesis 1 above.

'If whole-genome comparisons had revealed that the two QEUH isolates were highly genetically similar, this would have strengthened the argument that they arose from a point source and thus, were likely linked to a single nosocomial source'

JH: – but they were not!

'However, the fact that they are genetically distinct does not necessarily rule out a common source of infection, given that pigeon guano from different birds and even from the same bird, may contain a variety of unrelated genotypes due to the general diversity of environmental isolates'.

JH: Any evidence of this, in this instance?

They went on to say:

'Although other *Tremellomycetes* yeasts were found in the locality, there were no environmental isolation of *C. neoformans* from the hospital buildings or from the wide-scale air sampling undertaken following the identification of the second case ...'

'While an epidemiological link in time and place to a pigeon infestation and guano detection on the hospital site suggested a common source, genome sequencing of the two cryptococcal isolates did not provide evidence of a single genotype causing infection'.

'However, there were several limitations in the environmental sampling including both culturing conditions and the cleaning of potential source sites, which may have decreased the likelihood of detecting *C. neoformans* in subsequent samples. Therefore, we cannot exclude a point source consisting of multiple cryptococcal strains. Indeed, genetic diversity of clinical and environmental isolates within a city has been described'. JH: New York City.

But they go on to say: 'While wider sampling might reveal some isolates with closer genetic links, this study, including isolates from two other infections from the same geographical area, highlights the diversity of genotypes causing infection in the UK.'

JH: Question: How can the authors say 'highlights the diversity of genotypes causing infections in the UK'?

Email from Rhys Farrer to Teresa Inkster 17th April 2019: 'The 2 Glasgow isolates are the only representatives from the UK in the tree, so it may be helpful to include some others, yes'

JH: Were other UK strains inserted (apart from the other 2 strains isolated from GGC patients, noted above) and if so, how many? and where from?

CONCLUSIONS:

Reasons why Case-patients unlikely to have contracted *C. neoformans* infection while in QEUH/RHC.

1. Cases: [redacted] Child and one Adult [redacted] Please also see page 6 of the Report.

2. Note that Nosocomial (hospital-acquired cases) cases are very very rare (worldwide). Please see: *Farrer et al*, 2021 & *Vallabhaneni et al*, 2015.
   Quote from Farrer *et al*, 2021 commenting on *Vallabhaneni et al*, 2015:'Only one other cluster of *C. neoformans* infection in hospitalized patients has been reported in the literature*. In Arkansas in 2013, six patients in a community hospital developed blood stream and respiratory infections. Bird habitats at the hospital and staff who had contact with birds were investigated, but no definitive source was established, and environmental sampling was negative. Isolates from the clinical cases appeared genetically diverse, as three separate MLST (multilocus sequence typing) types were identified.'
   *The other cluster being the two cases described by them (Farrer *et al*, 2021) in Glasgow.

3. Please also note the very significant issue of dormancy and reactivation - especially in Children. Please see pages 6 & 8 of the Report. Please also see: *Goldman, DL et al*, 2001 & *Kao, C* & *Goldman*, *DL*, 2016.

4. Please note that the Genomics of the above 2 cases and 2 others from the community (in Greater Glasgow & Clyde, around the same time and as described in *Farrer et al*, 2021) showed 4 completely different Genotypes.

5. There were no environmental isolates of *C. neoformans* found, within or near, QEUH/RHC in some 3000 air samples.

6. Infection caused by *Cryptococcus neoformans* is a rare disease in Adults and even rarer in Children. Commoner in Males than Females - twice as common in Males than Females (see page 6 of the Report and *Guess, TE et al*. 2018). [redacted]

7. The Adult [redacted] was in Ward 4C for [redacted] entire hospital stay. Note that 4C had/has the best 'control of the air' around it compared to both 4B (Bone Marrow Transplant Unit) and Paediatric Ward 6A (poorest control of the air between 6A, 4B & 4C). 4C has the best control of the air around it, not only around entrances/exits but also Voids and Risers - just does not have HEPA filtered air as in 4B.

8. Importantly, it should also be noted that Ward 4C has a cohort of Renal beds and carries out some 140 Renal Transplants per year. Note that there has never yet been any cases of *Cryptococcus neoformans* infections in any of these patients. Again, why not? as this group of patients are at risk of contracting *C. neoformans* infections. Please see Marr, KA et al. (2020) and 'OTHERS AT RISK FROM INFECTION WITH CRYPTOCOCCUS

NEOFORMANS.' See Pages 61 – 62 of the Report: Underlying Disease, No 1: Solid Organ Transplant (SOT).

9. Opening of AHUs (Air Handling Units) serving the two case – patients. Please see Hypothesis Number 1, Plant Rooms – pages 12 to 21.

Theory: 'Pigeon ingress and then fouling in Plant Rooms leading to cryptococcal spores (if present) entering the Plant Room air and then gaining access to the Air Handling Units (AHUs) ventilating the rooms/wards where the case-patients were.
The theory was that when the AHU was shut down, opened, with the final filter removed and changed, there was – believed at that time – the opportunity for *C. neoformans* spores (if present in the Plant Room Air) to be 'sucked' into the open AHU, then into the duct and then down it to the 'at risk' patients.'

Findings:

Firstly: AHUs in Plant rooms related to case-patient rooms were not opened when the case-patients were in these rooms/wards.

Fifthly: The Hypothesis was that air from a Plant Room (postulated to contain aerosolised spores of *Cryptococcus neoformans*, from the postulated presence of pigeon guano) could possibly gain access to the patients via the AHUs, when they were shut down and opened to replace the Final Filter – thus allowing aerosolised spores (if present in the Plant Room air) down the then 'filter-less' duct. The theory was that the air would be 'pulled' into the AHU through its open door and proceed down the duct to the patient(s).

In reality the OPPOSITE happens. When the AHU is shut down and its door opened – and the Final Filter removed – air is driven, at some force OUT of the duct and into the Plant Room – a presumed thermal effect – NOT down the duct to the patients.
Perhaps, more importantly, in terms of the two case-patients, NO AHUs that served any of the Wards/individual PICU room(s) were shut down and opened, during the time that that either of the two case-patients were present in these Wards/individual PICU room(s)

Membership of the group

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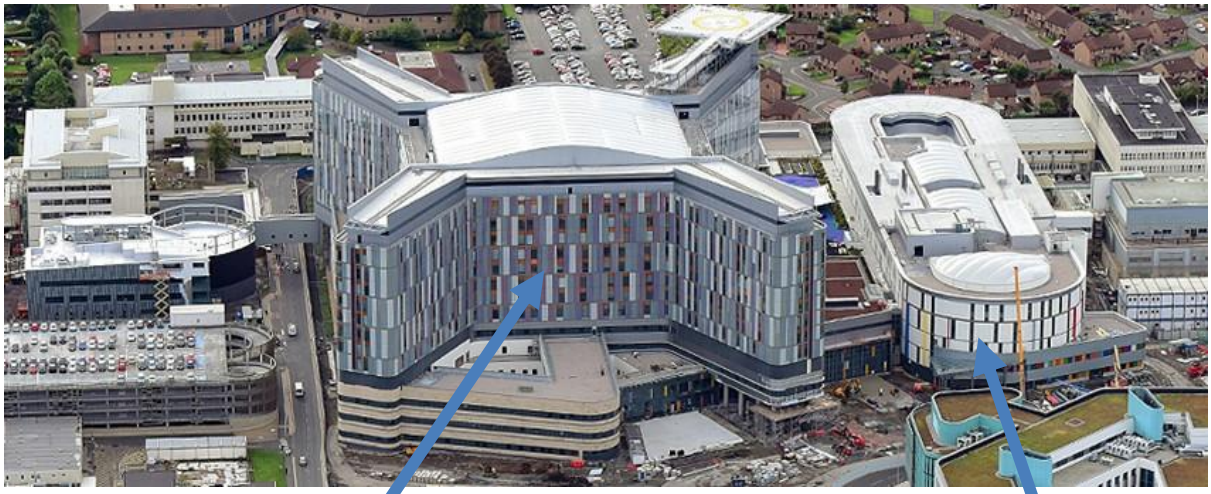
Appendix 1 – Site Map



Appendix 2 – Report helipad

Report on the Computational Fluid Dynamics Simulation of the External Flow Around Queen Elizabeth University Hospital by Quesada Solutions Ltd. - 14th June 2019. Report is detailed below.

21.06.19 - Revised CFD Model - QS Repo

Appendix 3 – Literature Review

Literature Review carried out by Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) – June 2021. Report is detailed below.

Cryptococcus Literature Review_V1

Glossary of Terms

ACH	Air Changes per hour
AHU	Air Handling Units
CFU	Colony-forming unit. In microbiology, a colony-forming unit (CFU, cfu, Cfu) is a unit used to estimate the number of viable bacteria or fungal cells in a sample. Viable is defined as the ability to multiply via binary fission under the controlled conditions.
HEPA	High Efficiency Particulate Absorbing
F7 Filters	The F7 **Pleated Panel Filter** is from the HVDS F7 HVAC panel filter range, and is designed for use in HVAC systems. Offering superior performance and more energy efficient than standard panel filters.
NIPCM	National Infection Prevention and Control Manual.

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Asterisks represent an important paper and/or a good Review

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NHSS Assure: Response to Questions regarding NSS involvement as requested by NHS GGC in respect of all or any Cryptococcus incidents at QEUH/RHC between 2018 and 2022.

1. **Confirm why NSS attended the Cryptococcus Sub-Group IMTs and not the IMTs in respect of Cryptococcus incidents at QEUH/RHC between 2018 and 2019;**

   Response: NSS were not invited to attend the Incident Management Team (IMT). Health Facilities Scotland (HFS) and Health Protection Scotland (HPS) representatives were invited to attend the Expert Advisory Group by NHS Greater Glasgow and Clyde (GGC).

2. **In respect of the Report from the Cryptococcus Incident Management Team Expert Advisory Sub-Group dated 5th April 2022:**
   a. **Provide confirmation of when this report was submitted/ sent by NHS GGC to NSS, along with any accompanying correspondence.**
   b. **Details of the response, if any, from NSS in respect of the report, along with any communications from NSS to NHS GGC in respect of the views of NSS regarding the report.**
   c. **Details of why NSS did not approve the final report of the IMT sub-group, and any communications provided to NHS GGC by NSS in respect of this matter.**

   Response: As agreed, a response will be submitted by 17th April 2024.

3. **Full details of all or any engagement from NHS GGC in respect of Cryptococcus cases in Ward 6A in or around July and August 2020, to include but not limited to details of all support given, advice tendered, and actions followed up on. If within the knowledge of NSS full details of the reporting action taken by NHS GGC in response to Cryptococcus in Ward 6A in or around July 2020, including any NSS, ARHIORT or other reporting action taken including HIAAT ratings, actions taken in response to any advice given by either internal or external agencies**.

   Response: Information contained in the documents and emails provided contain Patient Identifiable Information which if put into the public domain would likely mean individual patients could be identified. We request this information is not placed into the public domain.

   NHSGGC reported a possible Cryptococcus case on [redacted]/07/2020 via Healthcare Associated Infection Outbreak Reporting Tool (HAIORT) as per document number 2. Healthcare Infection Incident Assessment Tool (HIIAT) Green support from ARHAI requested. ARHAI Nurse Consultant attended the IMT on 02/07/20. NHSGGC closed the incident on 09/07/20 as per document number 9 following confirmation for the Reference Lab in Bristol that the sample was negative. Details of actions reported to have been taken by NHSGGC within the HAIORT. Additional relevant emails have been provided numbered 1 and 3 to 8.

4. **Full details of any further engagement from NHSGGC in respect of any cases of Cryptococcus cases in QEUH/RHC from July 2020 to date, to include but not limited to details of all support given, advice tendered, and actions followed up on.**

   Response: No further incidents relating to Cryptococcus have been reported into ARHAI by NHSGGC since the possible case reported on [redacted]/07/20 as referenced in response to Q3.

Question 2: In respect of the Report from the Cryptococcus Incident Management Team Expert Advisory Sub-Group dated 5th April 2022:

Note

Responses are based on a compilation of emails, and documents contained within, minutes of meetings and draft reports. Due to the content of minutes and draft reports being difficult to follow, and version control being limited, this response has been somewhat challenging for NSS to compile.

A. Provide confirmation of when this report was submitted/ sent by NHS GGC to NSS, along with any accompanying correspondence.

NSS Response

A final report was issued to NSS on 7th April 2022, by NHSGGC (**email chains 1 and 7**). Over the lifespan of the Cryptococcus Incident Management Team Expert Advisory Sub-Group there were a number of draft reports shared with NSS by NHSGGC. In addition to draft reports some meeting minutes would include text for inclusion within the draft reports. There was no version control of draft report documents and therefore it was difficult to tell which version was most up-to-date, or indeed on which document NSS was being asked to comment.

NSS's search has identified 10 draft reports shared prior to the final report being shared on 7th April 2022. Noting the difficulties previously stated regarding version control, NSS cannot be confident that this represents the total number of draft reports shared by NHSGGC.

B. Details of the response, if any, from NSS in respect of the report, along with any communications from NSS to NHS GGC in respect of the views of NSS regarding the report.

NSS Response

NSS first received the "draft 2" version of the report on 16th August 2019 for discussion at the subgroup meeting that same day (**email 9**).

On the 23rd August 2019, an email containing Draft 2 of the report was shared for comments and discussion at the meeting scheduled for the same day. The document entitled "Draft 2" was watermarked "Draft 1 130819" (**email 10**).

NSS shared information from the literature on Pneumatic Tube Systems with the Sub-Group chair on 27th August 2019, to help inform the report (**email 11**).

A document was then shared with NSS on 16th December 2019 entitled "18 12 19 Crypto John Hood comments - word" (**email 12**). This document was laid out as an SBAR and issued to members of the subgroup for discussion at the meeting on 18/12/19.

On 17th December 2019 NHSGGC shared an updated version of the document shared the previous day. The updated version was entitled "CRYPTOCOCCUS JOHN HOOD COMMENTS – Update 171219" (**email 13**).

On 18th December 2019 NHSGGC shared a further document entitled 'item 7 – 18.12.19 - CRYPTOCOCCUS JOHN HOOD COMMENTS - WORD (002) v1.doc" (**email 14**).

The meeting held on 18th December 2019 focused on (i) a presentation by the Director of Facilities, and (ii) the preparation of the Board's position paper. NSS sent the Chair and members of the Sub-Group comments regarding the position paper on 23rd December 2019 (**email 15**):

> *"HPS and HFS have reviewed the document circulated on 18/12/19 and comments/suggested changes are attached. We have tried to put it into a more structured format and kept it specifically about hypothesis 1.*
>
> *We feel that should any further information be sought in relation to the additional hypotheses it should come from the final report to ensure that all the relevant points are captured in the correct context given the complexity of the investigations. I know we agreed to meet again on 9th January when we are more than happy to attend. However, If there are no ongoing investigations in regards to Cryptococcus, we wondered what the purpose of the group meeting again prior to a draft of the final report being available for discussion is?"*

On 24th February 2020, NSS was made aware of NHSGGC QEUH and RHC Update Paper No. 20/04. Paragraph 3.4.5 and Minute of Finance and Performance Commit ee Page 4 Para 3 (**email 16**).

QEUH and RHC Update Paper No. 20/04 stated:

> *"Section 3.4.5*
>
> [redacted]
>
> *The hypothesis that the air from the plant rooms, via the AHUs, was the likely source of the cryptococcal spores, specifically those of C. neoformans, which were then breathed in by the case patients, has subsequently been categorically ruled out as it is not technically possible.*

Paper number 19/06 – Minutes of the Meeting of the Finance Planning and Performance Committee stated:

[redacted]

> *Section 99 Estates and Facilities review*
>
> *Mr Steele went on to provide an overview of the work carried out in respect of Cryptococcus neoformans. He described 6 hypotheses considered and the outcomes of investigations of each of these. Mr Steele advised that all of the hypotheses considered were ruled out due to a number of factors and it was concluded that the likely source was that the spores were brought into the building from the incoming outside air. "*

NSS Sub-Group members did not agree with the statements included in the NHSGGC Board papers, and on the day that they became aware of them an email was sent to the Chair of the Sub-Group, sharing the NSS members' concerns that the findings reported in the Board papers did not reflect the Sub-Group's investigations(**email 16**):

"I am concerned that the statements below are not the view of the wider group and certainly not my understanding of the hypotheses to date. At previous meetings I have expressed concern about the findings from this group being discussed out with the group before the final report is written given the complexities of the findings. My concerns with the statements below as follows;

- *As far as Hypothesis 1 goes, my recollection is, although it was thought by the group that this was an unlikely source, it was certainly not 'categorically ruled out'.*
- *As per the second section noted below, the remaining hypotheses have been 'ruled out'. This is not the status of the hypotheses as I believed them to be at previous meetings. Furthermore, the group also agreed that the additional hypotheses explored would not be commented upon outwith the group until the report was complete, again due to the complexities of these findings.*
- *The conclusion summarised in the second section below 'that the spores were brought into the building from the incoming air outside' raises more questions for me than it answers and needs more discussion at the group should this be one of the conclusions within your report.*
- *Overall, I feel that the group have discussed many of the findings in depth which would form your report and conclusions within that report which we would then discuss further and approve as a group once available. To date, what we have is a set of minutes and notes which are open to interpretation hence the need for a formal report capturing the entirety of the investigations, findings (and interpretation of those findings which is extremely complex) and discussions of the group as a whole."*

The Chair agreed with NSS's concerns, and on 25th February 2020 shared an email that they, in their capacity as Sub-Group chair, sent to Professor Bain outlining these concerns (**email 17**).

The first detailed written feedback provided by NSS was in response to "Draft 7" of the report, received on 14th September 2020. NSS responded on 8th October 2020 (**email 2**):

"Please find comments on the draft report contained within the attached from myself, Ian and Annette. Overall, we feel that;

- *There is no clear methodology given in terms of study selection/inclusion;*
- *From the layout of the report it reads as though it is bias and appears that the selected evidence base is being used to back up a (potentially) biased view of the situation;*
- *Patient identifiables should be removed throughout – instead of referring to* [redacted] *a more appropriate discourse would be 'the patient'.*

It may be more appropriate for a more transparent literature review to be included from which conclusions can be drawn which ARHAI are happy to support. In doing so, this will

allow the report to be laid out in a clearer fashion (lay out suggested below). In completing the final report I think it also needs to be considered for whom this report is intended and sections which will have to be summarised and simplified for the reader."

After this draft (draft 7) many of the discussions regarding the report took place at the Sub-Group meetings. NSS sent an email to the chair of the Sub-Group and the Infection Control Manager highlighting that the discussions were confusing and that the minutes were not reflecting the discussion at the meetings. Issues included minutes recording actions that had not been shared or discussed with the Sub-Group, and cases being referenced despite not having been discussed or agreed by the Sub-Group (**emails 33 and 18**). NSS members escalated their concerns internally to the ARHAI Clinical Lead and the NHS Procurement Commissioning and Facilities Director.

On 15th January 2021, NHSGGC shared with NSS two sets of minutes and two documents for comment. The two documents are NSS comments on Draft 7 of the report, with additional comments from the chair of the Sub-Group (**email 19**).

NSS members emailed the chair of the Sub-Group on 16th March 2021 **(email 20**) asking him to confirm how the group planned to move ahead with the report and what the governance route for the final report was, given that the IMT had been disbanded. Also highlighted was the amount of time the Sub-Group had spent going through comments. Yet no documentation had been made available recording whether the comments had been accepted or declined.

Following internal discussions around the governance and NSS remit within the Sub-Group, a meeting took place between the NSS NHSGGC Chief Operating Officer, the Infection Control Manager, the NSS NHS Procurement Commissioning Facilities Director, and the ARHAI Clinical Lead on 16th March 2021.

The summary of the meeting was shared by email from the ARHAI Clinical Lead to the NSS Sub-Group members on 16th March 2021 (**email 34**):

"Gordon and I met with Jonathan and Sandra this afternoon to discuss the ongoing issues and concerns and have agreed:

- *NHSGGC will finalise the minutes and share with NSS by CoP today – I have not received anything can you let Gordon and myself know if you have received please?*
- *We agreed to have comments back by end of week/Monday am at the latest.*
- *Sandra and Jonathan agreed NHSGGC will provide documentation on the final comments received from NSS.*
- *We agreed you would provide availability to meet asap – Susie I know you have sent an email can you keep me up to date with when you are meeting.*
- *Jonathan agreed that if there were areas where agreement could not be reached this should be documented.*
- *Gordon sought to understand the governance process for the final report and NHSGGC stated it would be submitted to the chair of the IMT that commissioned*

the work to be done prior to going through NHSGGC internal governance processes"

NHSGGC shared further documents with NSS Sub-Group members on 17th March 2021 (**email 3**). NSS Sub-Group members considered the documents difficult to follow and NSS advised NHSGGC of concerns on 19th March 2021 (**email 3**):

"Please find attached comments previously submitted on 26/11 and 3/12/20. We (ARHAI/HFS) are finding the documents rather confusing (document on 'crypto meeting 101220' and minute 171220 Q and As to 11 to 77' list responses to our previously submitted comments on the report. Document 'Post1712' then goes onto to repeat all the questions and responses but with 'added comments') and therefore it is difficult to say with any confidence whether this is a true minute of the meetings and what are post meeting points/discussions/comments.

We await your comments table and perhaps this will make things clearer. Can we also have, as previously requested, an updated terms of reference that accurately reflects the existing membership and an update on the additional potential cases that have previously been discussed.

The meeting proposed to go over the final draft: we have not seen the final draft and request that once we receive the final draft that we are afforded adequate time for us to read and consider prior to a meeting to discuss this and therefore as we have not yet had sight of the final draft or received an update on comments submitted, we propose that you consider a delay in the meeting until we have all had sufficient time to review the finalised documents".

Included in the email were the original documents and an email sent by NSS on 15th December 2020 with two at achments of previously submit ed comments.

NHSGGC responded on 19th March 2021, advising that NHGGC ICM would summarise the 77 comments received from NSS (**email 4**) to allow a decision to be made against each. NHSGGC issued a table of NSS comments on the draft report (**email 21**) on 24th March 2021. NHSGGC shared by email on 9th April 2021 an updated draft report ("Crypto Report Draft 8") for members to review prior to the Sub-Group meeting on 14th April 2021 (**email 22**). NHSGGC shared a further updated draft report by email on 13th April 2021 ("Crypto Report Draft 9") for the same purpose (**email 23**).

On 30th April 2021 NSS–emailed NHSGGC with comments on Draft 9. The comments were shared via an at achment (**email 5**). That email summarised them as follows:

"NSS would not consider the report to be in a final stage and therefore NSS are not in a position to sign off this version as contributing authors.

- *It would be helpful if the introduction included a summary of the timeline for investigation and production of report.*
- *The discussion section needs serious consideration as it contains a large volume of highly confidential patient related information and NSS would ask NHSGGC to*

ensure good governance around this information being shared through the suggested groups and boards for sign off – our recommendation would be to remove this section and refer to the findings of the significant adverse event findings without disclosure of the patients age, gender or detailed diagnosis. The purpose of this report was to investigate the hypothesis for transmission not to review the cases.

- *We would recommend a formal literature review is carried out to support the report as a recommendation (as discussed ARHAI Scotland are undertaking) the literature currently referenced appears to have been selected to support the groups finding and could be viewed as selection bias.*
- *A summary of the air samples carried out across the sites would be helpful as an appendix."*

NHSSGGC ICM contacted NSS on 11th May 2021 requesting a formal systematic literature review by ARHAI to support the production of the report (**email 24**). NSS shared its literature review with NHSGGC on 24th June 2021 (**email 25**).

NHSGGC shared a further draft report (draft 15) on 17th September 2021 (**email 26**). NSS responded on 24th September 2021 (**email 27**):

"We have started to review the report and wondered if you are able to share whether our comments were accepted or declined from our previous feedback (email attached) as this would help speed up the review at our end?

Can you also confirm that the authorship is now NHSGGC and the subgroup are the supporting group for the investigations rather than authors of the report?"

NHSGGC responded on 24th September 2021 (**email 28**):

"Thank you for reviewing this report again. As you know there were almost 90 comments on an earlier draft which we had hoped were reflected in the updated draft we sent you in April. After we received your comments on the April draft I hope you will agree that as a result of these comments this report was changed significantly and Dr Hood has expanded it to hopefully reflect the complexity and scope of the review undertaken by the members of the sub group and their professional expertise and opinions. I have spoken to Jonathan and we are happy to list members of both the main IMT and the sub group if this is more acceptable?"

On 24th September 2021 NHSGGC shared with NSS air sampling results they intended to include in the final report (**email 29**). NHSGGC shared a further draft of the report on 8th October 2021. NSS responded on 26th October 2021 **(email 30**):

"I think there has been some misunderstanding - I had been expecting for the updated version to be sent to me as I had been liaising directly with you for the last 2 versions. Therefore the team have not reviewed this version shared by Ann.

I have had a quick look at this version and I am not able to identify the changes from the last version. I do note that much of what I commented on has remained in the this version.

Can you confirm this is the latest version that you are looking for comments on?"

NHSGGC responded on 26th October 2021 (**email 31**):

"Thanks for getting back to me. I apologise if there has been a miscommunication but I hope it's apparent that your helpful informal feedback was taken on board and that this is evidenced in the final draft of this report. The report is significantly different to the versions previously circulated so with that in mind, we had hoped that your team could view this as a more expansive document and could take the time to fully review it to inform the final version.

We communicated with members of the group on the 8 October with comments due by Friday 22 October; I apologise I assumed your team would have been in contact with you and then me if there was an issue with the deadline. As you will be aware we have heard nothing back from your team and have put in the usual gentle reminder on Friday. I also informed Jane Grant and Jonathan Best that this had been sent on the 8th with two weeks for comments to be returned.

This is the proposed final version which we would welcome comments on and I have set up a resource (Natalia Hedo) as it's the final version to list and respond to each of the comments received before the final version is agreed. We have had feedback from GGC members of the group and Peter Hoffman has been in touch with John Hood with his comments so it is the ARHAI/HFS which remain outstanding.

If we can agree on a tight turnaround I would be very grateful. We intend to submit this to the COO and CE on 5th November."

NSS shared comments on "Draft October Report" on 4th November 2021 (**email 6**):

"Sorry I never got to this before now. I have provided tracked changes and comments throughout this most recent final version of the report.

From reviewing this version I still do not feel this is ready as a final report for submission however I note from our previous email communication that the report is a NHSGGC report summarising the investigations and findings of the expert sub group and the actions taken within NHSGGC and that NSS are not authors.

- *NSS have submitted multiple comments since April – no feedback was received in terms of whether these have been accepted or rejected and most have not been considered in the latest version.*

- *Previously submitted comments were seeking clarity on data used to inform the text e.g timeline of cases – this has not been provided. Again we note that this may be part of the NHSGGC internal investigation and if so feel it is important to highlight these data were not shared/discussed with the sub group.*
- *Feedback about the report layout or grammar have not been considered or accepted including the changes in tense used, the layout, terminology etc. The layout makes the report quite difficult to follow.*
- *Inclusion of the copy and paste of extensive minutes included in the report (see hypothesis 5), could this report not summarise the discussions and actions of the sub group to support the summary/conclusions of the report rather than have direct lifts from minutes?*
- *Throughout the report, individual group members are identified by initials and the person tense changes - suggest the whole document is in the third tense.*
- *Mitigations added have not been discussed by the sub group (which is absolutely acceptable) - as above should be clear what are actions taken independently by the Board and not part of the sub group remit.*
- *There is a huge amount of PII – aware that advice from clinical governance has been sought however raising again in these final comments as NSS members still consider the amount and level of PII within the report unnecessary.*

Happy to talk through if you need further clarity – was aware of your tight deadline so apologies if anything is not clear."

NHSGGC responded on 4th November 2021 (**email 32**), acknowledging receipt of NSS's comments.

NHSGGC sent an email on-7th April 2022 with "Crypto Report Final REDACTED 05 04 22" and "16 02 22 Response to ARHAI HFS Comments on DRAFT Crypto Report" at ached (**email 7**).

NSS responded to NHSGGC on-28th April 2022 (**email 8**):

"Many thanks for sharing the final version of the NHSGGC report. I note the majority of our comments appear to have been rejected or "answered". For clarification can you confirm where the NSS comment has received an answer that this comment as been rejected?

Considering the input from the NSS members who were part of the IMT sub Group I would like to once again highlight that the title "Report from the Cryptococcus Incident Management Team Expert Advisory Sub-Group" is not a true reflection of the authors and we had previous assurance that this was a NHSGGC report on the finding of the sub group."

NHSGGC responded on 3rd May 2022 (**email 8**):

"I had hoped that John's summary would have covered all the comments made by ARHAI/HFS colleagues but if you would like to highlight any outstanding issues that you feed are germane to the report I'm happy to take back to BICC who commissioned the sub group. As you would expect we collected comments from all members of the group and we hope this is reflected in the final report. I can also take back your comments re authors, the report is a summary of the conversations and hypotheses explored in the 29 meetings of the group (I'm happy to send you all of the minutes) and colleagues from ARHAI/HFS attended 25 of these meetings."

NHSGGC shared a zip file of all the NHSGGC minutes of the Expert Advisory Sub Group Meetings on 10th May 2022. There has been no subsequent correspondence with NHSGGC about the report.

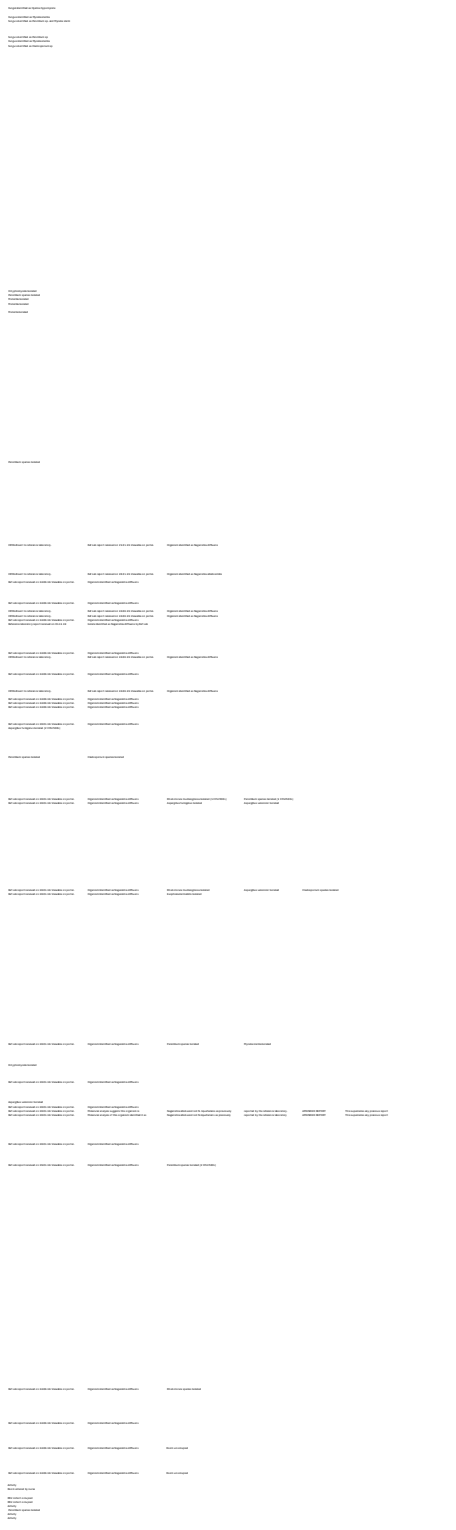
C. Details of why NSS did not approve the final report of the IMT sub-group, and any communications provided to NHS GGC by NSS in respect of this matter.

NSS Response

NSS had a number of concerns about how the work of the group was documented and recorded. Version control for minutes was confusing and there were examples of when minutes did not reflect discussion at the group meetings. A position paper had been developed for presentation to HSE which NSS were concerned did not reflect conclusions by the group. Papers then submit ed to the NHSGGC board were found to contain incorrect statements about the work of the group and the conclusions associated with the hypotheses.

There was no version control of the draft reports or documentation of Sub-Group members' comments and whether they had been accepted or declined, and the basis for the decisions. Within the report NHSGGC included data on cases that NSS had no knowledge of and actions that NHSGGC had taken out with the Sub-Group.

Emails from NSS to NHSGGC in respect of these concerns are referred to above in the response to 2B.



Exophiala dermatitidis Isolated	Penicillium species Isolated		
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia diffluens		
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia diffluens		
1 Bacterial CFU isolated			
Penicillium species Isolated	Ref Lab report received on 18.6.19. Viewable on portal.	Mucor plumbeus	
Penicillium species Isolated (6 CFU/500L)			
Penicillium species Isolated	Ref Lab report received on 18.6.19. Viewable on portal.	Mucor plumbeus	
Penicillium species Isolated	Ref Lab report received on 18.6.19. Viewable on portal.	Mucor plumbeus	
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia diffluens	Penicillium species Isolated (11 CFU/500L)	
1 Bacterial CFU isolated			
Penicillium species Isolated	Ref Lab report received on 18.6.19. Viewable on portal.	Mucor plumbeus	
Penicillium species Isolated			
Penicillium species Isolated	Ref Lab report received on 18.6.19. Viewable on portal.	Mucor plumbeus	
1 Yeast CFU isolated	Unable to identify		
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia diffluens	Penicillium species Isolated (14 CFU/500L)	
1 Yeast CFU isolated	Candida parapsilosis Isolated		
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia diffluens	Exophiala dermatitidis Isolated	Penicillium species Isolated
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia diffluens	Exophiala dermatitidis Isolated	Penicillium species Isolated
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia diffluens	Door opened	
Door opened			
Rhodotorula Species Isolated (1 CFU/500L)			
Exophiala dermatitidis Isolated (1 CFU/500L)			
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia albida	Door opened	
Penicillium species Isolated			
Plate Contaminated			
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia diffluens		
Ref Lab report received on 24.06.19. Viewable on portal.	Organism identified as Naganishia diffluens		
-			
Unable to Identify - Plate Contaminated			
Unable to identify - Plate Contaminated			
Penicillium species Isolated	Mycelia sterilia Isolated		
Penicillium species Isolated			
Mycelia sterilia Isolated			
Penicillium species Isolated	Cladosporium species Isolated		
Fungal CFU (8 CFU/500L)	Unable to identify - Plate contaminated		
Mycelia sterilia Isolated	H.hyphomycete Isolated		
Unable to identify further - Plate contaminated			
Penicillium species Isolated	H.hyphomycete Isolated		
Fungal CFU (14 CFU/500L)	Unable to identify - plate contaminated		
Fungal CFU (24 CFU/500L)	Penicillium species Isolated	H.hyphomycete Isolated	

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Report on the Computational Fluid Dynamics Simulation of the External Flow Around Queen Elizabeth University Hospital

Date: 14th June 2019

Presented to:	Mr Ian Powrie Deputy General Manager (Estates)
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Report number:	RT/QEUH01v3

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1. Introduction

This report summarises the finding from Computational Fluid Dynamics (CFD) simulations of the flow around the Queen Elizabeth University Hospital and adjacent Royal Children's Hospital in Glasgow. The purpose of the project is to determine whether potentially contaminated air from the region below the hospital helipad is being drawn into the ducts that supply ventilation to the various parts of the hospital. This location is a particular concern due to the roosting of pigeons on the struts under the helipad. The influence of the downwash from a helicopter approaching to land is also considered.

CFD is a computational method to simulate fluid flow. It uses discretization of both the underlying equations and geometrical domain and an iterative process to solve the Navier-Stokes equations. Turbulent behaviour can be captured using models, allowing simulations to be performed in steady-state conditions. When used correctly, the results capture the physical behaviour; however, it should be noted that the use of any approximation or model is a potential source of error. Good practise in the design and solving of simulations minimises this.

The simulations were carried out using the SimScale cloud platform which uses the OpenFoam CFD solver. This industrially established tool is based on the finite volume approach and is used widely in many industries. The finite volume approach for CFD has been used successfully for industrial applications since the 1980s. It is well suited for air flows of the type of interest here.

2. Basis of Model and Assumptions

A 3D CAD model was generated to include the main building structures and helipad region. Geometrical details with an insignificant influence on the flow were omitted. The model was created from the available data, which came from architectural elevations, construction drawings, operational diagrams and a site visit.

Appendix A summarises the air flow into the ventilation intakes and associated air handling units (AHUs). This is captured using velocity outlet conditions with the appropriate velocity values and directions for perpendicular flow. The velocity is relatively low compared to the local wind conditions at between 0.5 and 2.5 m/s. The flow out of the exhaust vents is not modelled explicitly as it is also low, so would have little impact on the wind in the area.

The wind strengths and directions are taken from the wind rose data in reports produced by WSP Energy Ltd from 2010 and 2011. This data is the CIBSE (Chartered Institute of Building Services Engineers) Test Reference Year (TRY) for 1978 to 1999 for Glasgow (Abbotsinch). More than half the time, the wind is from the prevailing direction, south-west and was reported up to an averaged value of 18m/s (approximately 40 mph). The next most frequent wind direction is east-north-east where the maximum average wind strength is 9 m/s.

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The helipad is closed at wind speeds greater than 36.4 knots (18.7 m/s). Since this value is slightly higher than the maximum average wind speed in the CIBSE data, it will be used as the maximum wind speed in the CFD simulations. The most common wind speed, for nearly 20% of the time, is 1 m/s. Simulations were therefore also considered for this speed.

The influence of the downwash from an approaching helicopter is of interest. To capture the effect, a momentum source is used to represent the helicopter rotor, with a similar diameter to the aircraft rotors (14m). The downwards velocity used was 25 m/s. The approach for landing will always be into wind.

The project proposal was for two simulations:

1. The flow under maximum prevailing wind conditions.
2. The addition of a momentum source to represent the downwash caused by a helicopter hovering on approach to the helipad.

In addition, further simulations were considered to allow for the following variations:

- The most common wind speed of 1 m/s
- An intermediate wind speed of 5.5 m/s
- All three wind speeds with and without the rotor downwash present.
- Wind from the second most frequent direction at the maximum, intermediate and most common wind speeds (18.7, 5.5 and 1 m/s)
- Four rotor locations during approach: 22, 32, 47 and 117m horizontally from the center of the helipad.

3. Computational Model

The computational model consists of a mesh of approximately 7 million mixed-type computational cells, the majority of which are hexahedral. Care has been taken to ensure the regions of interest and influence have good cell density, based on previous experience.

Turbulence is captured using the 2-equation, k-ω SST model.

All simulations were isothermal and steady state (time invariant).

There is interest in the transport of particulate matter, specifically pigeon debris. Light particles will travel with the airflow, whereas heavier particles will fall out of the flow. The angled louvres on the AHU intakes will prevent ingress by gravity so particle traces, that follow the flow path, are used to determine the path that air entering the intakes follows.

4. Results

CFD simulations generate pressure and velocity data for all locations within the simulated domain. To provide insight, it is necessary to extract reduced data sets or specific values. In this case, graphical plots of particle trajectories and coloured

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contour maps are used to show the flow behaviour in the areas of interest. It is important to note that there are different ranges for the colour scales used in the various figures in this report, so scale included within each figure should be referred to for each image separately.

For the main hospital building, particle traces are plotted from immediately in front of all four towers, at the height of the intakes. The particle traces are calculated in both directions (upstream and downstream) but only the upstream paths are of interest, since they show where the flow has passed before it enters the ducts. If any case shows that air is being drawn from beneath the helipad, then the more precise duct intakes can be used.

5.1 Maximum Prevailing Wind

At the maximum prevailing wind velocity of 18.7 m/s, without the helicopter present, the air that reaches the AHU intakes does not pass through the area below the helipad or any of the ventilation exhausts (Figure 1, Figure 2, Figure 3, Figure 4 and Figure 5). The simulations also showed that air from the ventilation exhausts of the main hospital building is not being re-entrained and passing back into the AHU intakes.

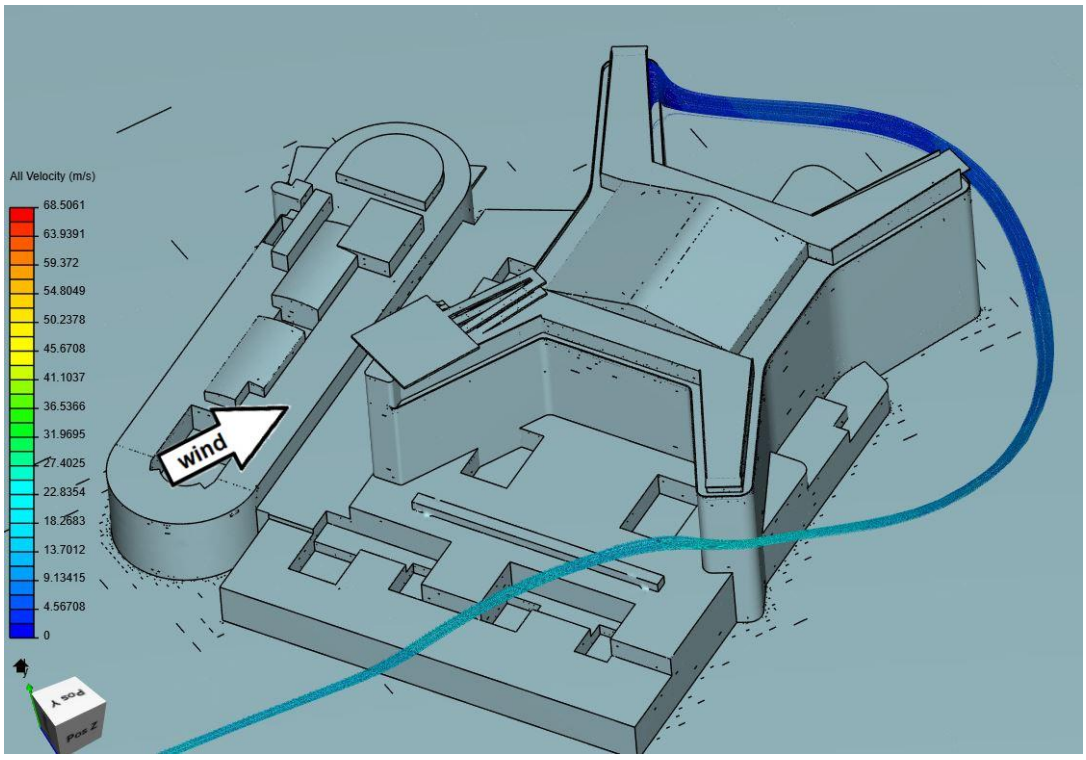

Figure 1: Prevailing wind direction showing airflow path to AHU intakes on tower A.

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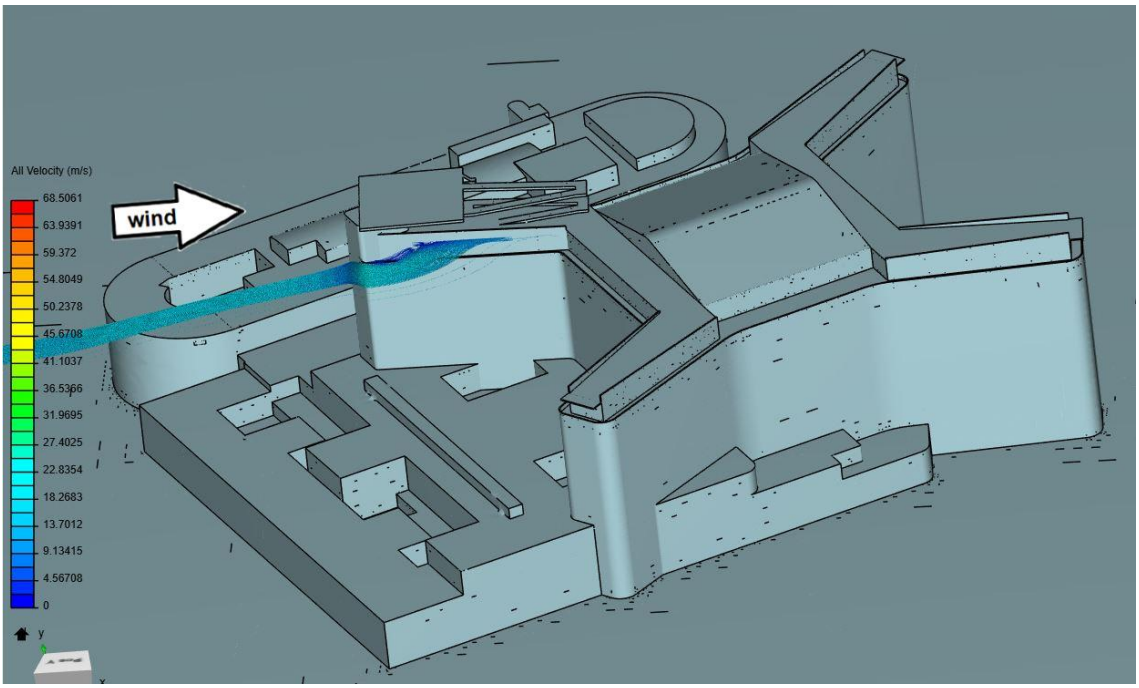

Figure 2: Prevailing wind direction showing airflow path to AHU intakes on tower B.

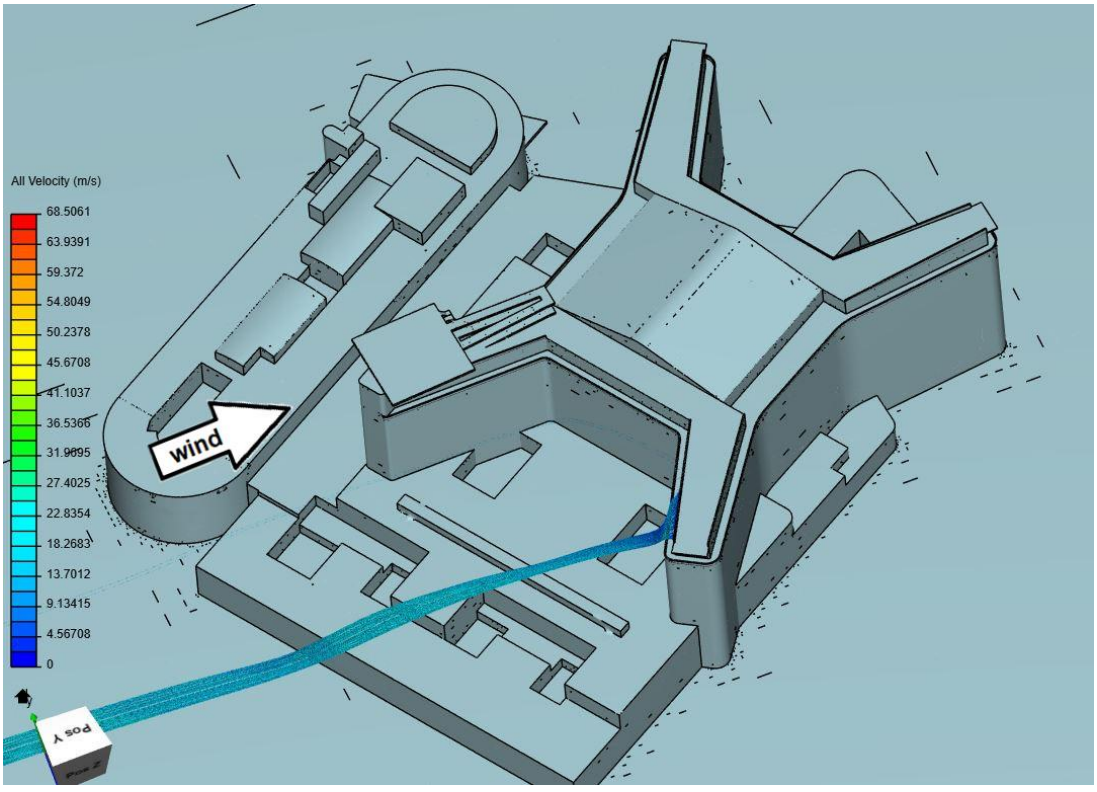

Figure 3: Prevailing wind direction showing airflow path to AHU intakes on tower C.

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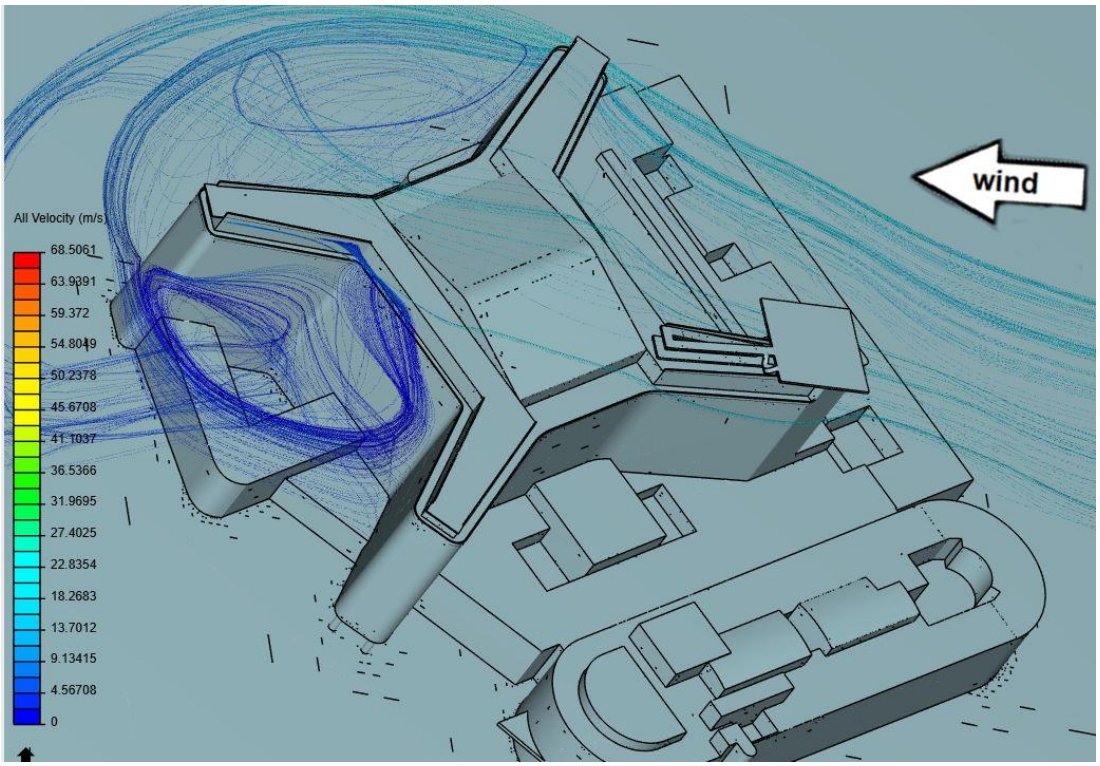

Figure 4: Prevailing wind direction showing airflow path to AHU intakes on tower D.

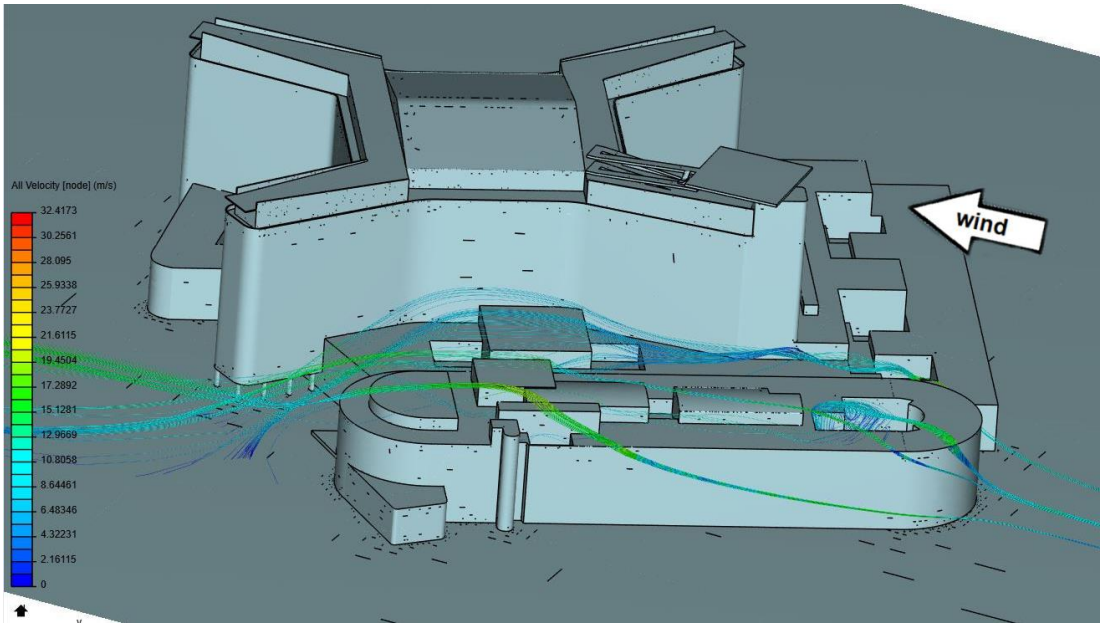

Figure 5: Prevailing wind direction showing airflow path to AHU intakes on Royal Children's Hospital.

Figure 6: Prevailing wind direction showing airflow path to intakes on Podium Level 3. Upstream and downstream.Figure 6 and Figure 7 show the flow to and from the light wells between Towers B and C, where intakes on Podium level 3 are located. The particle traces show both the flow arriving in the lightwell and also leaving it because

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flow intakes were not explicitly modelled in this location. The flow of interest to us is the flow upstream from the lightwells, to determine where it has travelled prior to reaching this location. However the software doesn't allow the upstream direction only to be shown, so the two images show both upstream and downstream flow and then just downstream flow. It is the upstream flow that is of interest. The difference between the two images shows the flow reaching the intakes on Podium level 3 doesn't pass through the area under the helipad or any of the ventilation exhausts.

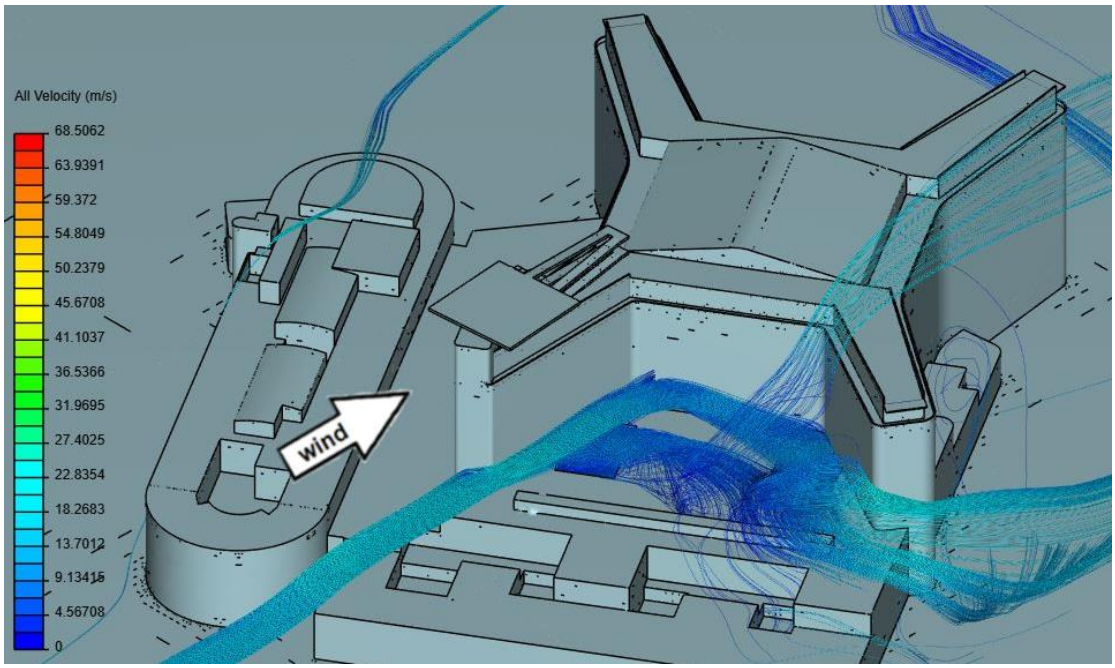

Figure 6: Prevailing wind direction showing airflow path to intakes on Podium Level 3. Upstream and downstream.

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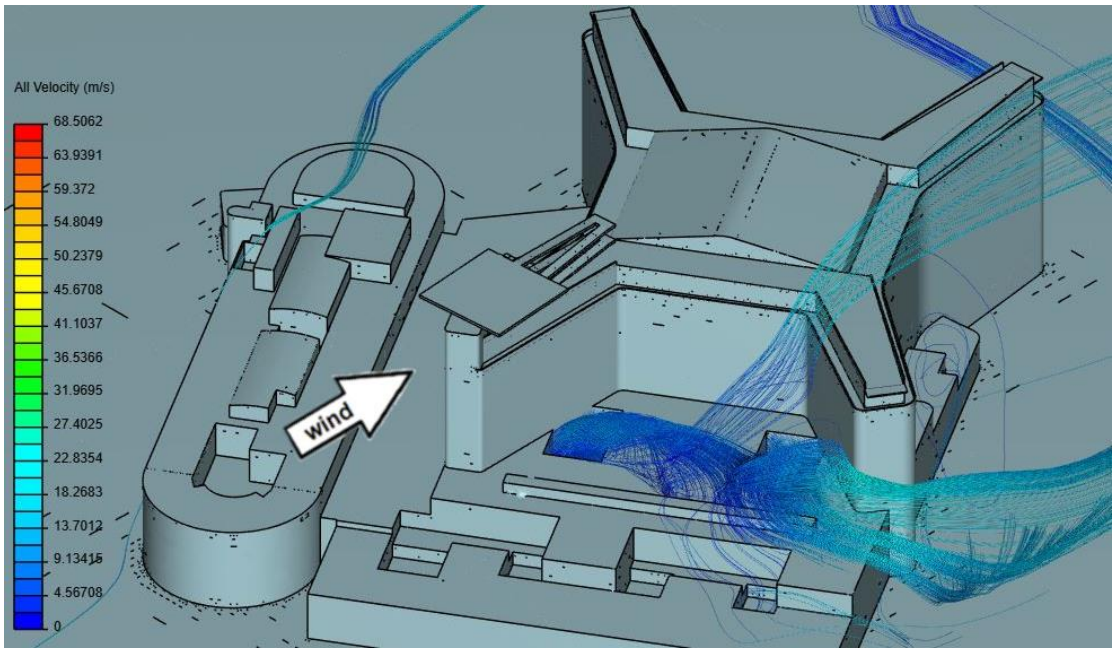

Figure 7: Prevailing wind direction showing airflow path to intakes on Podium Level 3. Downstream only.

5.2 Maximum Prevailing Wind with Helicopter Approaching

Three helicopter locations were assessed. The first was approaching at 22m from the centre of the helipad and at a height of 10m. This is close to the helipad and the AHU intakes of Tower B. The second was approaching at 47m from the centre of the helipad and at a height of 14m. This is further out over the main building with potential to affect the intakes in the other towers. The third was with the helicopter immediately over the centre of the helipad.

For the first case, with the helicopter 22m out from the helipad, at the maximum prevailing wind velocity of 18.7 m/s, the air that reaches the AHU intakes does not pass through the area below the helipad (Figure 8, Figure 9, Figure 10, Figure 11 and Figure 12).

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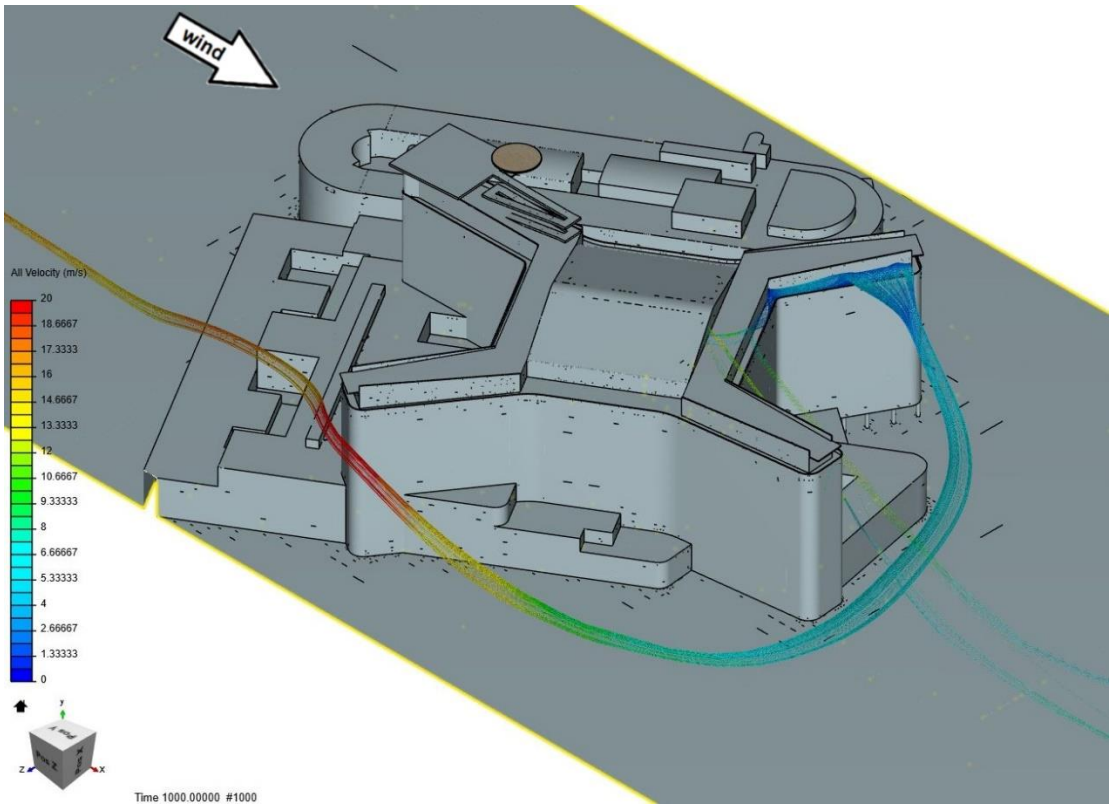

Figure 8: Prevailing wind direction with helicopter 22m from the helipad showing airflow path to AHU intakes on tower A.

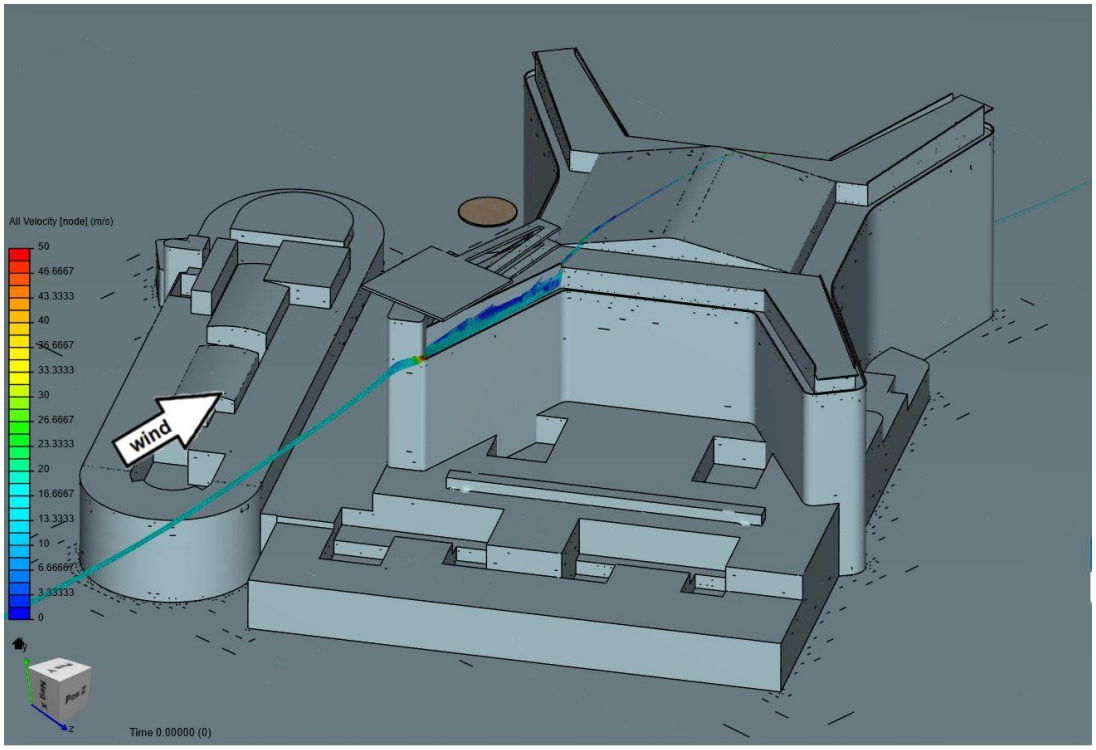

Figure 9: Prevailing wind direction with helicopter 22m from the helipad showing airflow path to AHU intakes on tower B.

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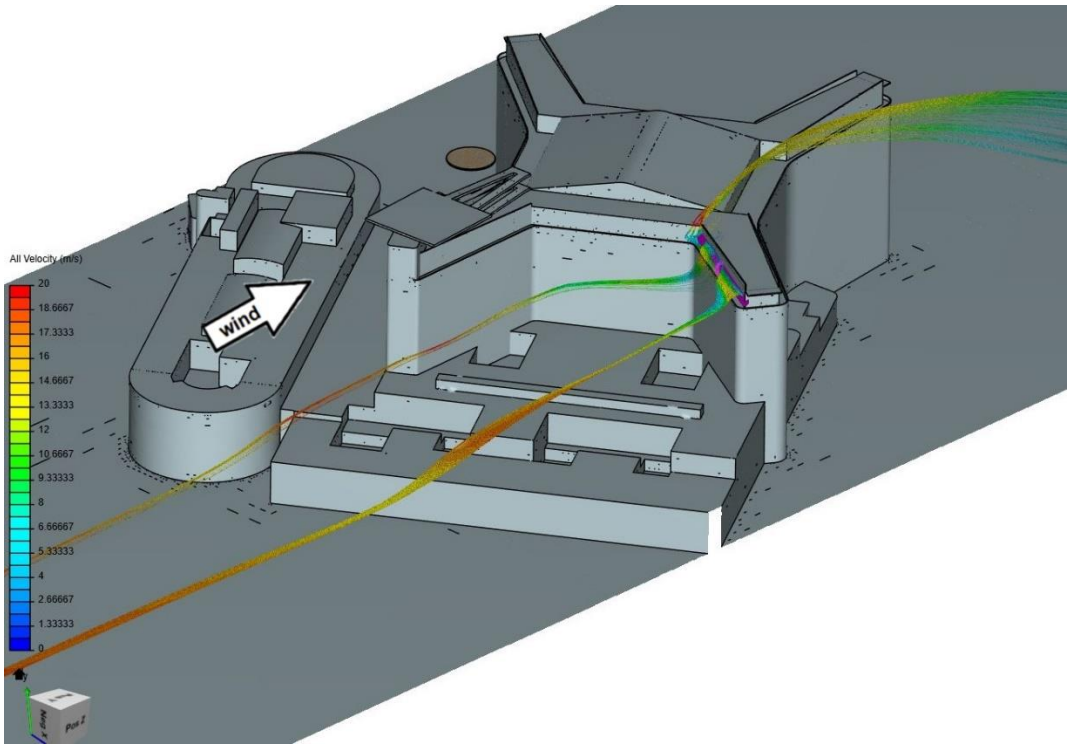

Figure 10: Prevailing wind direction with helicopter 22m from the helipad showing airflow path to AHU intakes on tower C.

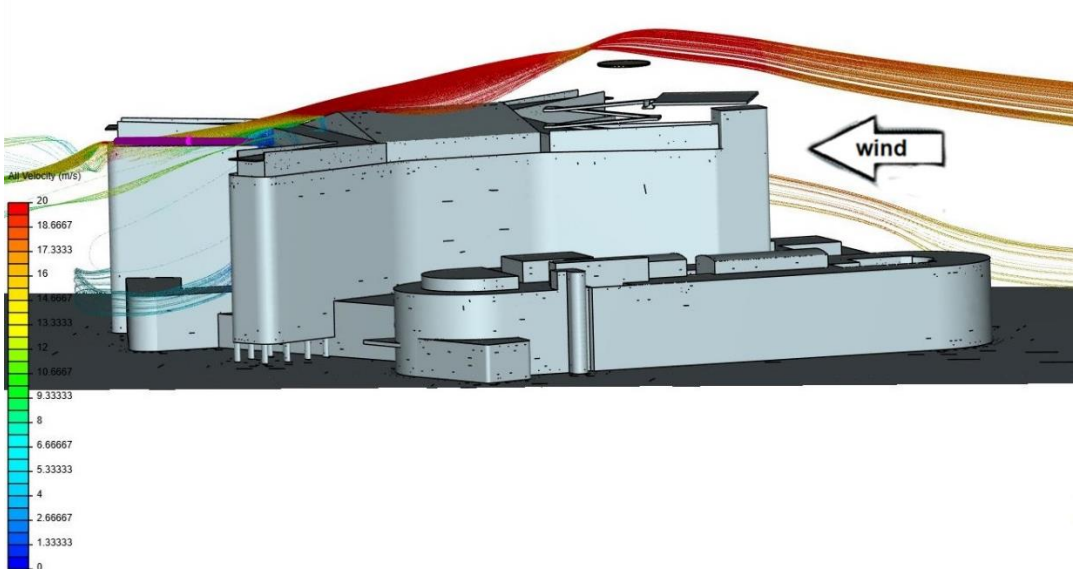

Figure 11: Prevailing wind direction with helicopter 22m from the helipad showing airflow path to AHU intakes on tower D.

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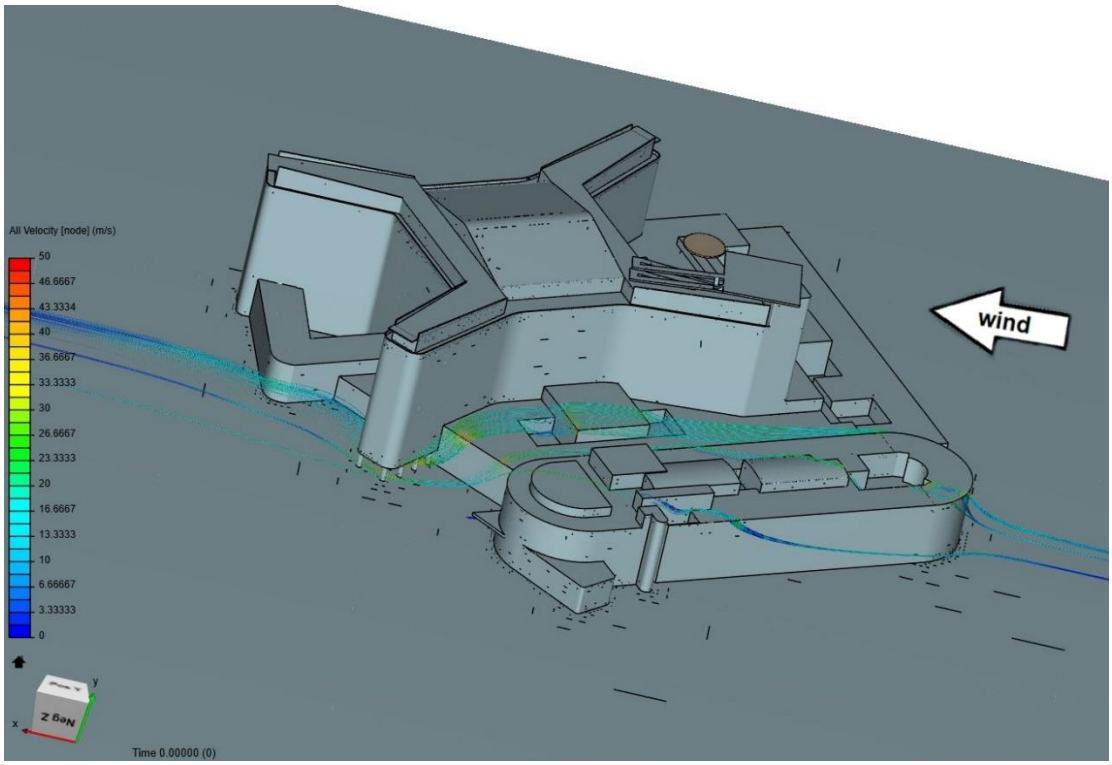

Figure 12: Prevailing wind direction with helicopter 22m from the helipad showing airflow path to AHU intakes on Royal Children's Hospital.

With the helicopter 47m out from the helipad and 14m above it, again, the air that reaches the AHU intakes doesn't pass through the area below the helipad (Figure 13, Figure 14, Figure 15, Figure 16 and Figure 17).

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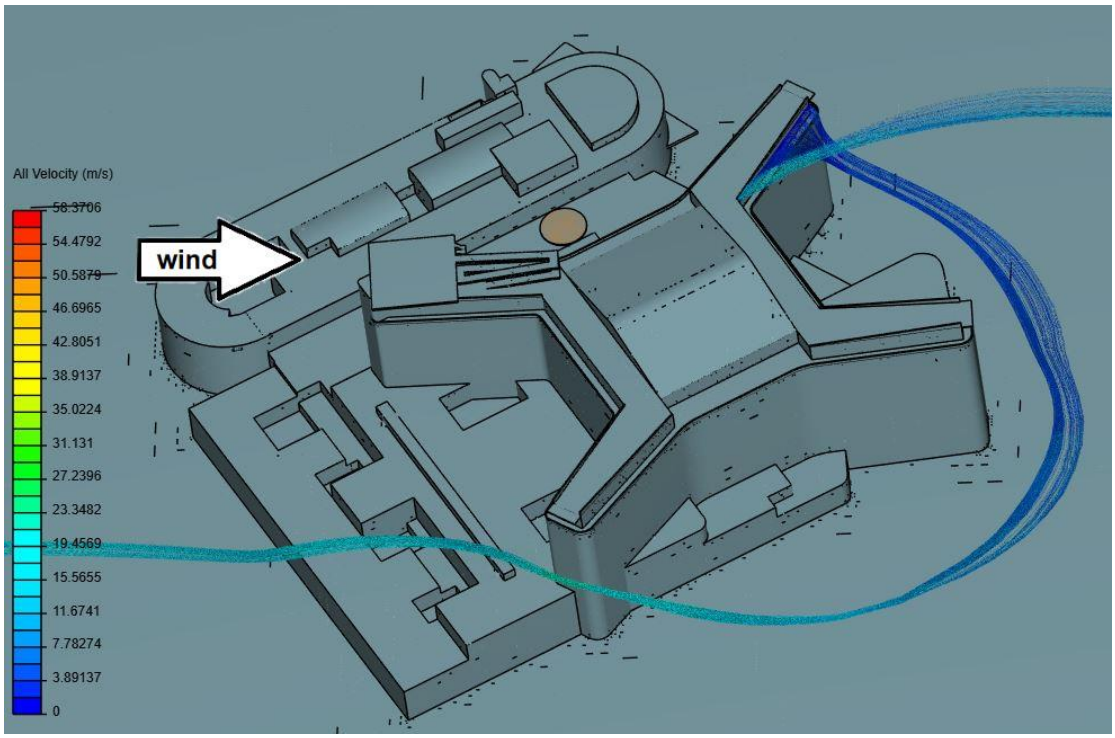

Figure 13: Prevailing wind direction with helicopter 47m from the helipad showing airflow path to AHU intakes on Tower A.

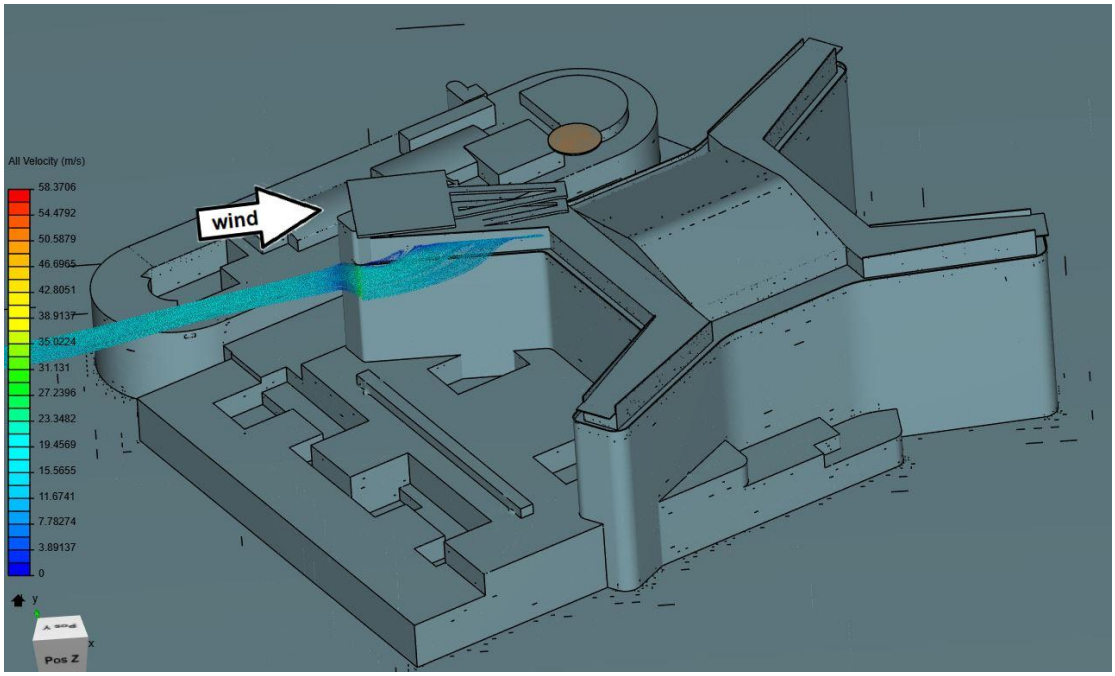

Figure 14: Prevailing wind direction with helicopter 47m from the helipad showing airflow path to AHU intakes on Tower B.

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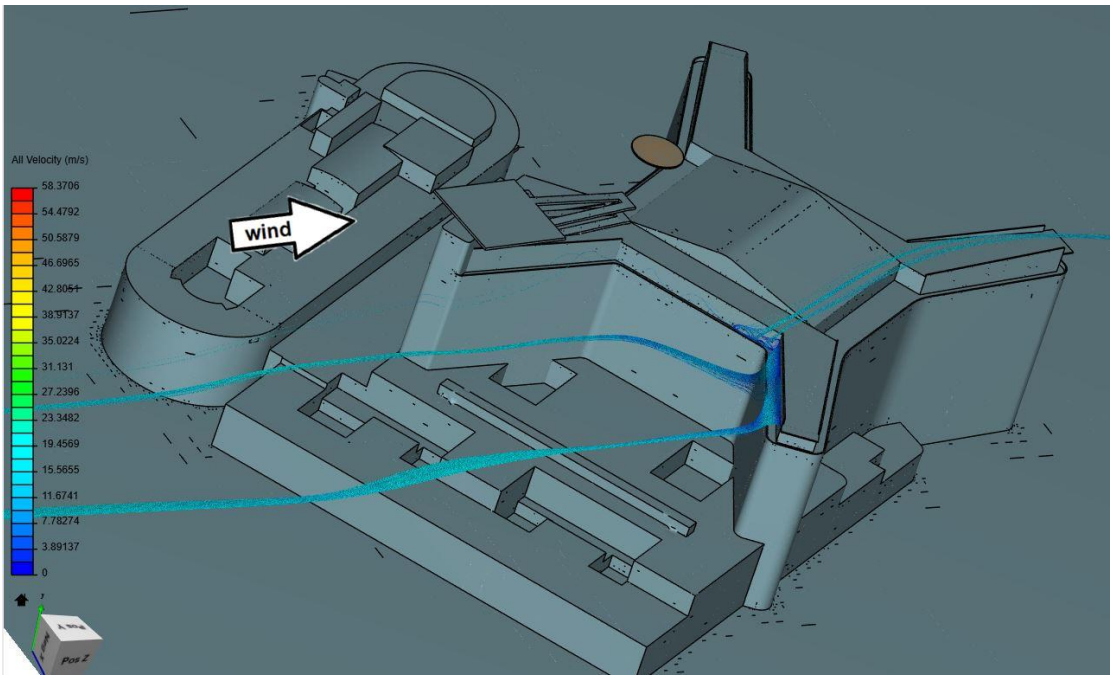

Figure 15: Prevailing wind direction with helicopter 47m from the helipad showing airflow path to AHU intakes on Tower C.

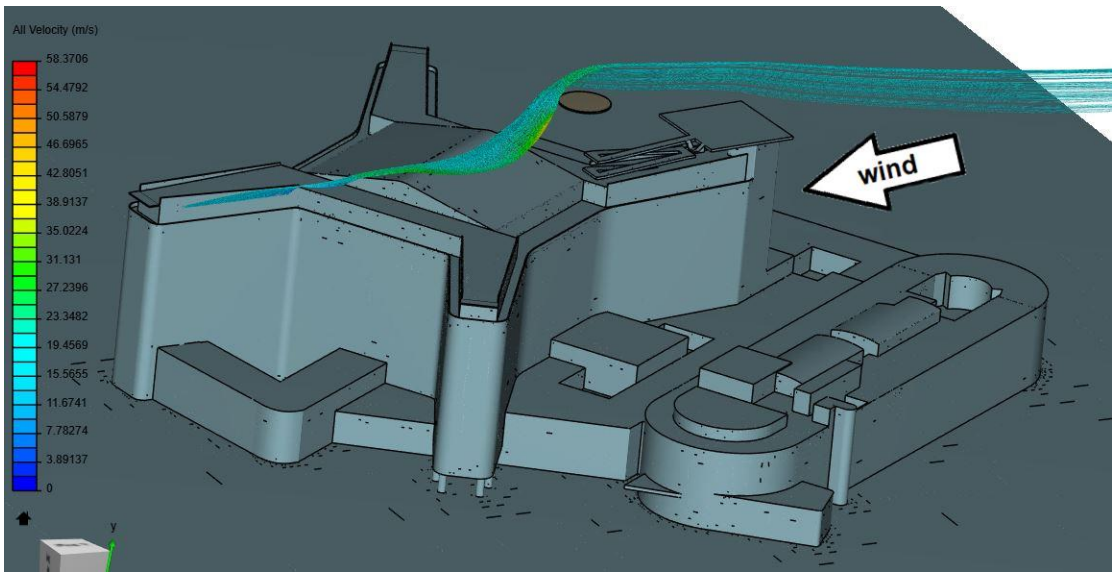

Figure 16: Prevailing wind direction with helicopter 47m from the helipad showing airflow path to AHU intakes on Tower D.

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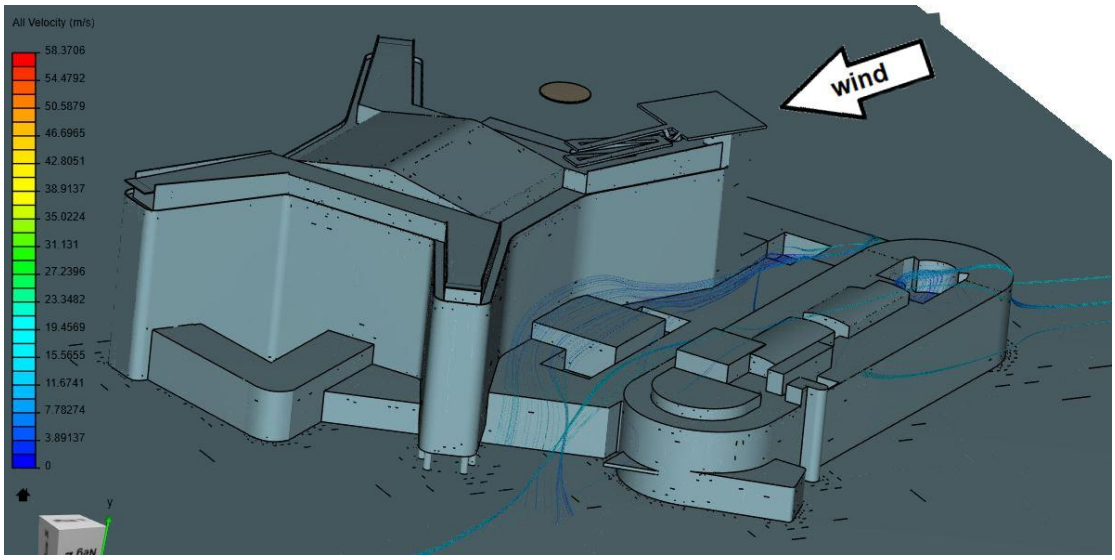

Figure 17: Prevailing wind direction with helicopter 47m from the helipad showing airflow path to AHU intakes on the Royal Children's Hospital

With the helicopter immediately above the center of the helipad, equivalent to immediately prior to landing, again, the air that reaches the AHU intakes doesn't pass through the area below the helipad (Figure 18, Figure 19, Figure 20, Figure 21 and Figure 22).

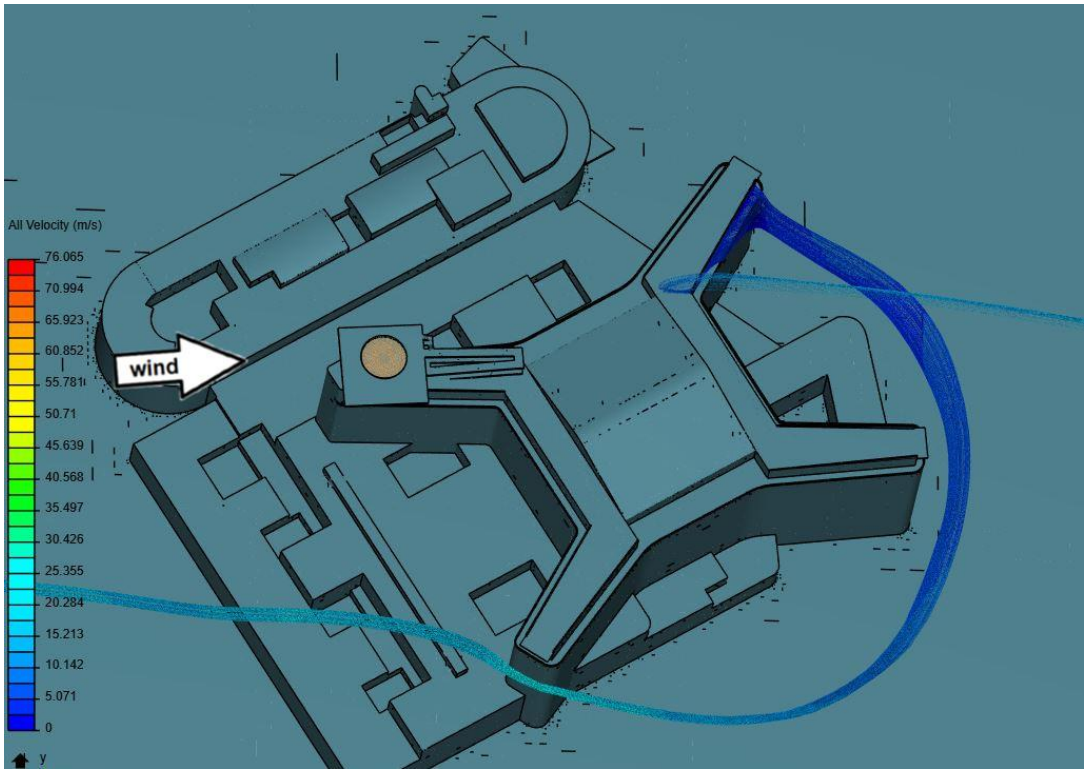

Figure 18: Prevailing wind direction with helicopter above helipad showing airflow path to AHU intakes on Tower A.

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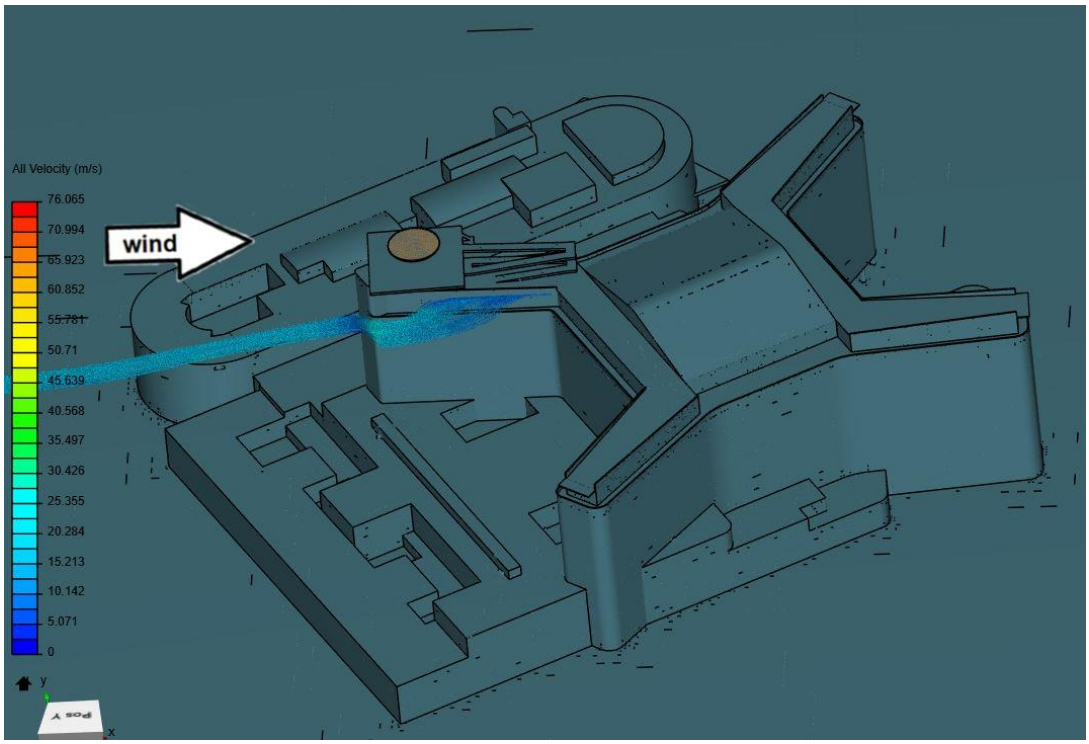

Figure 19: Prevailing wind direction with helicopter above helipad showing airflow path to AHU intakes on Tower B.

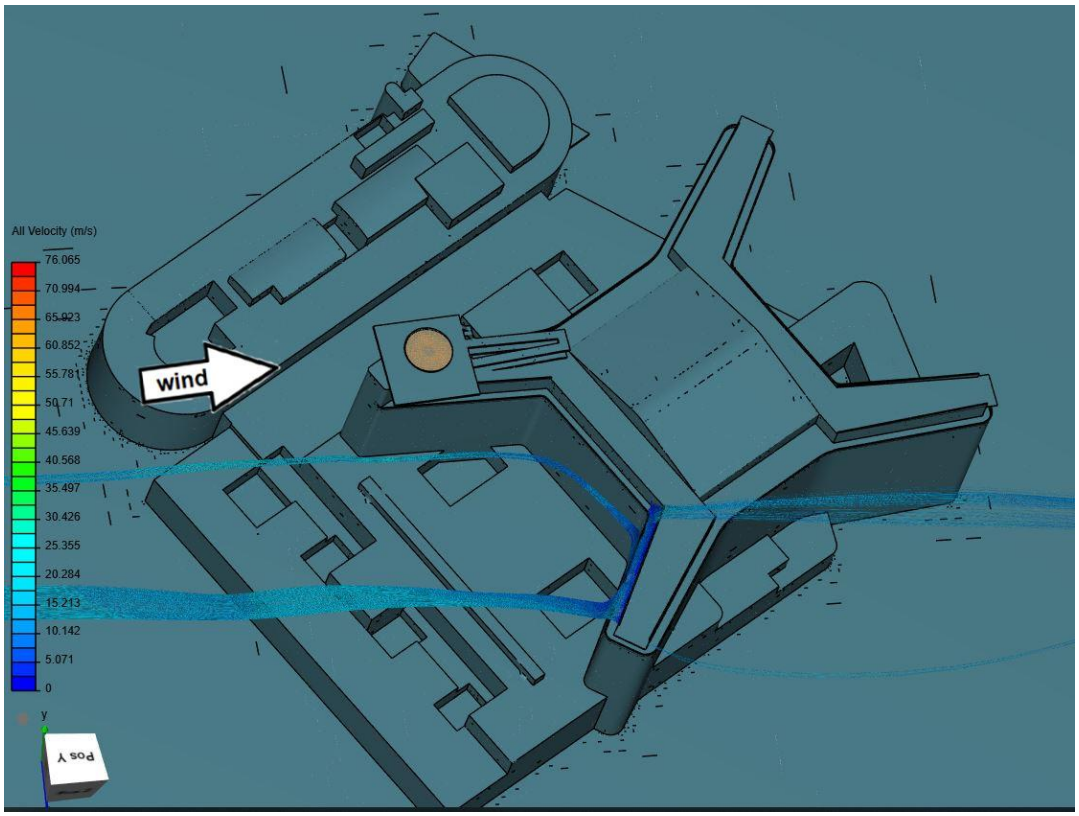

Figure 20: Prevailing wind direction with helicopter above helipad showing airflow path to AHU intakes on Tower C.

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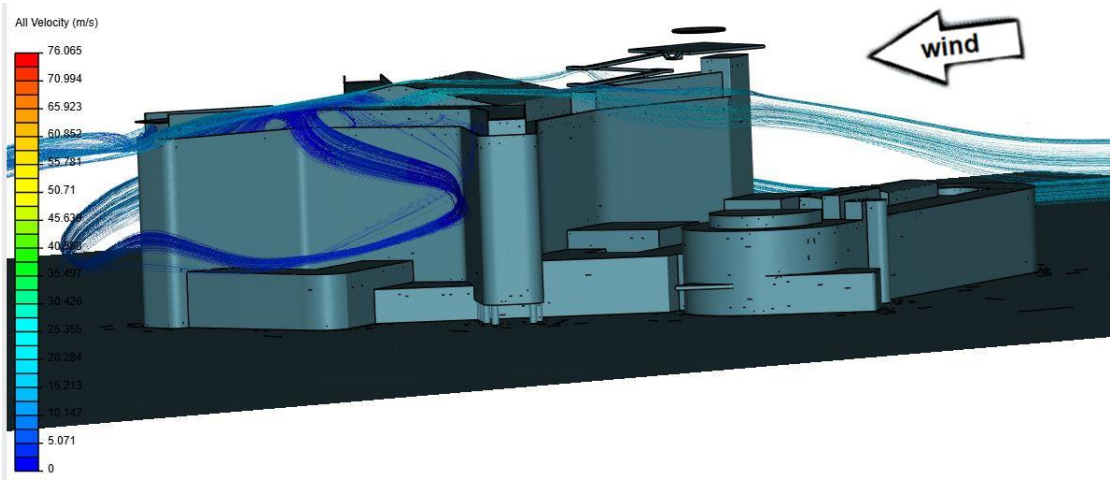

Figure 21: Prevailing wind direction with helicopter above helipad showing airflow path to AHU intakes on Tower D.

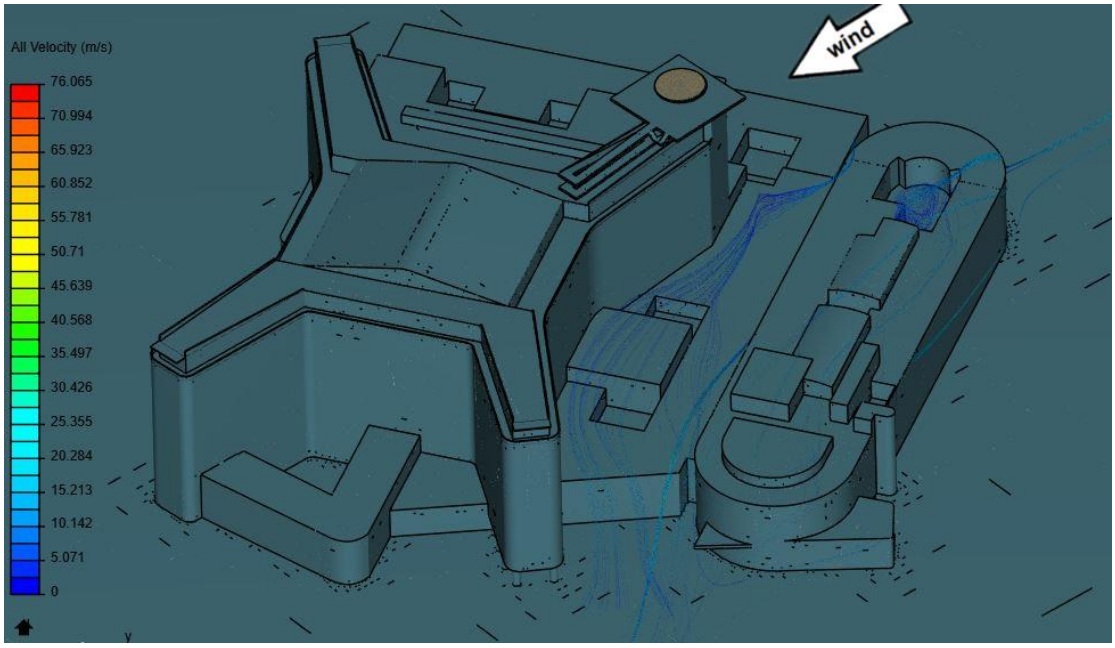

Figure 22: Prevailing wind direction with helicopter above helipad showing airflow path to AHU intakes on Royal Children's Hospital.

Figure 6: Prevailing wind direction showing airflow path to intakes on Podium Level 3. Upstream and downstream.Figure 23, Figure 24, Figure 25, Figure 26, Figure 27 and Figure 28 show the flow to and from the light wells between Towers B and C, where intakes on Podium level 3 are located under maximum prevailing wind conditions and with the effect of the helicopter in three different locations: 22m, 47m and above the helipad. Again the particle traces show both the flow arriving in the lightwell and also leaving it because flow intakes were not explicitly modelled in this location. The flow of interest to us is the flow upstream from the lightwells, to determine where it has travelled prior to reaching this location. However the software doesn't allow the upstream direction only to be shown, so there are two images for each case, showing

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both upstream and downstream flow and then just downstream flow. It is the upstream flow that is of interest. The difference between the two images shows the flow reaching the intakes on Podium level 3 doesn't pass through the area under the helipad or any of the ventilation exhausts.

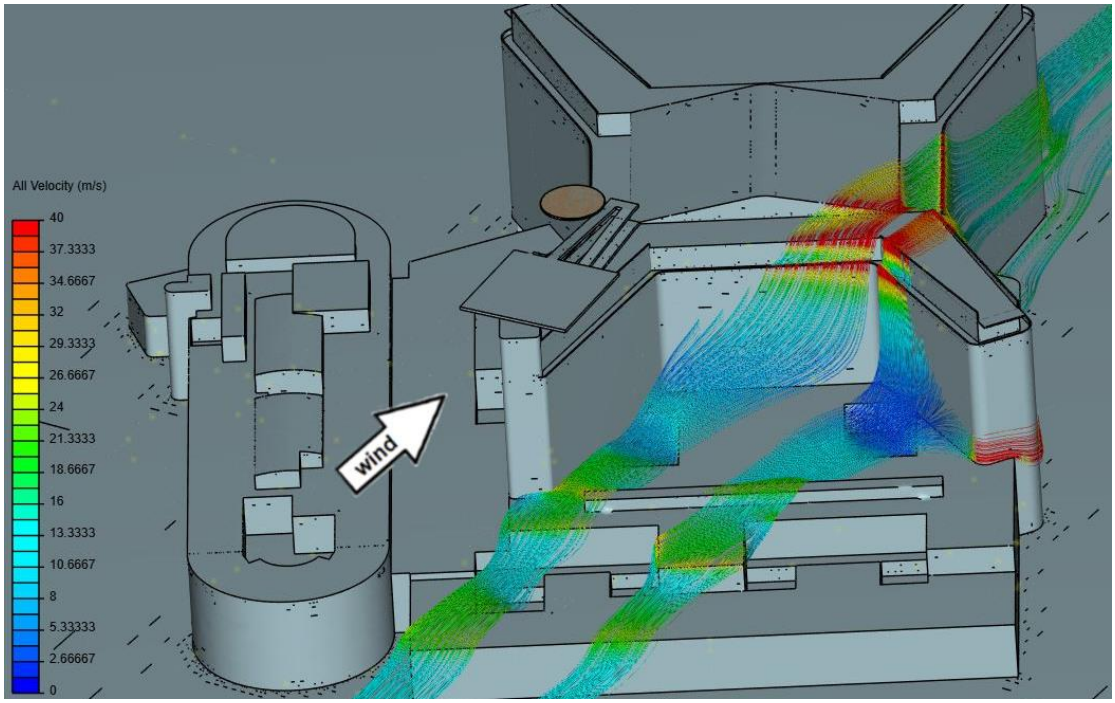

Figure 23: Prevailing wind direction with helicopter 22m from the helipad showing airflow path to intakes on Podium level 3. Upstream and downstream flow.

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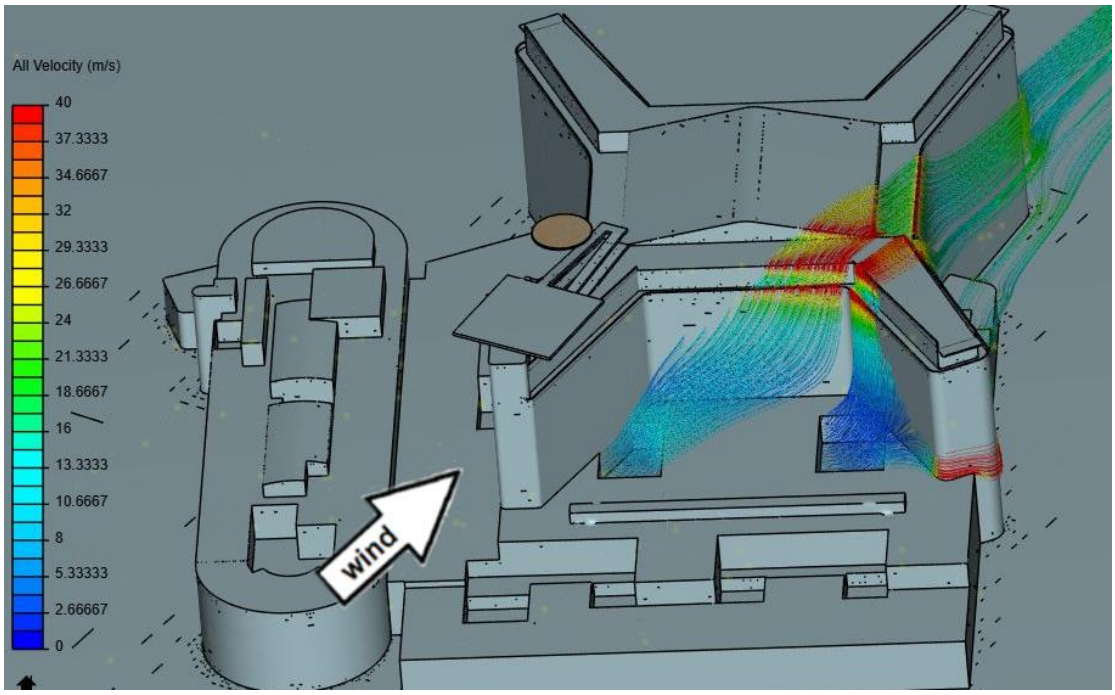

Figure 24: Prevailing wind direction with helicopter 22m from the helipad showing airflow path to intakes on Podium level 3. Downstream flow only.

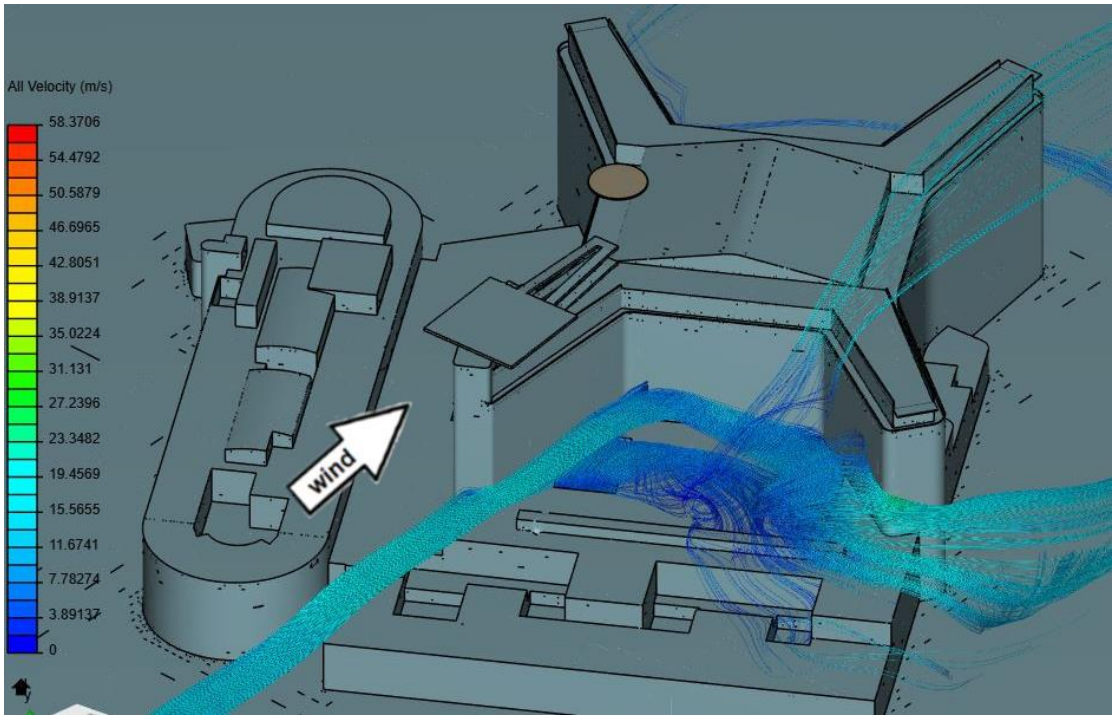

Figure 25: Prevailing wind direction with helicopter 47m from the helipad showing airflow path to Podium level 3 lightwells. Upstream and downstream flow.

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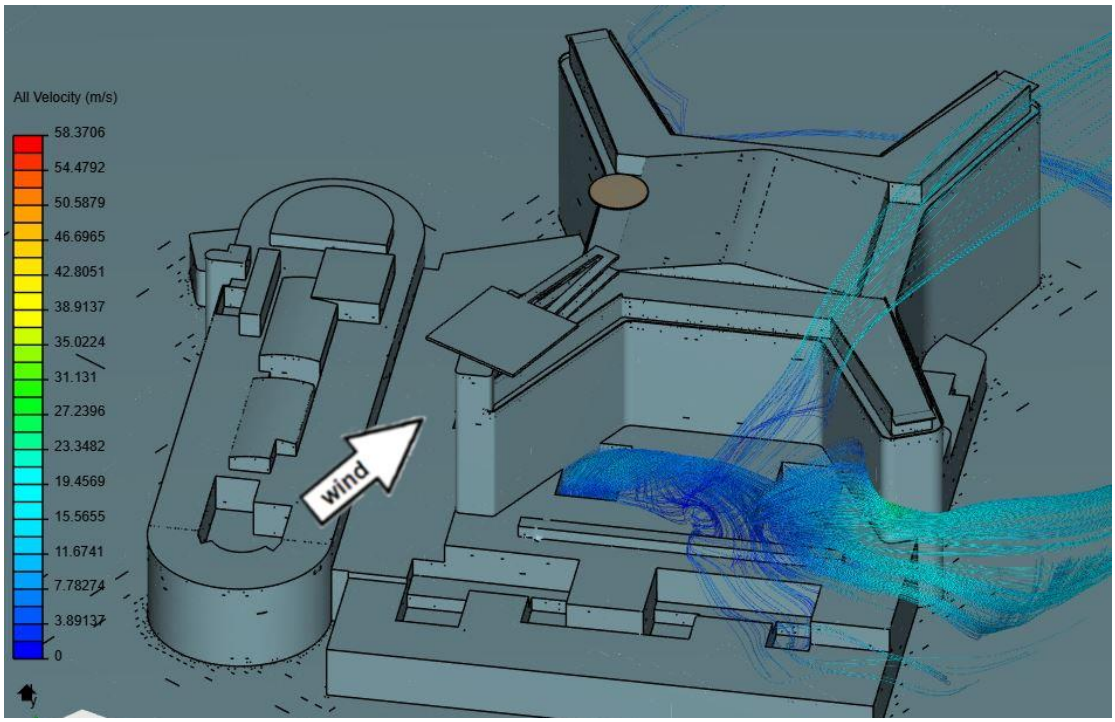

Figure 26: Prevailing wind direction with helicopter 47m from the helipad showing airflow path to Podium level 3 lightwells. Downstream flow only.

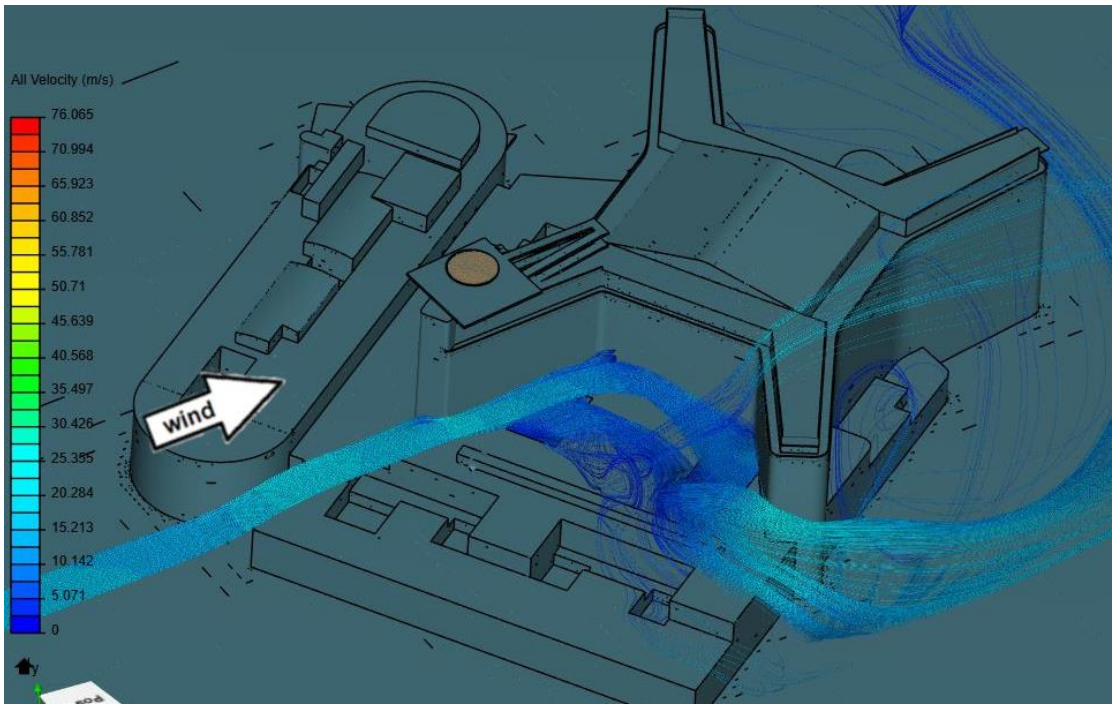

Figure 27: Prevailing wind direction with helicopter above the helipad showing airflow path to Podium level 3 lightwells. Upstream and downstream flow.

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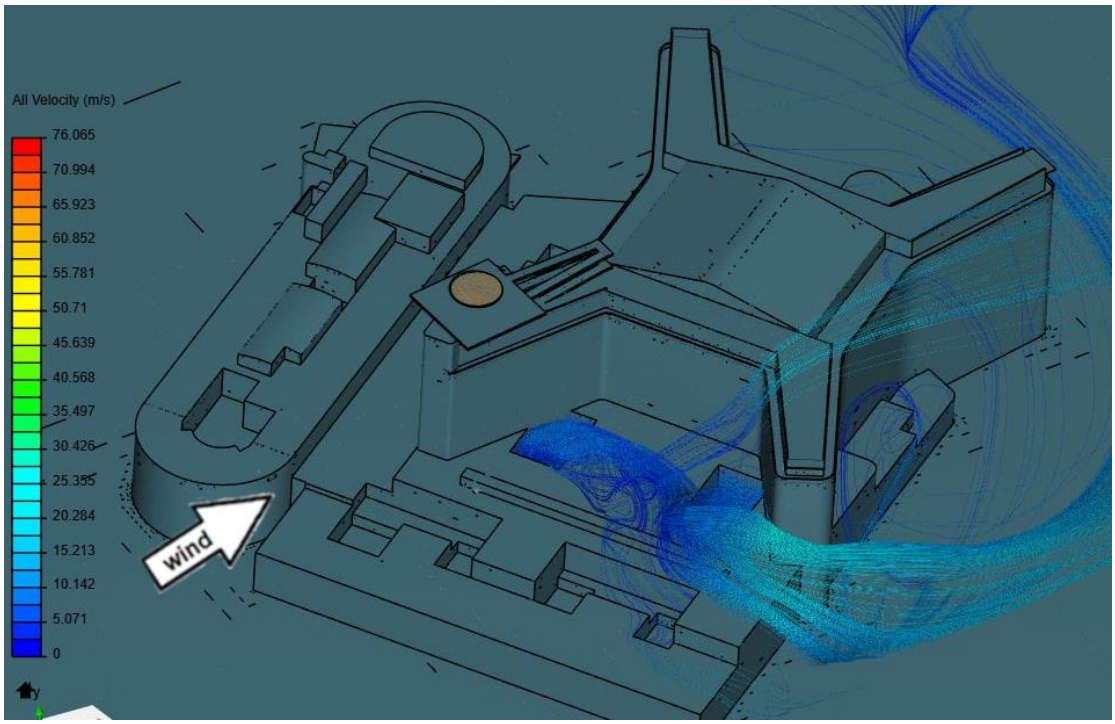

Figure 28: Prevailing wind direction with helicopter above the helipad showing airflow path to Podium level 3 lightwells. Downstream flow only.

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5.3 Secondary Wind Direction

The second most frequent wind direction is east-north-east. The maximum average recorded wind speed from this direction is much lower than from the prevailing wind direction, at 9 m/s compared to 18.7 m/s. However for this wind direction, the flow is from tower D towards tower B, passing over the helipad last. This means the flow is much less likely to be drawn from the helipad region into any of the vents, since they are all upstream and this was confirmed by the simulations.

A more interesting wind speed from this direction is 1 m/s, so this was simulated. Again, in all cases, the air reaching the AHU intakes does not pass beneath the helipad (Figure 29, Figure 30, Figure 31, Figure 32 and Figure 33).

Since the flow reaching the AHU intakes on tower C can be seen to pass round tower B (although much lower than the helipad location), this same wind direction was also simulated at the maximum wind speed of 18.7 m/s. The flow reaching the AHU vents in tower C was assessed and the air was shown to still not pass through the region beneath the helipad (Figure 34).

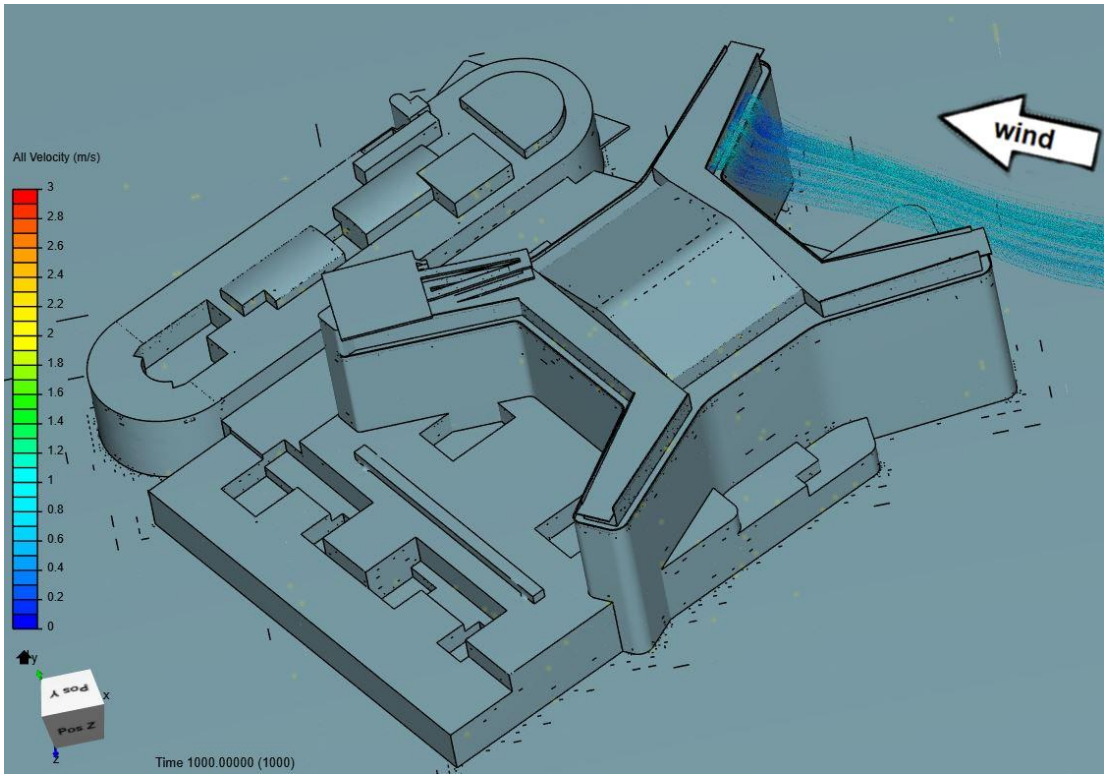

Figure 29: Secondary wind direction showing airflow path to AHU intakes on tower A.

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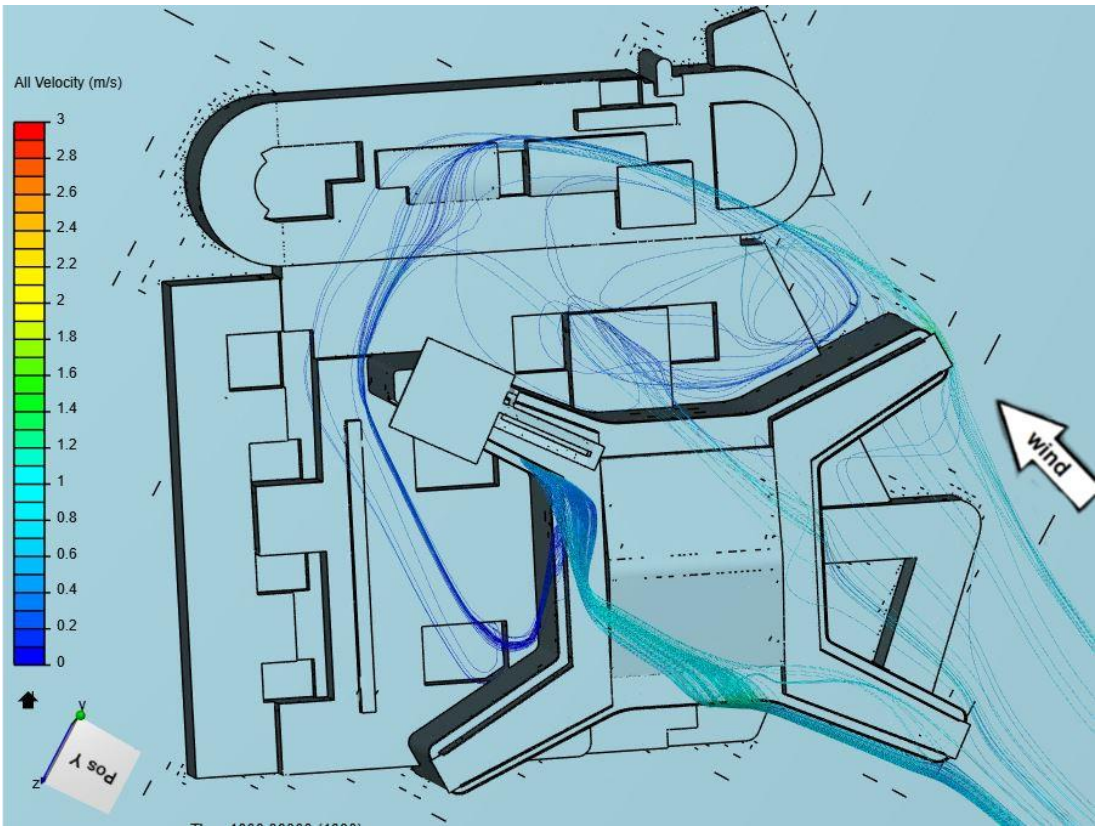

Figure 30: Secondary wind direction showing airflow path to AHU intakes on tower B.

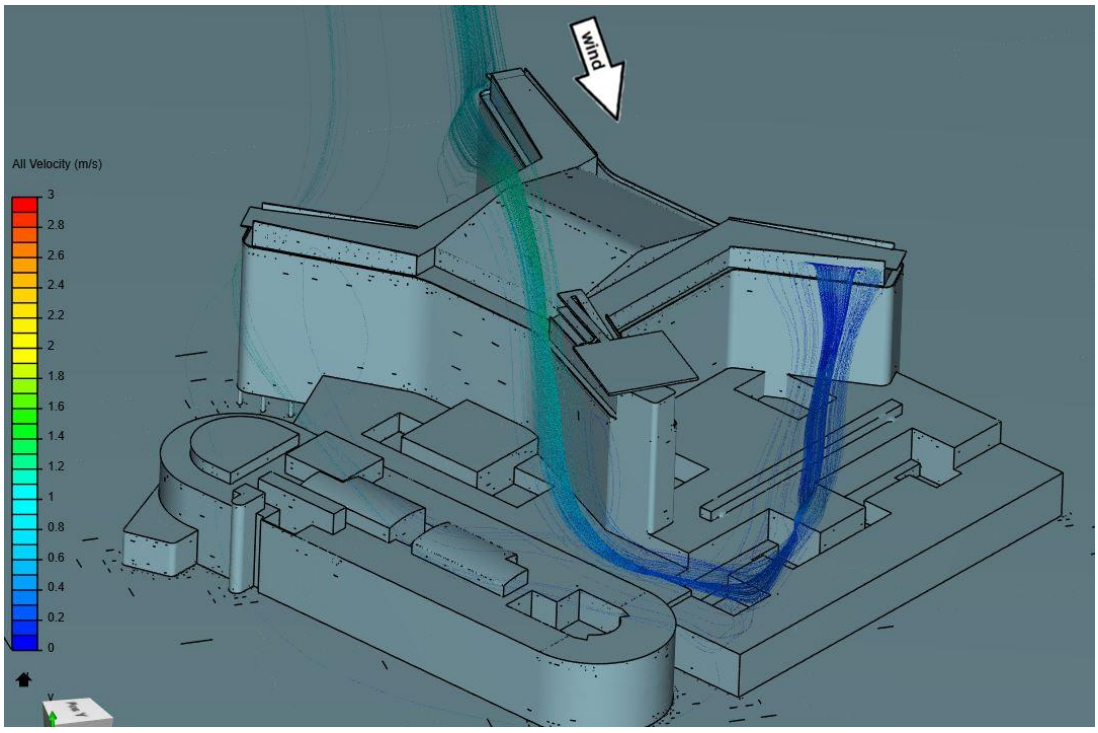

Figure 31: Secondary wind direction showing airflow path to AHU intakes on tower C.

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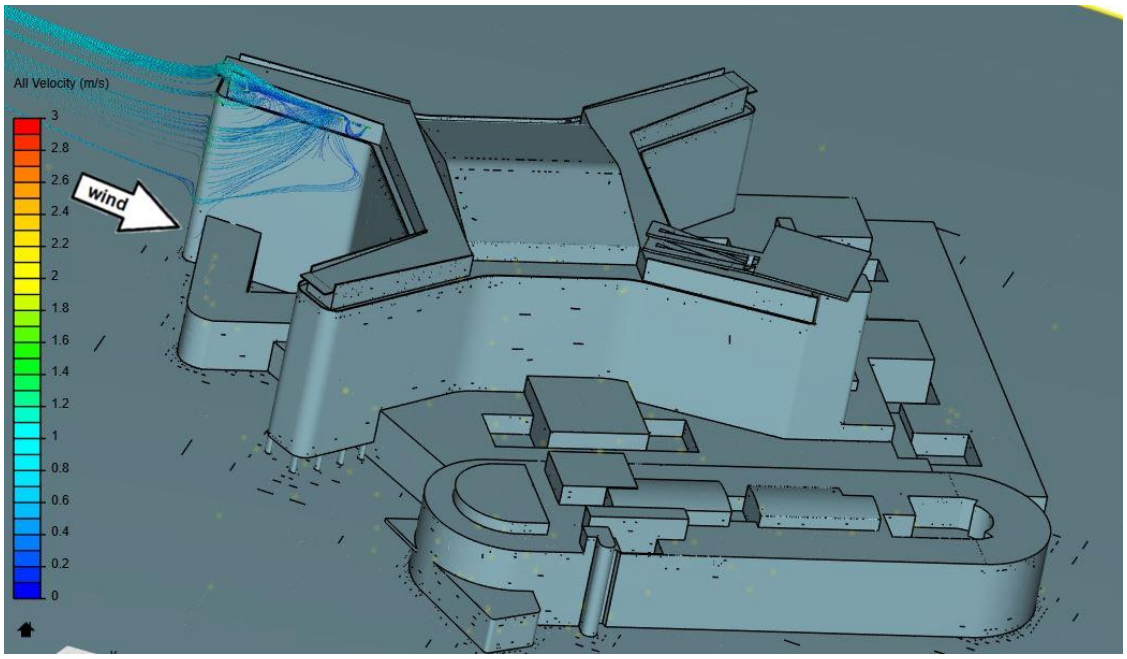

Figure 32: Secondary wind direction showing airflow path to AHU intakes on tower D.

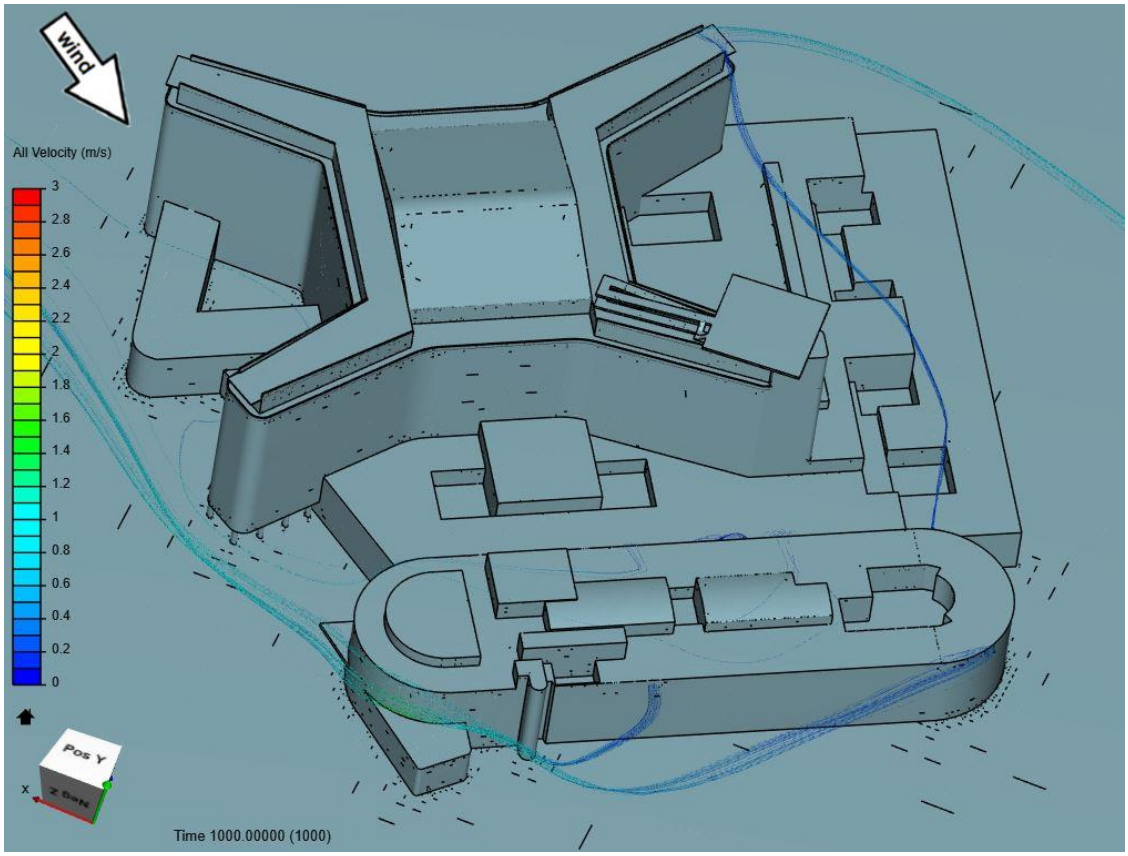

Figure 33: Secondary wind direction showing airflow path to AHU intakes on Royal Children's Hospital.

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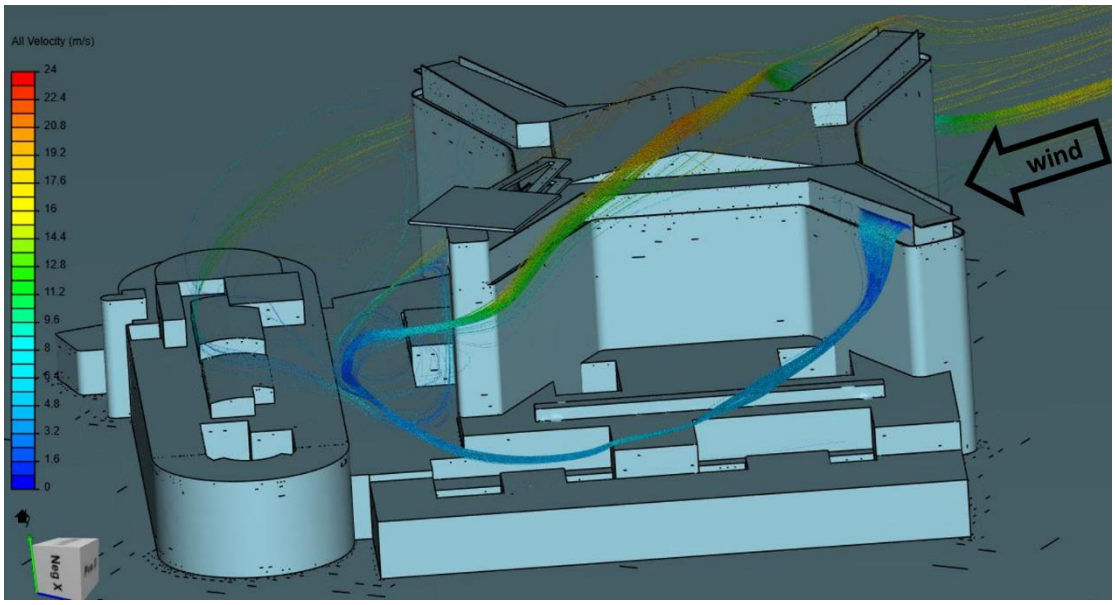

Figure 34: Secondary wind direction at 18.7 m/s showing airflow path to AHU intakes on Tower C.

Figure 6: Prevailing wind direction showing airflow path to intakes on Podium Level 3. Upstream and downstream.Figure 35, Figure 36, Figure 37 and Figure 38 show the flow to and from the separate lightwells between Towers B and C, where intakes on Podium level 3 are located. The particle traces show both the flow arriving in the lightwell and also leaving it because flow intakes were not explicitly modelled in this location. The flow of interest to us is the flow upstream from the lightwells, to determine where it has travelled prior to reaching this location. However, the software doesn't allow the upstream direction only to be shown, so the two images show both upstream and downstream flow and then just downstream flow. It is the upstream flow that is of interest. The difference between the two images shows the flow reaching the intakes on Podium level 3 doesn't pass through the area under the helipad.

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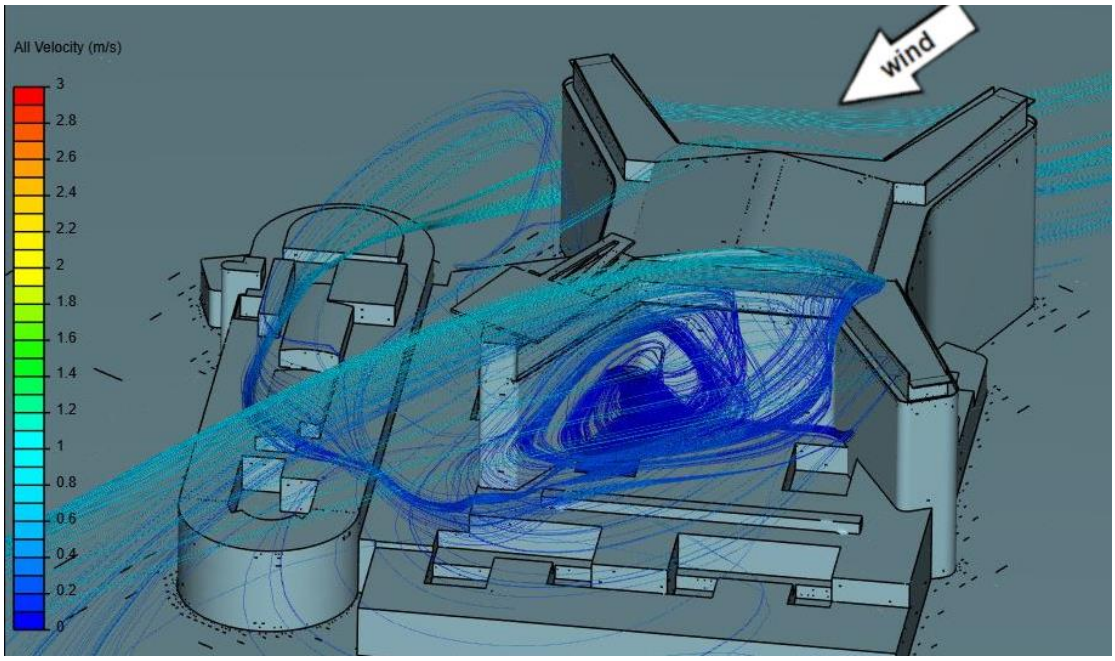

Figure 35: Secondary wind direction at 1m/s showing airflow path to left hand side Podium level intakes. Upstream and downstream flow.

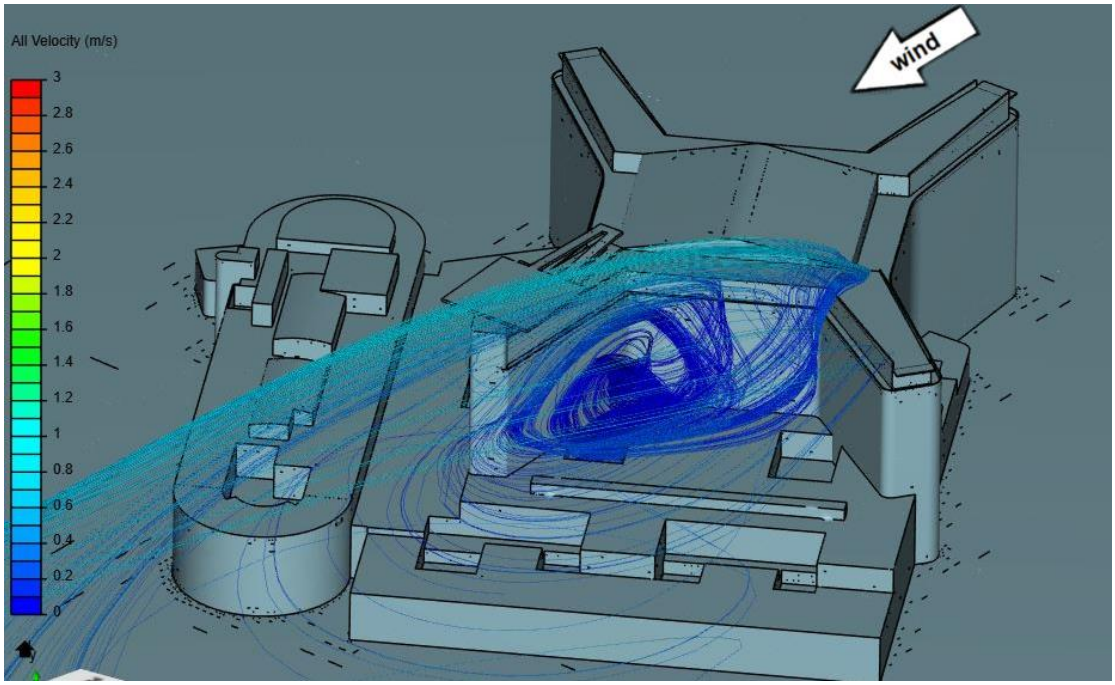

Figure 36: Secondary wind direction at 1m/s showing airflow path to left hand side Podium level intakes. Downstream flow only.

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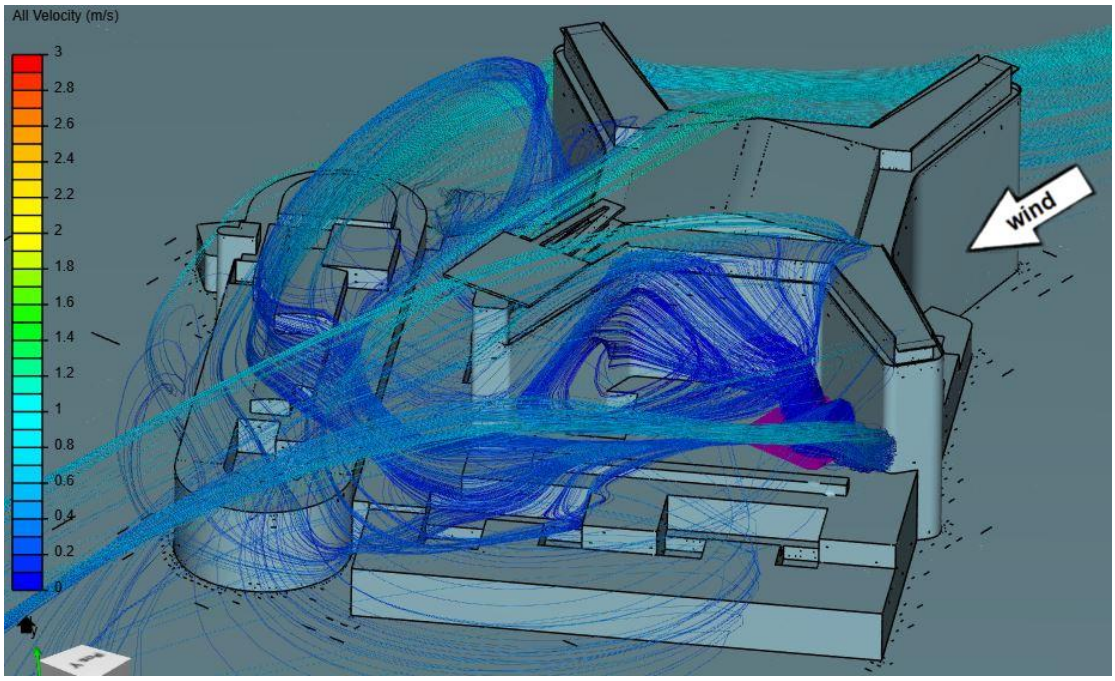

Figure 37: Secondary wind direction at 1m/s showing airflow path to right hand side Podium level intakes. Upstream and downstream flow.

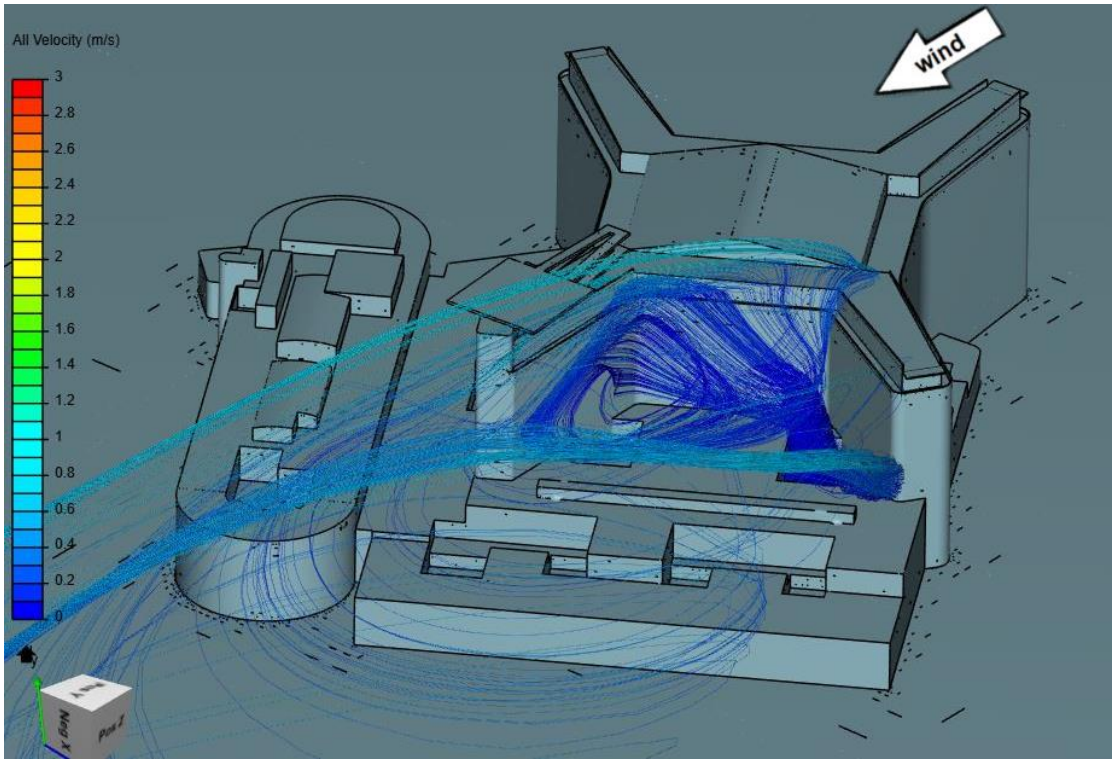

Figure 38: Secondary wind direction at 1m/s showing airflow path to right hand side Podium level intakes. Downstream flow only.

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5.1 Secondary Wind Direction with Helicopter Approaching

At the second most frequent wind direction but the maximum velocity of 18.7 m/s, with the helicopter approaching at 22m from the centre of the helipad and at a height of 10m, the air that reaches the AHU intakes does not pass through the area below the helipad (Figure 39, Figure 40, Figure 41, Figure 42, Figure 43 and Figure 44). Two different views are shown for flow into the vents of Towers B and C for clarity. This is as expected given the orientation of the helipad downstream of the vent locations and that the helicopter would approach from downstream.

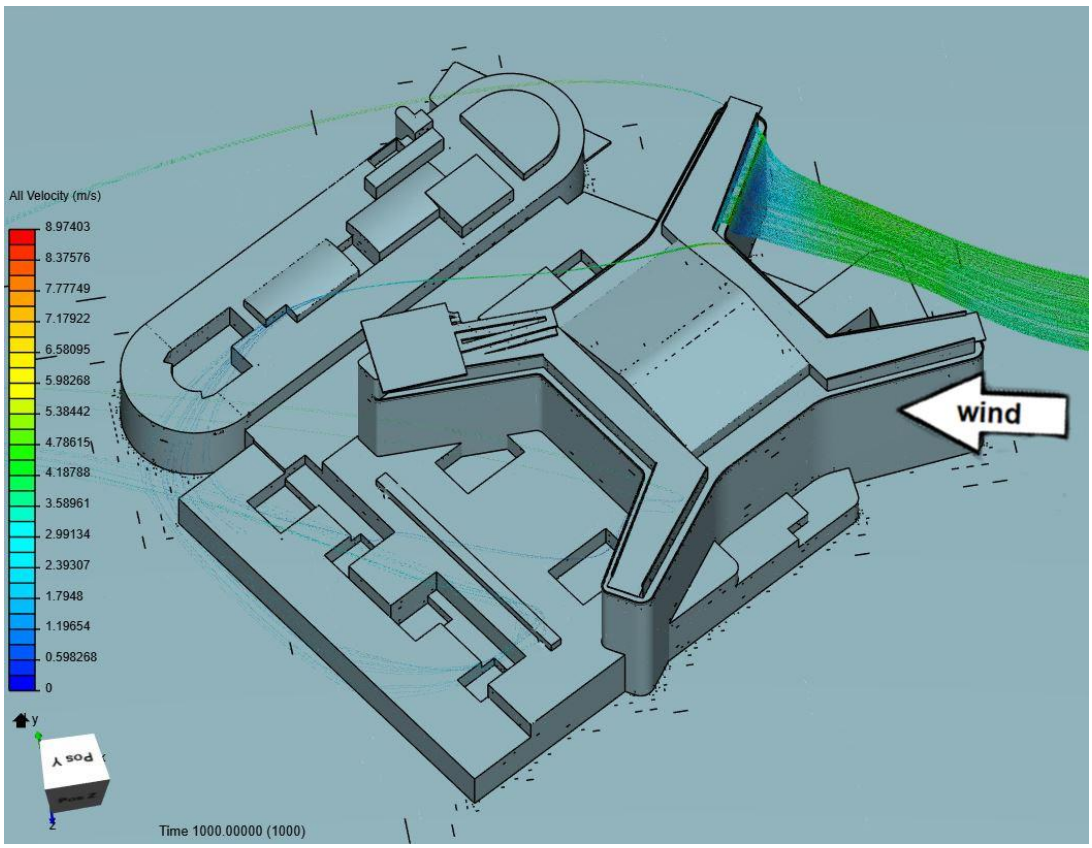

Figure 39: Secondary wind direction with helicopter approaching showing airflow path to AHU intakes on Tower A.

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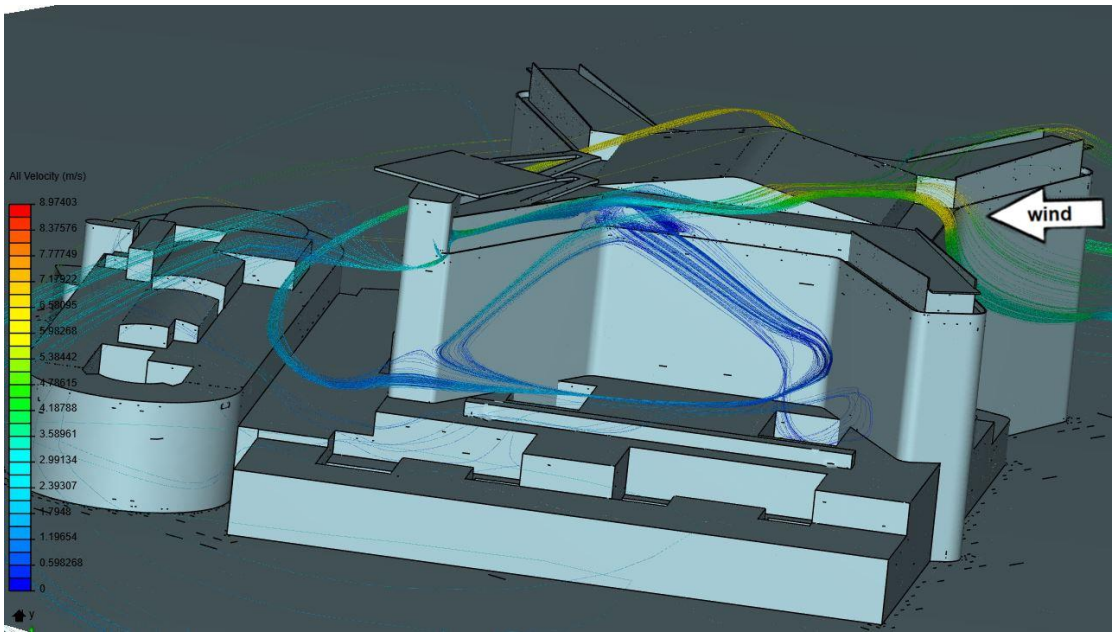

Figure 40: Secondary wind direction with helicopter approaching showing airflow path to AHU intakes on Tower B.

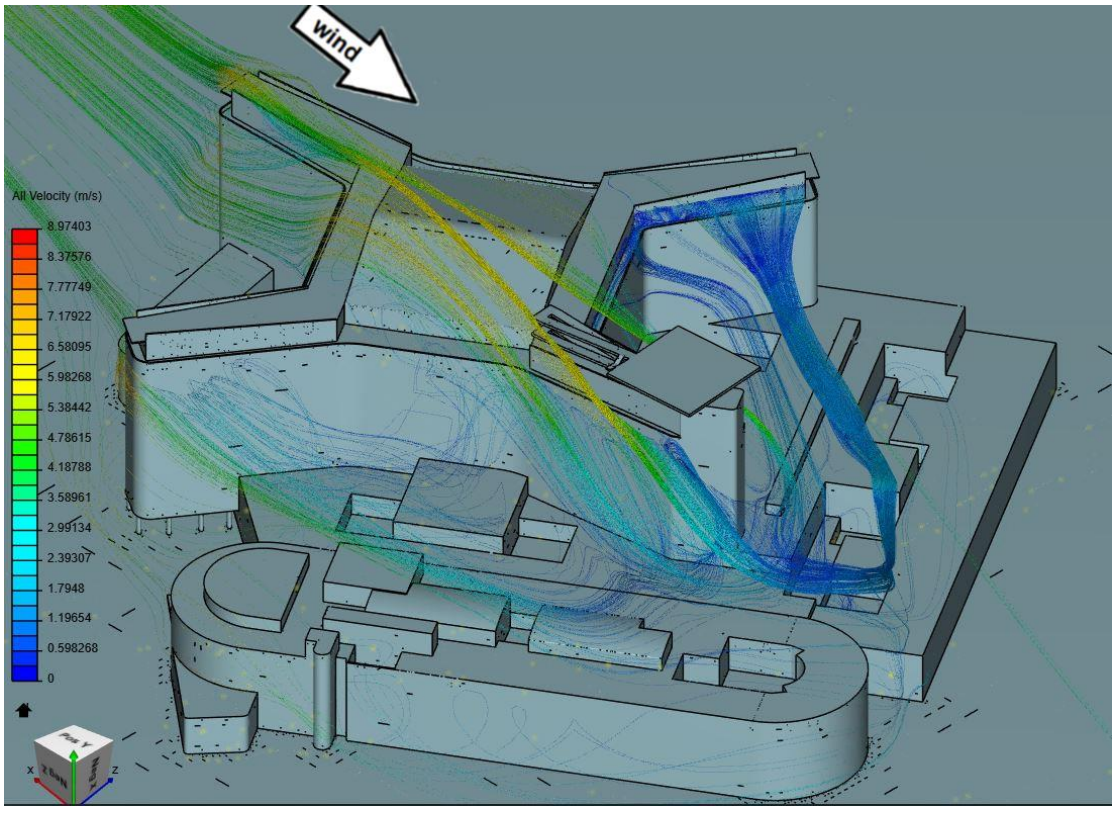

Figure 41: Secondary wind direction with helicopter approaching showing airflow path to AHU intakes on Tower C.

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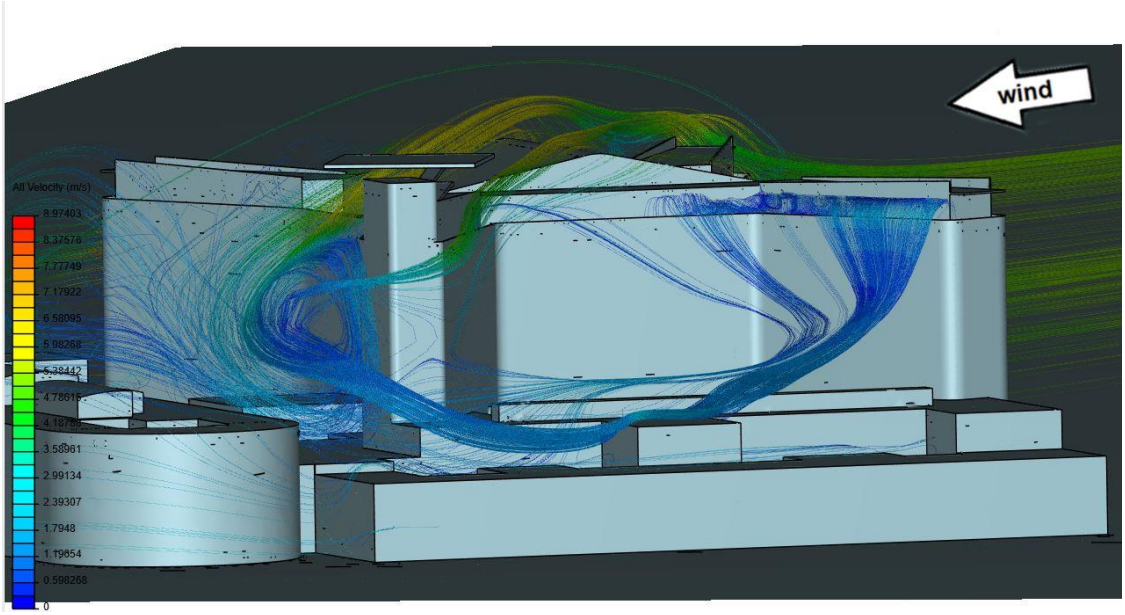

Figure 42: Secondary wind direction with helicopter approaching showing airflow path to AHU intakes on Tower C alternate view.

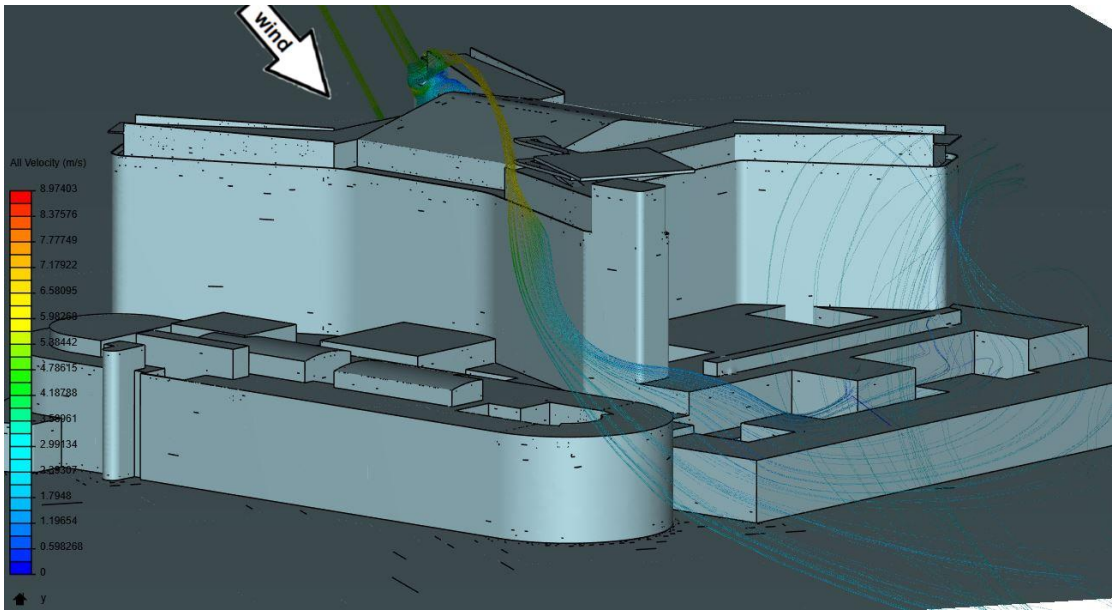

Figure 43: Secondary wind direction with helicopter approaching showing airflow path to AHU intakes on Tower D.

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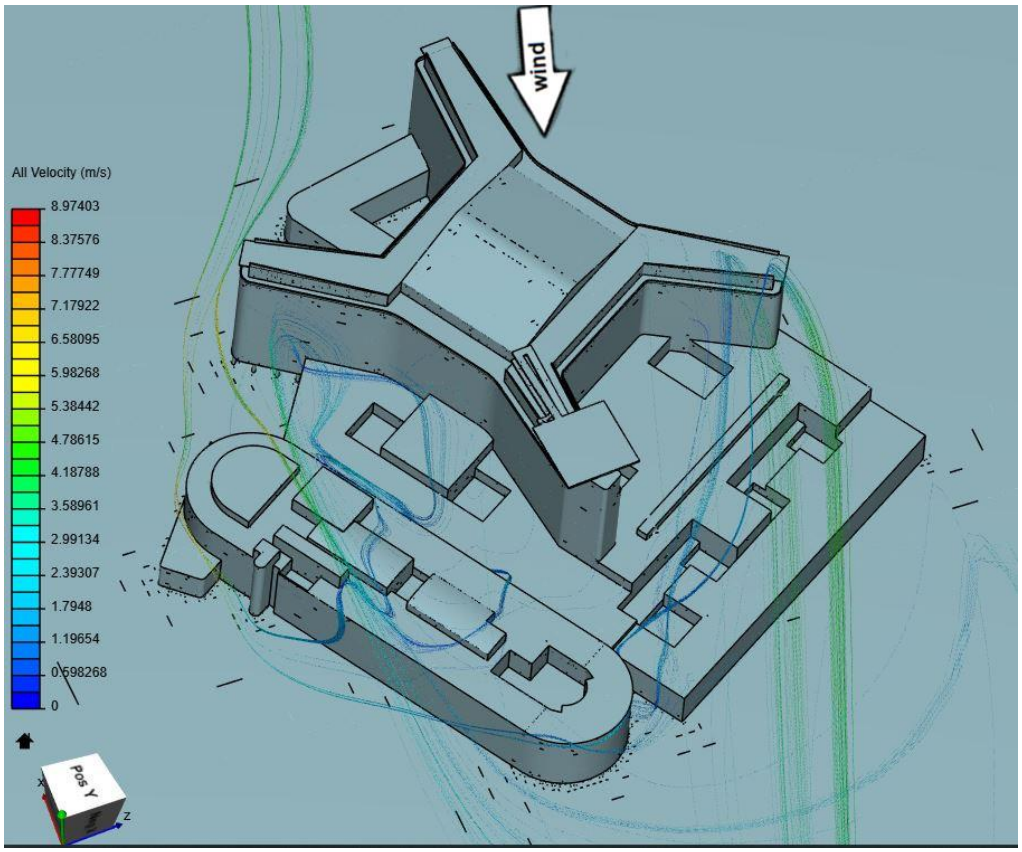

Figure 44: Secondary wind direction with helicopter approaching showing airflow path to AHU intakes on Royal Children's Hospital.

The helicopter will have a greater impact on the flow to the AHU intakes when it is closer to landing. With the helicopter immediately above the center of the helipad, equivalent to immediately prior to landing, the air that reaches the AHU intakes doesn't pass through the area below the helipad (Figure 45, Figure 46, Figure 47, Figure 48 and Figure 49).

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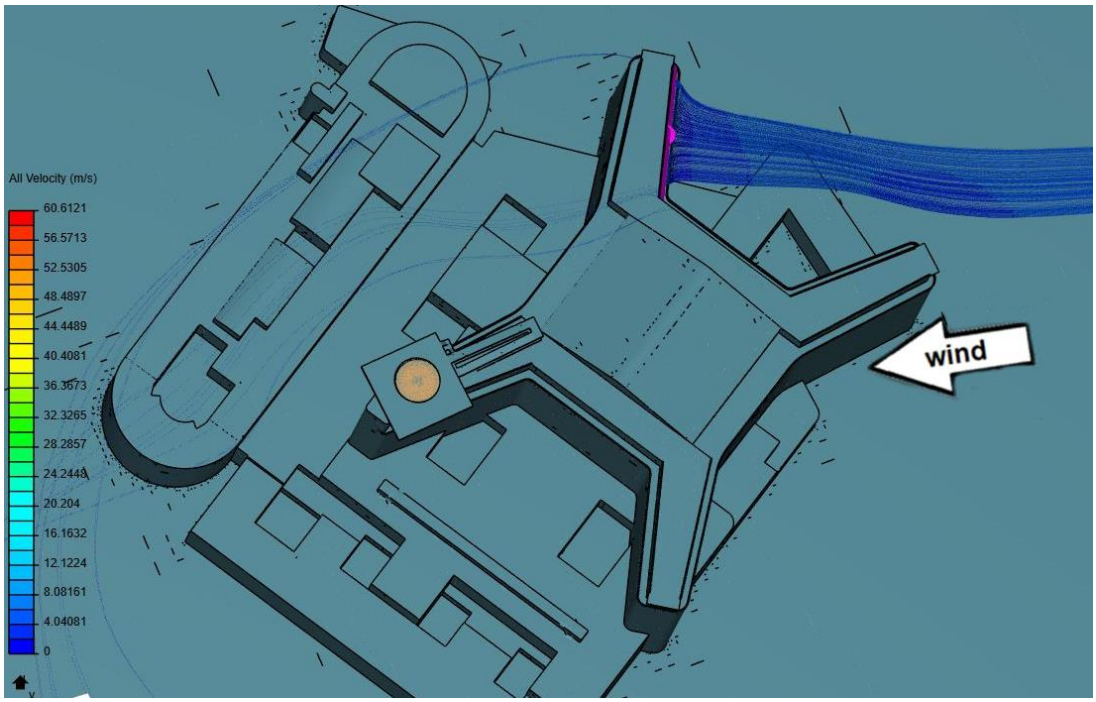

Figure 45: Secondary wind direction with helicopter above helipad showing airflow path to AHU intakes on Tower A.

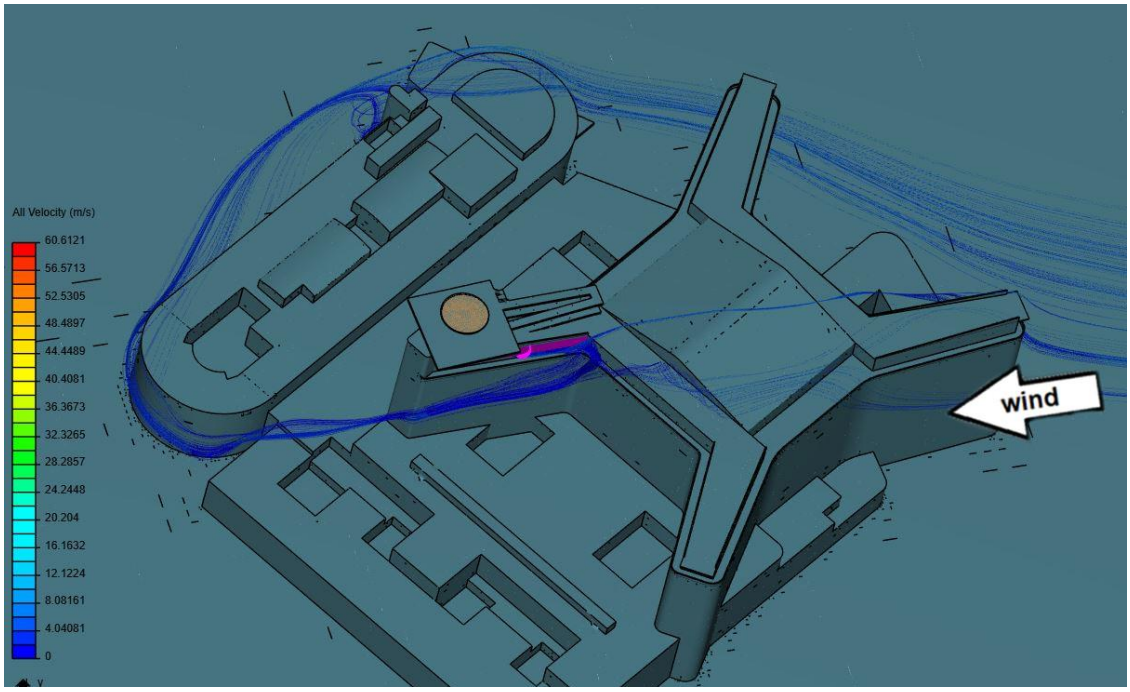

Figure 46: Secondary wind direction with helicopter above helipad showing airflow path to AHU intakes on Tower B.

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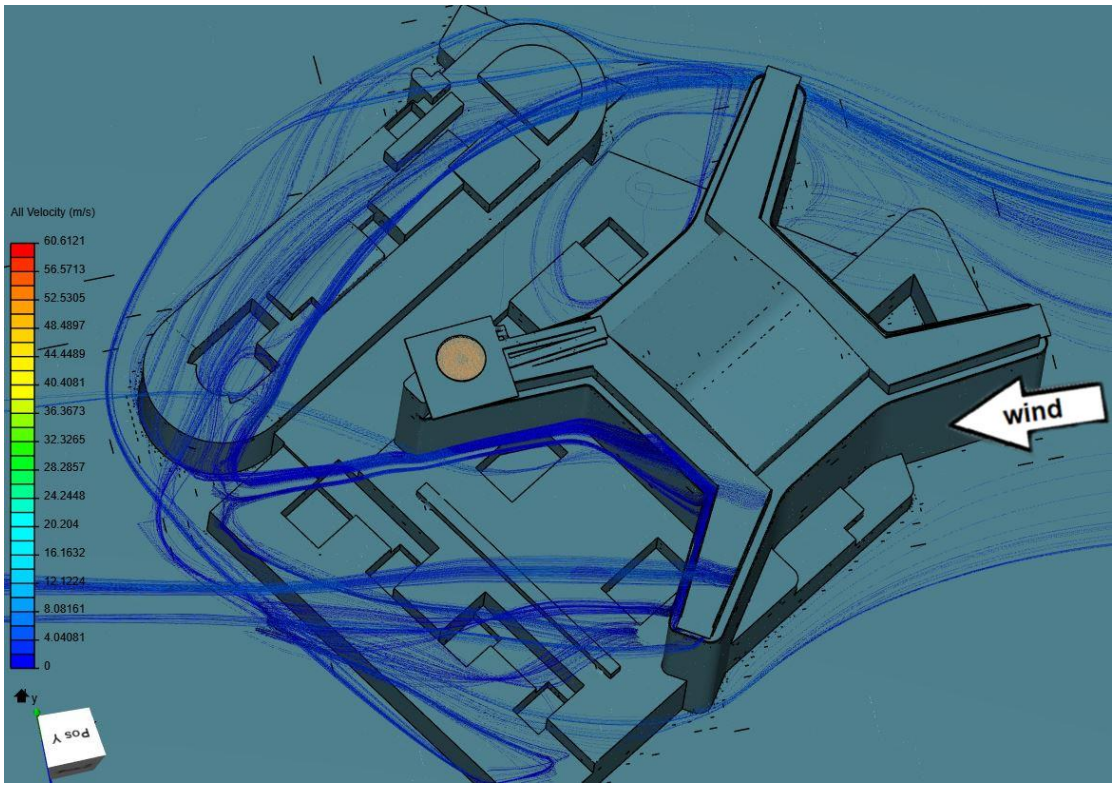

Figure 47: Secondary wind direction with helicopter above helipad showing airflow path to AHU intakes on Tower C.

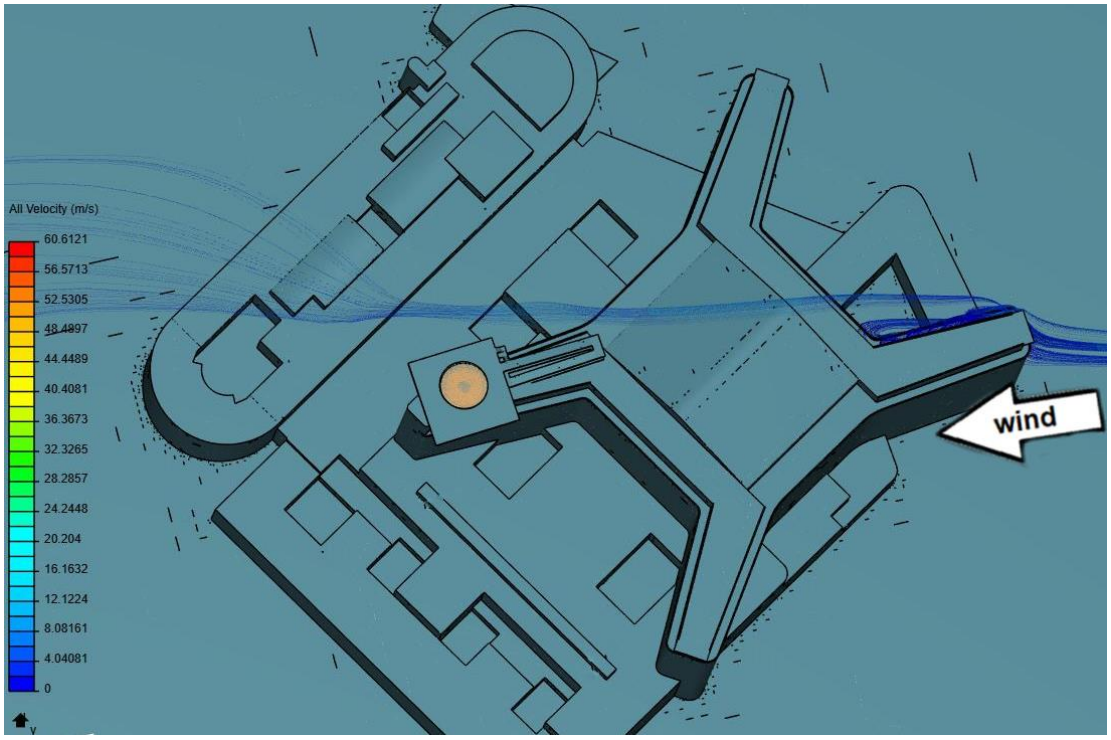

Figure 48: Secondary wind direction with helicopter above helipad showing airflow path to AHU intakes on Tower D.

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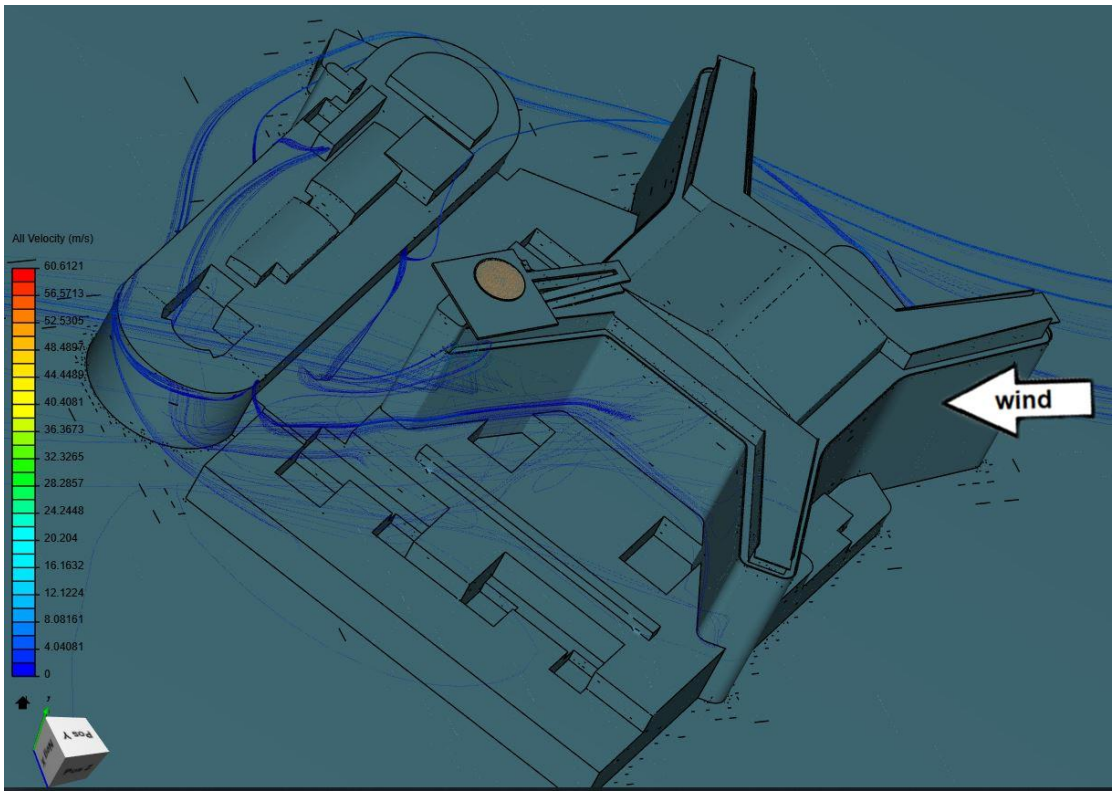

Figure 49: Secondary wind direction with helicopter above helipad showing airflow path to AHU intakes on Royal Children's Hospital.

Finally, since the flow entering the AHU intakes has not passed through the area beneath the helipad, any contamination entering the ducts is from the wider environment. This will be in the direction of the wind, so either south-weat or east-north-east.

Figure 6: Prevailing wind direction showing airflow path to intakes on Podium Level 3. Upstream and downstream.Figure 50, Figure 51, Figure 52 and Figure 53 show the flow to and from the separate lightwells between Towers B and C, where intakes on Podium level 3 are located, with the effect of the helicopter in approaching the helipad. Figure 54 shows to flow with the effect of the helicopter immediately above the helipad. Again, the particle traces show both the flow arriving in the lightwell and also leaving it because flow intakes were not explicitly modelled in this location. The flow of interest to us is the flow upstream from the lightwells, to determine where it has travelled prior to reaching this location. However, the software doesn't allow the upstream direction only to be shown, so the two images show both upstream and downstream flow and then just downstream flow. It is the upstream flow that is of interest. The difference between the two images shows the flow reaching the intakes on Podium level 3 doesn't pass through the area under the helipad or any of the ventilation exhausts.

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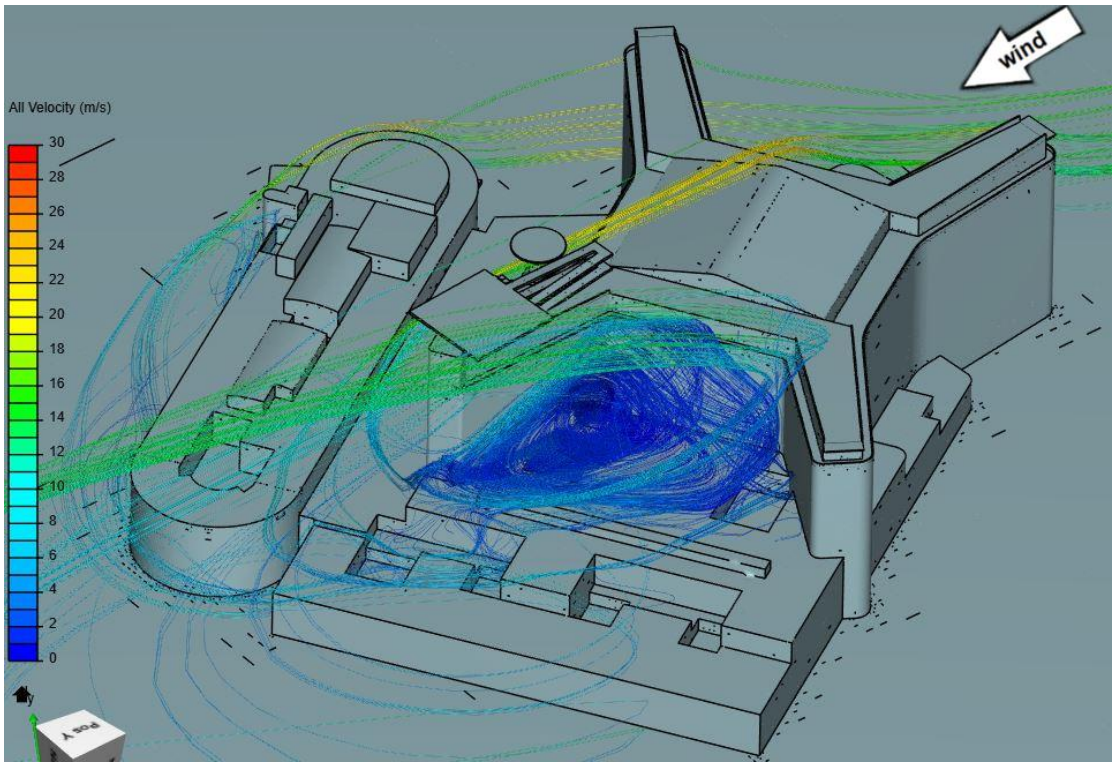

Figure 50: Secondary wind direction with helicopter approaching showing airflow path to left hand side Podium level 3 intakes. Upstream and downstream flow.

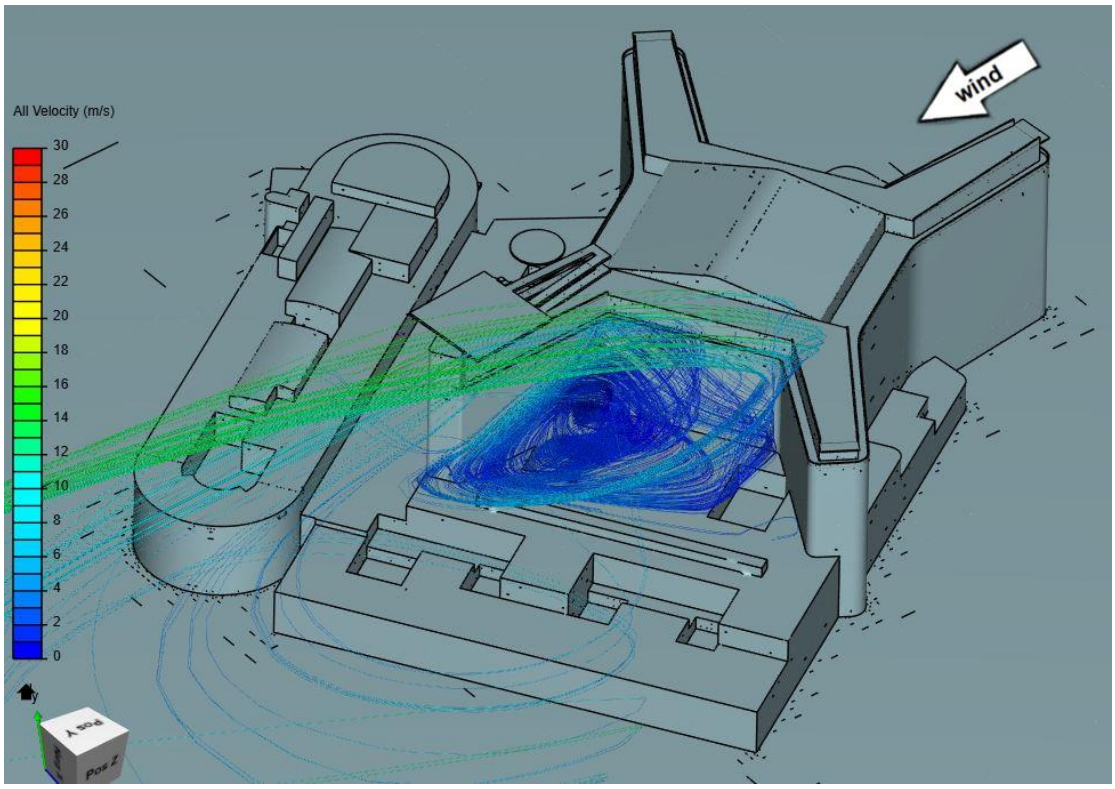

Figure 51: Secondary wind direction with helicopter approaching showing airflow path to left hand side Podium level 3 intakes. Downstream flow only.

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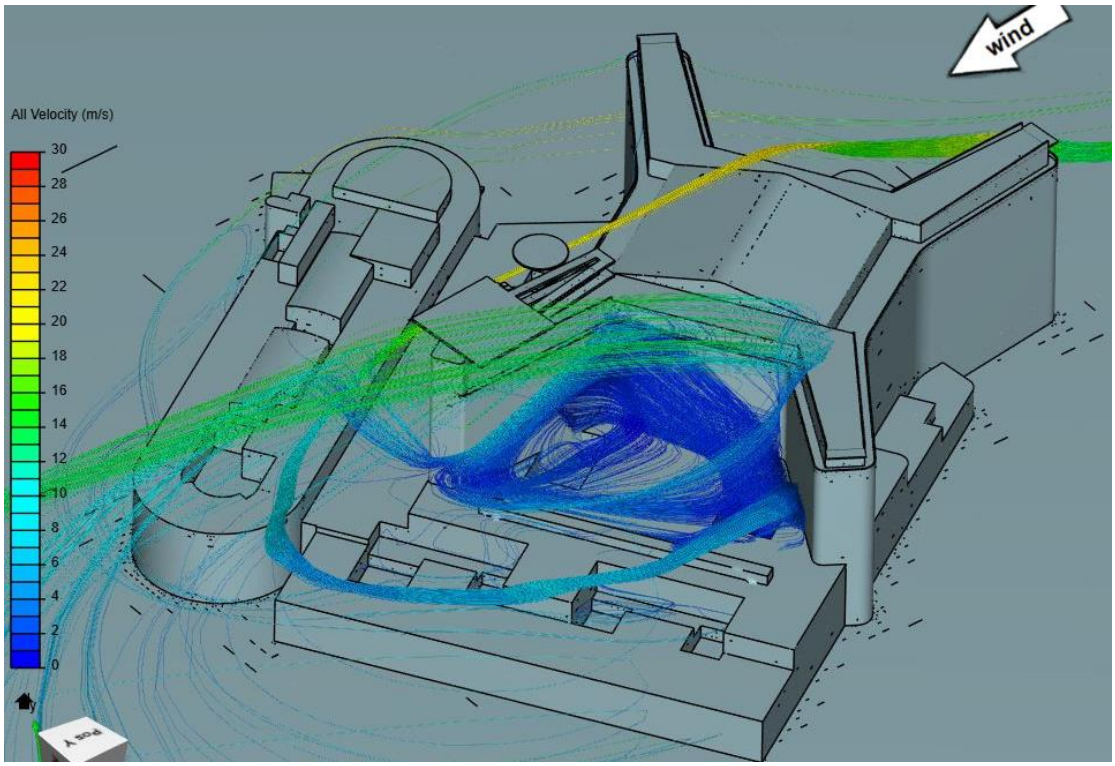

Figure 52: Secondary wind direction with helicopter approaching showing airflow path to right hand side Podium level 3 intakes. Upstream and downstream flow.

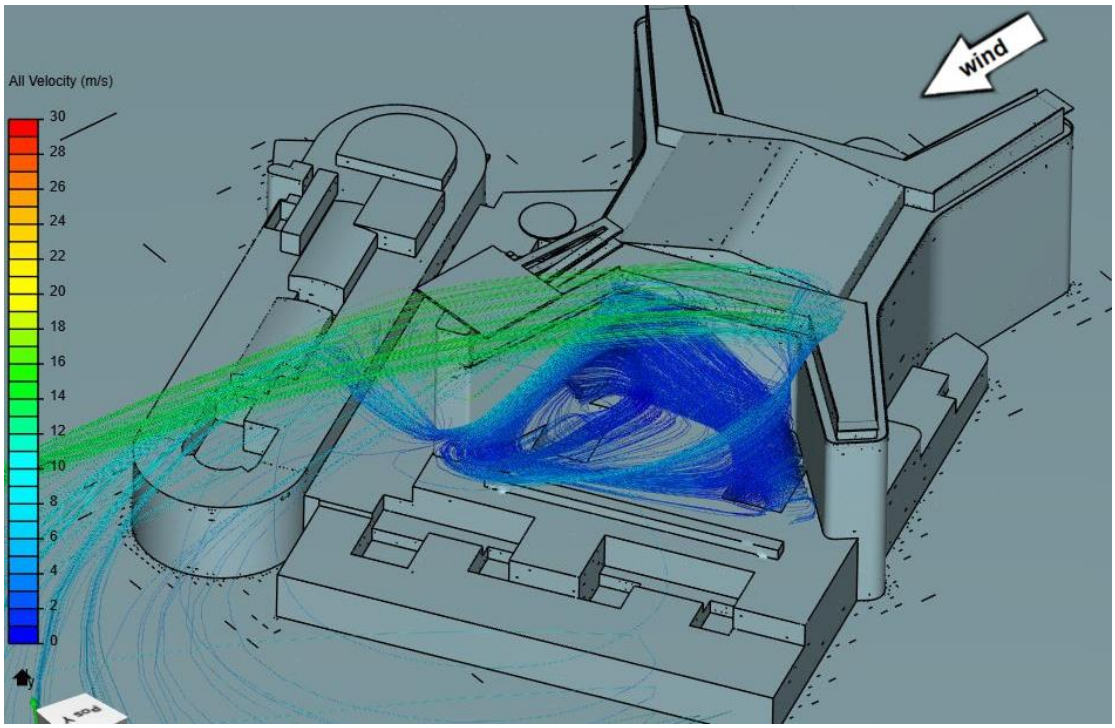

Figure 53: Secondary wind direction with helicopter approaching showing airflow path to right hand side Podium level 3 intakes. Downstream flow only.

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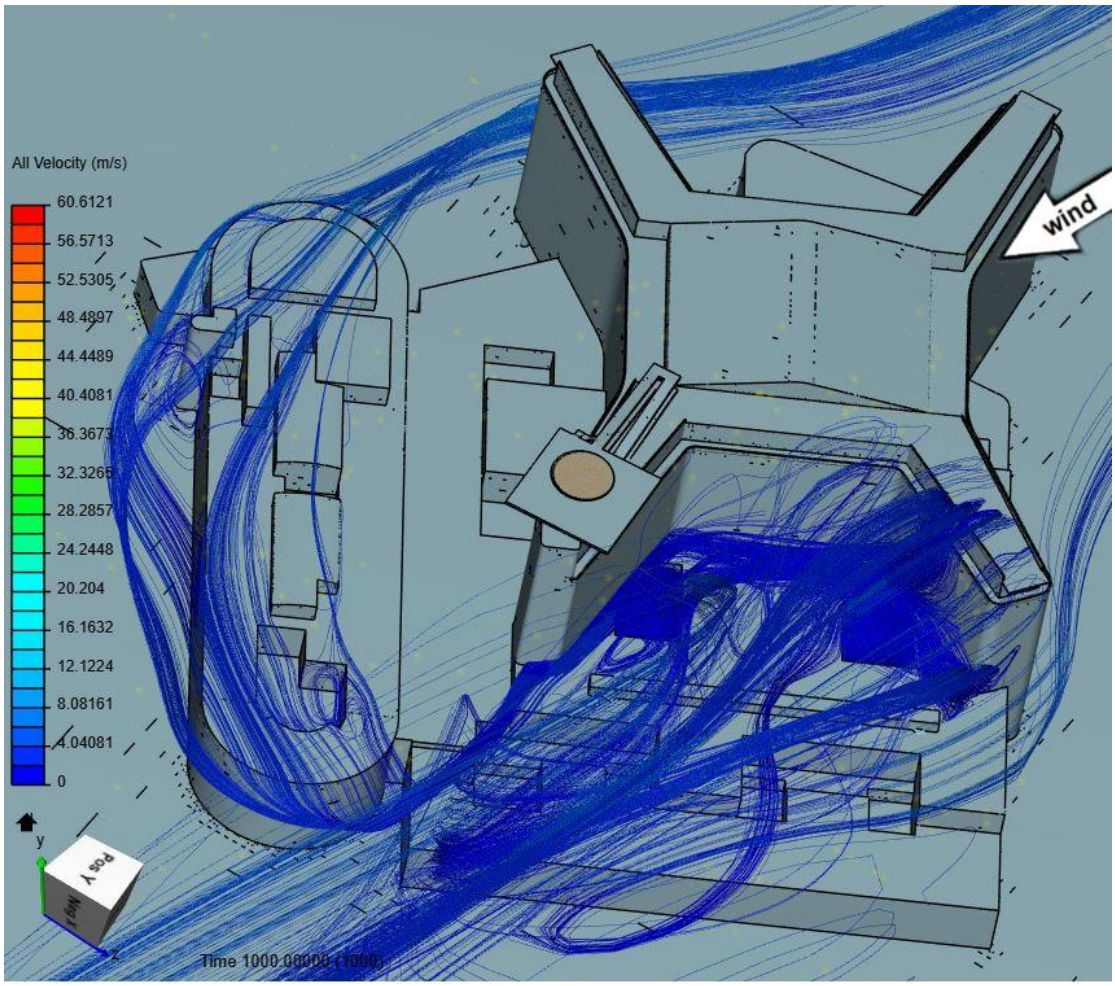

Figure 54: Secondary wind direction with helicopter directly over the helipad showing airflow path to Podium level 3 intakes. Upstream and downstream flow.

4.1 Ground level wind effect

Although it wasn't the focus for this study, the nature of CFD means that there is data for all locations included in the model. Since there is anecdotal evidence and concern about strong winds around the front entrance of the main hospital, this was also plotted for the two wind directions.

The velocity contour plots show that in prevailing wind conditions (south-west), the wind velocity in the area in front of the hospitals in low, below 6m/s and according to Lawson's comfort criteria, should not cause pedestrian discomfort (Figure 55). This is not the case when a helicopter is arriving, with high wind velocities over 20 m/s in the area (Figure 56). However, it should be noted that this would only occur briefly during helicopter landing.

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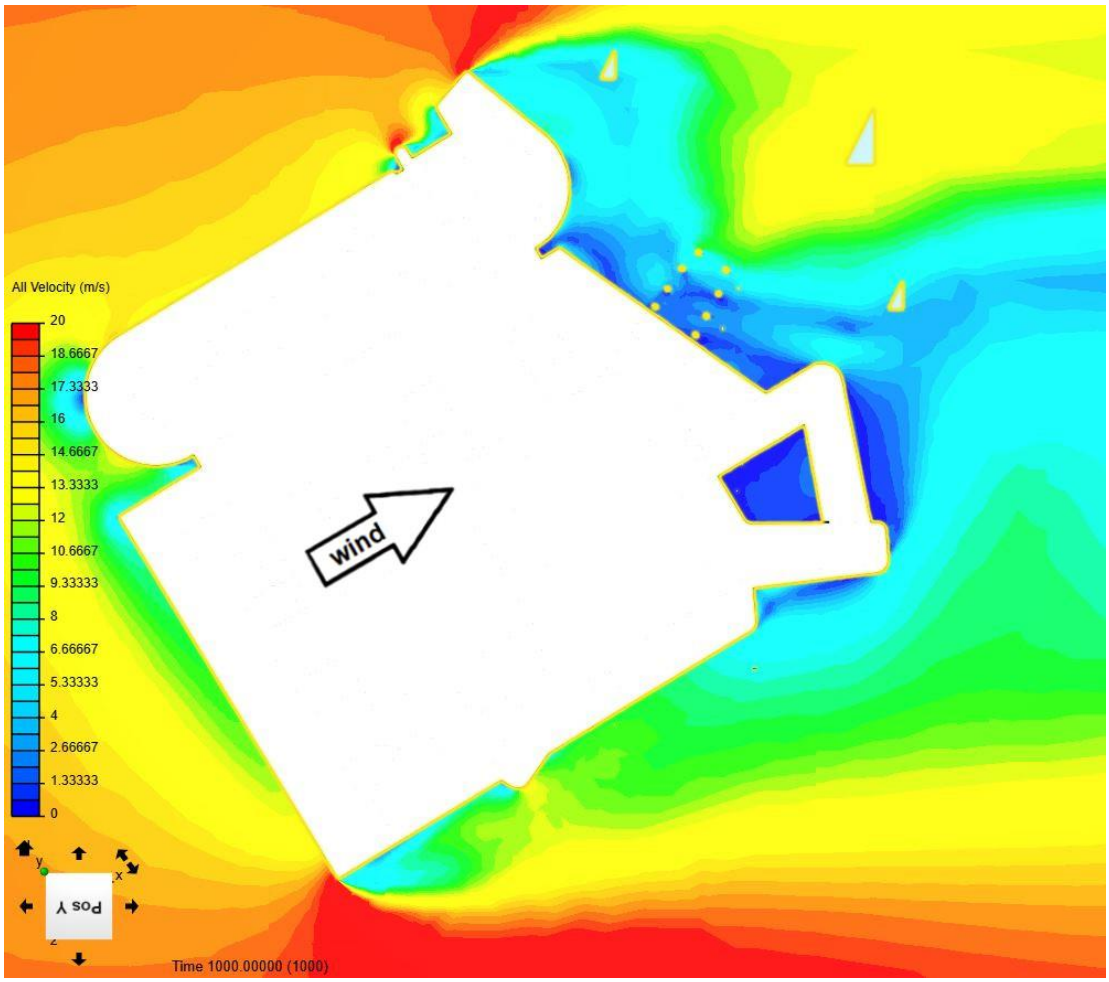

Figure 55: Prevailing wind of 18.7 m/s without helicopter present. Velocity contours 1m above the ground.

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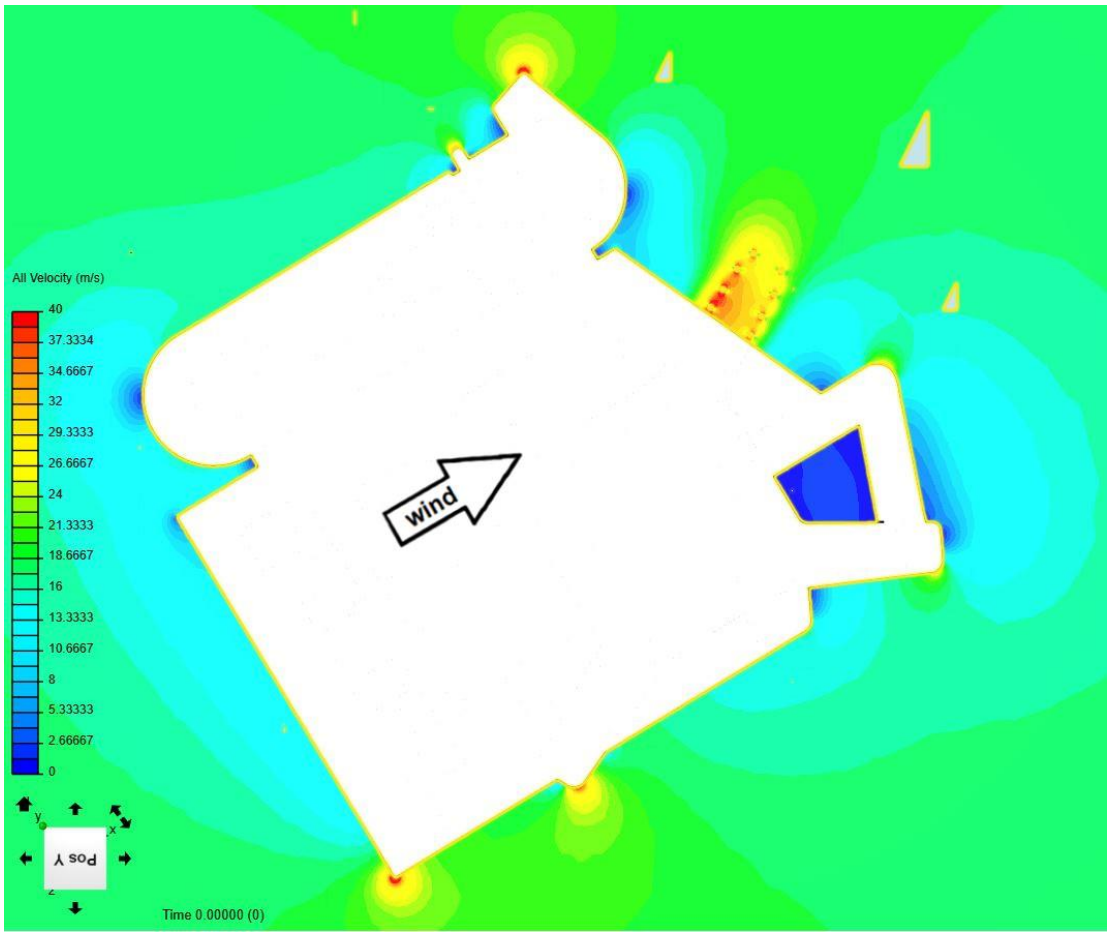

Figure 56: Prevailing wind of 18.7m/s with helicopter present. Velocity contours 1m about the ground.

For the second most common wind direction (east-north-east), the flow is very different. It is now towards the front entrance, without the sheilding effect of the main building. Figure 57 shows that for this wind direction, at the maximum overall wind speed of 18.7 m/s, high wind speeds are present around the front entrance. The values are significantly over 10 m/s which is the upped limit for Lawson's comfort criteria. However, it should be noted that this is at a higher wind speed than occurs from this direction.

At the more common speed of 5.5 m/s, the wind in the area is more acceptable, below 7 m/s, although this would still be uncomfortable for anyone standing or sitting in the area. Figure 58 shows this with overlaid velocity ventors showing the flow directions. For the maximum average wind speed in this direction (9 m/s), the effect would be worse and likely to be beyond the Lawson comfort criteria.

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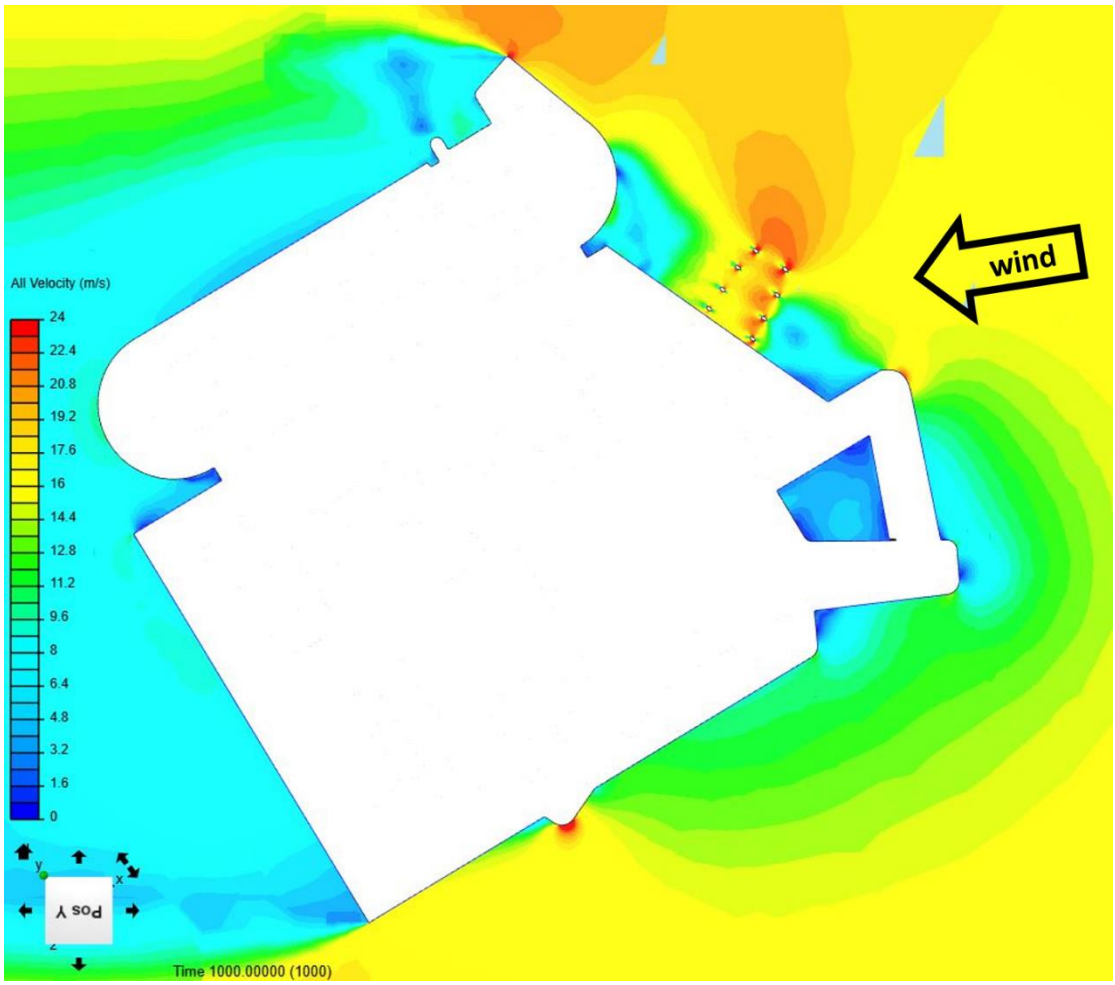

Figure 57: Second wind direction at 18.7 m/s without the helicopter present. Velocity contours 1m above the ground.

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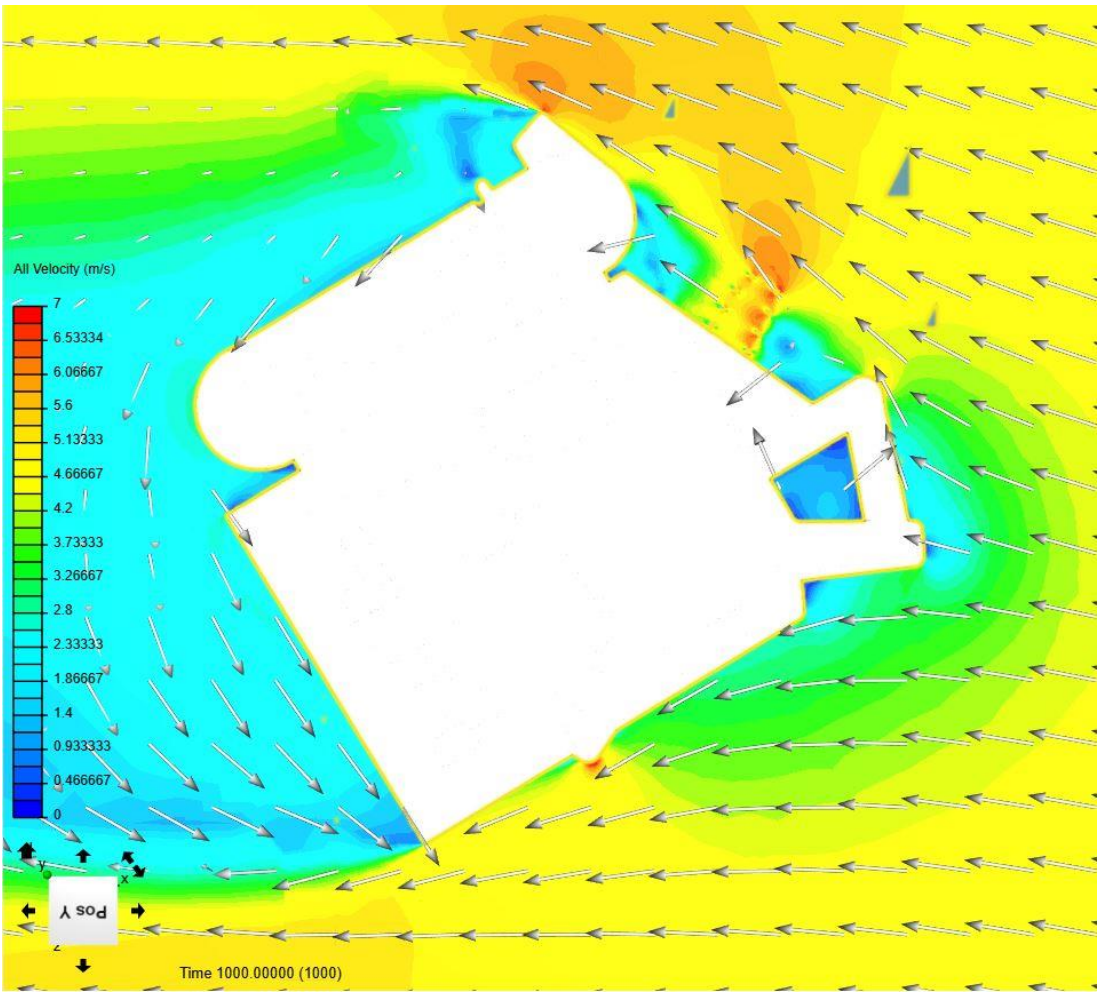

Figure 58: Second wind direction at 5.5 m/s without the helicopter present. Velocity contours 1m above the ground.

5. Conclusions

The CFD simulations undertaken demonstrate that the air arriving at the AHU intake locations does not originate in the region beneath the helipad for any of the scenarios considered. It is therefore, unlikely that debris from the helipad area is being carried into the hospital ventilation system so anything drawn into the AHU will come from the wider environment. Whilst it is not possible to determine how far away potential contamination will originate, it should be noted that anything carried in the flow will be lightweight, since heavier matter will fall out due to gravity.

Additionally, the simulations show that with the maximum wind from the prevailing direction (south-west) and when there is no helicopter in the area, the air speed around the front entrance of the main hospital should be under 6 m/s, which would not be excessive for pedestrian comfort for walking or standing. However, when a helicopter is approaching, gusts of over 20 m/s may be experienced in the area.

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With wind from the second most frequent direction (east-north-east) at the maximum average wind speed of 18.7 m/s, wind speeds over 10 m/s are present around the front entrance, which is above the Lawson's comfort criterion for any activity. However this is a higher wind speed than the average recorded for this direction.

At the more likely speed of 5.5 m/s, the wind in the area is more acceptable, below 7 m/s. This would be uncomfortable for sitting or standing but acceptable for walking. However at the maximum wind speed form this direction (9 m/s) the wind speed in the area would be higher and likely to be above the Lawson comfort criteria of 10 m/s

It is understood that remedial work is being undertaken to add canopies in the area to protect against falling debris, but these have not been included in the model. Further work would be required to evaluate how these will influence the flow in the area.

6. Appendix A

Summary of ventilation intakes and associated AHUs.

Tower	Plant Room/AHU Ref:	Area service	Air intake elevation	Exhaust Elevation	Intake volume (l/s)
A	122-AHU-01	LEVEL 8-11	North-West	West	2594.83
	122-AHU-02	LEVEL 8-11			2429
	122-AHU-03	LEVEL 4 -11			4906
	122-AHU-04	Level 4 - 7			2283
	122-AHU-05	Level 4 - 7			2246
	122-AHU-06	Level 4 - 7			3228
	122-AHU-07	LEVEL 8-11			2923
	122-AHU-08	Level 4			329
	122-AHU-09	Level 4			326
B	121-AHU-01	LEVEL 8-11	South-West	West	2599
	121-AHU-02	LEVEL 8-11			2582
	121-AHU-03	LEVEL 8-11			3210
	121-AHU-04	Level 5 - 7			1971
	121-AHU-05	Level 5 - 7			1967
	121-AHU-06	Level 4 - 7			3150
C	124-AHU-01	LEVEL 8-11	South-East	East	2626.9
	124-AHU-02	LEVEL 8-11			2341
	124-AHU-03	LEVEL 8-11			2911
	124-AHU-04	Level 4 - 7			2778
	124-AHU-05	Level 4 - 7			2502
	124-AHU-06	Level 4 - 7			3168
	124-AHU-07	Level 4 - 7			2868
D	123-AHU-01	LEVEL 8-11		East	2722

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	123-AHU-02	LEVEL 8-11	North-East		2386
	123-AHU-03	LEVEL 8-11			4913
	123-AHU-04	Level 4 - 7			2638
	123-AHU-05	Level 4 - 7			2236
	123-AHU-06	Level 4 - 7			3304
	123-AHU-07	Level 4 - 7			2831

And for the Royal Children's Hospital

AHU	Area service	Air in take elevation	Exhaust Elevation	Intake volume (l/s)
41 AHU 13	PICU (Isolation Room)	East	Roof/court yard	322
41 AHU 14	PICU (General)	East		3262
41 AHU 46	PICU (General)	West		4093
41-AHU-20A	Ward 2A (Haem\TCT)	East		4151
41-AHU-24	MDU/Day case (2B)	West		2565

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

Bundle 24 - Documents referred to in the Expert Report by Allan Bennett regarding Cryptococcus, and Supporting Documentation

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Volume 3