Expert Report for the UK Covid-19 Public Inquiry

Module 1 – virology, epidemiology, threat agencies, international organisations and comparisons

Author: David L. Heymann, MD, CBE

Author statement

I confirm that this is my own work and that the facts stated in the report are within my own knowledge. I understand my duty to provide independent evidence and have complied with that duty. I confirm that I have made clear which facts and matters referred to in this report are within my own knowledge and which are not. Those that are within my own knowledge I confirm to be true. The opinions I have expressed represent my true and complete professional opinions on the matters to which they refer.

David L Heymann

19/05/2023

Contents

Preamble

1. I am a USA trained medical doctor (BA, Penn State University and MD, Wake Forest University School of Medicine); and a medical epidemiologist with a Diploma in Tropical Medicine and Hygiene (DTM&H, London School of Hygiene and Tropical Medicine). Currently I am Professor of Infectious Disease Epidemiology at the London School of Hygiene and Tropical Medicine.

2. In 1976, after spending two years working in India as a field epidemiologist to the World Health Organisation (WHO) smallpox eradication programme, I joined the US Centers for Disease Control (CDC) and was a member of the CDC team that investigated the first (1976) Ebola outbreak in the Democratic Republic of Congo (DRC). After that I stayed on in sub-Saharan Africa for 13 years with CDC, working within ministries of health, and with national counterparts conducted field research during Ebola outbreaks as they occurred; and investigated outbreaks of human monkeypox, Lassa Fever, malaria and other tropical diseases in order to better understand the epidemiology of these and other tropical diseases in sub-Saharan Africa.

3. From 1989 to 1997 I was seconded from CDC to the WHO, and in 1997 retired from CDC and stayed on at WHO as a staff member until 2009. During my time at WHO I held various leadership positions in infectious diseases, established the emerging infectious diseases programme, and in 2003 headed the WHO global response to Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-1) in my role as executive director for communicable diseases, after which I led the WHO polio eradication activities and became assistant director general for health security.

4. From 2009 to 2017 I was non-executive Chair of the UK Health Protection Agency (HPA) and then Public Health England (PHE), and during this period I also led the Centre on Global Health Security at Chatham House (London).

5. As Chair of the HPA I worked closely with the Chief Executive, and led monthly meetings of the non-executive board that included non-executive directors from England and one representative each from the devolved administrations. The board reviewed and commented on strategic directions for health protection in England, and on issues concerning the UK related to chemical and nuclear hazards. At its meetings reports were provided to the board with both background documents and oral presentations by HPA senior technical staff, with follow up discussion including any specific questions raised by the chief executive or the technical staff, and reports and updates were provided on management issues ranging from the review of budgets and spending, remuneration and audits. As chair I did not become involved in day to day implementation activities of HPA but met at least weekly with the chief executive to informally discuss both technical and management issues, occasionally being asked to speak with members of the technical staff, for example when there were difficult issues related to performance. In addition I was tasked by the Chief

Medical Officer with two specific functions: to help shape and unify activities in the HPA that had been developed as a statutory body from over 70 existing organisations dealing with biological, chemical radiological and nuclear hazards; and to help increase the global footprint of the Agency by increasing bilateral and multilateral technical support to lower and middle income countries. The latter was in support of the Health is Global Strategy of the UK, developed after the SARS-CoV-1 outbreak in 2003 when there was clear understanding that the health security of the UK depended on strong capacity to detect and respond to infectious disease outbreaks in all countries (Primarolo, 2008).

6. In addition to routine functions, the board worked closely with the Chief Executive during the response to the H1N1 influenza pandemic, and afterwards advised when specific issues were raised at board meetings on the development of cross government pandemic influenza response exercises, and on other cross government public health issues such as antimicrobial resistance and tuberculosis screening at international airports.

7. During my time as non-executive Chair of the advisory group of PHE the functions of the board were limited to strategic and technical issues, and budget updates and workplans were regularly provided for information only. The strategic plan was regularly reviewed by the board and updated, and in addition to technical issues related to biological, chemical, radiological and nuclear hazards, the board addressed public health issues related to health promotion and non-communicable health problems such as obesity, diabetes and smoking, in addition to those related to biological, chemical and nuclear hazards. Though my functions in PHE did not include implementation, in 2014, at the request of the chief executive, I accompanied the PHE team to the Kingdom of Saudi Arabia to discuss and review the data on a Middle East Respiratory Syndrome Coronavirus (MERS-CoV) coronavirus outbreak, and to offer technical support for outbreak investigation.

8. In 2017, after two four year periods as Chair of HPA and then PHE, I left UK government service.

9. My involvement with HPA and PHE remained at an advisory and strategic level throughout and I was not involved in making any recommendations or decisions on behalf of those organisations.

10. From 2017 until November 2022 I was Chair of the WHO Strategic and Technical Advisory Committee on Infectious Hazards (STAG-IH), and I remain a member of the STAG-IH since then. The STAG-IH is the principal external advisory body to the WHO Emergencies Programme, and it provides recommendations on strategic directions of the Programme. I have also chaired the WHO Polio Eradication Containment Advisory Group (CAG) since 2017, and in 2020-2021 I chaired the UK Research and Innovation / Department for Health and Social Care Covid-19 Rolling Call proposal review panel at the request of the chief medical officer.

11. I have published over 275 peer reviewed articles and book chapters on communicable diseases. I am editor of the Control of Communicable Diseases Manual, and am an elected member of the UK Academy of Medical Sciences and the US National Academy of Medicine. In 2009 I was named an Honorary Commander of the Most Excellent Order of the British Empire for services to global health.

12. This report is based on my own work and understanding, and a list of references that I have used is found in Annex 1. All facts stated in the report are within my own knowledge. I understand my duty to provide independent evidence and have compiled this report with that duty in mind. For transparency, I have set out above the details of my roles as non-executive Chair of the HPA and PHE between 2009 and 2017. I do not believe that my limited involvement with those organisations has hampered my ability to provide impartial expert opinion on the matters contained in my report.

13. Finally, I have knowledge about and commented on the reach across the devolved administrations of HPA and PHE, and of the HAIRS group; and of the PHE reach across government during the period of transfer of HPA to PHE when I was seconded to the DHSC board for a period of approximately 12 months to represent the PHE board concerns that arose, mostly having to do with continuation of activities in DHSC that were involved in the transfer.

A. Coronaviruses (matter 1)

14. A coronavirus is an infectious agent that can only be visualised by using an electron microscope, and images of a coronavirus under an electron microscope can be compared to a ball covered with spikes; within that ball (surrounded by a fatty or lipid membrane) is a piece of genetic material called RNA – ribonucleic acid – its genome. The coronavirus spike binds to the surface of a human cell by attaching to receptors called ACE2, and the virus particle is then drawn through the receptor into the cell where it takes over the cell's reproductive mechanisms to replicate itself. Replicated viruses are then released from the human cell into the human body.

15. Coronaviruses are common in animals, such as bats, cats and camels. There are thought to be hundreds of types, and there were six known coronaviruses that infect and transmit among humans prior to the emergence of SARS-CoV-2, the virus that causes Covid-19. Each of these six coronaviruses is an RNA virus with a distinct genetic sequence (V'kovski et al, 2020).

16. Four of these human coronaviruses (coronavirus 229E, NL63, OC43, and HKU1) are endemic (habitually present) in humans and cause mild upper respiratory infections. These human coronaviruses were first identified and characterised during the mid 1960s (Hamre and Procknow, 1966). All four of them are zoonotic – ie they are thought to have come from a reservoir animal in nature to humans by breaching the species barrier, either directly from the reservoir animal in nature – thought to be a bat or rodent – or indirectly from an animal that had been infected by the natural animal reservoir (Corman et al, 2018). Such breaches in the species barrier occur when there is an alignment of risk factors at the animal-human interface in such a way that emergence occurs. Risk factors vary with each emergence, but all include close direct or indirect contact with infected domestic or wild animals including with their body secretions, blood, and/or waste materials. Emergence is a random event and which risk factors will align, and when and where they align, cannot be predicted with current technologies.

17. The human immune response to these four endemic coronaviruses does not provide longstanding protection against infection – and reinfection with the same virus can occur after a period of time, usually quoted as 12 months, though some reinfections occur within 6 months of the initial infection (Galanti, 2021). Immunity, and natural boosting by repeat infection, is thought to keep disease caused by these viruses mild in most persons, though serious disease can occasionally occur in the elderly, those with immunosuppression or co-morbidities, and in young children. Minor mutations appear to occur at irregular intervals, and they do not appear to alter virus transmissibility or virulence.

18. A molecular clock analysis of one of these four human coronaviruses, coronavirus OC43, was conducted in 2004 to attempt to identify its possible date of emergence (Vijgen, 2005). The genetic sequence of human coronavirus OC43 is similar to that of

a bovine coronavirus (BCoV), and human coronavirus OC43 is thought to have emerged in humans from bovine species because of the genetic sequence similarity.

19. By calculating a rate of mutation of the genetic sequences of human coronavirus OC43 from the 1960s to 2003, and by applying this rate backwards on both the bovine and the human coronavirus genetic sequences, it was suggested that they could have been identical at a time between 1850 and 1890, at the same time a pandemic of influenza was reported to have occurred. Over 1 million deaths are thought to have occurred during that pandemic, but virus specimens are not available to confirm the cause. The authors of the molecular clock analysis hypothesise that because, in addition to deaths, neurological symptoms were reported that are uncommon in influenza, this pandemic was in fact caused by the emergence of human coronavirus OC43 that has now become endemic and less virulent in humans because of the development of population immunity to the virus over time.

20. Three additional human coronaviruses – SARS-CoV-1, MERS-CoV and SARS-CoV-2 – have been identified in humans during the 21st century, and the extensive research that has occurred following their emergence provides much information about these viruses, their possible origins, their epidemiology, and the associated clinical manifestations and outcomes.

21. The Severe Acute Respiratory Syndrome coronavirus (SARS-CoV-1) is thought to have emerged from an animal in a live animal market in the Guangdong Province of China sometime late in 2002. It is thought to have then amplified in transmission among health workers in provincial health facilities who were likely to have been infected by medical procedures that caused pulmonary aerosols, and by other interventions used in the management of infected patients that involved physical contact with an infected patient. Droplet and aerosol transmission then continued to amplify among patients who inadvertently became infected by health workers because of substandard infection prevention and control; among family members with whom they had close contact; and in turn among their close contacts in communities (WHO, 2003).

22. Global spread of SARS-CoV-1 began among persons who had stayed in a Hong Kong hotel on the same floor as a medical doctor who had been treating patients for this as-yet unknown virus in the Guangdong Province of China. He had travelled to Hong Kong in February 2003 and spent one night in the hotel during which it is known that he had high fever and cough, but his movements within the hotel are not known, nor is the means by which others became infected. During the investigation of the outbreak several weeks later, Polymerase Chain Reaction (PCR) fragments of SARS-CoV-1 were identified in scrapings of the hallway carpet in front of his hotel room and in front of the lifts, adding evidence to understanding that he was infected with SARS-CoV-1, and the source of infection of the other hotel guests on the same floor. These persons travelled onwards either within Hong Kong or to Vietnam, Singapore, Canada and Taiwan while still in the incubation period, to become ill at their destination. Their families, health workers and others managing their illness likewise became infected and amplified transmission within health facilities and in

communities. The virus was first identified as a novel coronavirus by genetic sequencing in March 2003, over three months after its emergence, and was given the name SARS-CoV-1 (Peiris, 2003).

23. The majority of transmission of SARS-CoV-1 was face to face by droplets, and transmission usually occurred from patients several days after the onset of signs and symptoms of infection. Though some asymptomatic transmission may have occurred, it was not fully documented as described during the outbreak (Wilder-Smith, 2005).

24. A major factor in the control of SARS-CoV-1 was the location of the virus in the respiratory system – it reproduced deep in the lungs and required deep coughing or pulmonary procedures that created droplets or aerosols to transmit to others, though there was at least one outbreak that was thought to be caused by virus excretion in faecal material that contaminated bathing areas of persons living in the same high rise apartment building in Hong Kong (McKinney, 2006).

25. The percentage of those persons with diagnosed SARS infection who died (the case fatality rate) is generally considered to have been close to 10%. By contrast, the case fatality rates for MERS-CoV and SARS-CoV-2 are estimated to be approximately 35% and 0.5-1% respectively (Parashar, 2004; Kim, 2017; Salzberger, 2021).

26. The case fatality rate estimates for SARS and MERS coronavirus infections are likely to be higher than the actual case fatality rates because of under-reporting of total numbers of cases, as the case fatality rate is defined as the number of reported deaths divided by the total number of reported cases. It is known that in most outbreaks of infectious disease, case reporting is not as accurate as mortality reporting, and that under-reporting occurs. Under-reporting of infections is even more likely if some of the infections are asymptomatic as may be the case for both SARS-CoV-1 and MERS-CoV, though definitive information on asymptomatic infection is not fully understood (Wilder-Smith, 2005; Grant, 2019). The case fatality rate for SARS-CoV-2 has been estimated by epidemiological modelling based on a large database of reported infections, and it is possibly more accurate.

27. Some of those who survived SARS and MERS coronavirus outbreaks have been found to have chronic pulmonary disease caused by fibrosis that began as the body developed immunity to the virus in the acute phase, and the same outcomes are occurring in patients with SARS-CoV-2 infection.

28. The SARS-CoV-1 outbreak was fully contained by July 2003 after infection had spread to 28 countries from China. A total of 8,098 persons were reported as infected and 774 (10%) as dead, and it is estimated that 20% of all SARS infections occurred in health workers, most of whom were in good health.

29. SARS-CoV-1 was transmitted primarily, but not exclusively, in health care and hospital settings from patients five or more days after the onset of disease, and from patients who were severely ill. The majority of persons infected were adults between 25-70 years of age. Infections resulting from casual or social contact were

uncommon, but transmission occurred occasionally after close contact with a patient with SARS in the workplace, on an aeroplane, or in a taxi. Investigations did not identify groups at greatest risk of serious outcomes after infection (such as persons with co-morbidities or the elderly), but because persons other than health workers who were infected in hospitals were hospitalised patients, serious outcomes of infection could be assumed to have occurred in some of those with co-morbidities and/or elderly. A few suspected infections occurred, but were not verified by laboratory testing, in persons under the age of 15 years (Peiris, 2003).

30. Factors leading to the containment of the SARS-CoV-1 outbreaks included strengthening of infection control measures in health facilities including the wearing by health workers of personal protective equipment (PPE – clothing, helmets, gloves, face shields, goggles, facemasks and/or particle respirators or other equipment designed to protect the wearer from infection); isolation of patients and their contacts; and a global coordinated effort to voluntarily follow WHO recommendations to curb travel to sites where uncontrolled outbreaks were being identified.

31. Without explanation, China refused to share any information about its domestic outbreak with the World Health Organisation until after having been confronted in public by the director general of WHO in early April 2003, approximately five months after the outbreak is thought to have begun and during which period WHO had made repeated attempts to freely obtain this information. This resulted in a rapid political response with apology to WHO by the highest level of the Chinese government, and rapid containment of the ongoing outbreak in China.

32. There are no vaccines to prevent SARS-CoV-1 and there are no proven antiviral drugs. Vaccines were not required to stop this outbreak as by using the measures outlined above, the outbreak was fully contained within a period of just over six months. Research that was being conducted to develop vaccines and antiviral drugs was stopped in most instances after the outbreak had been contained when it was understood that SARS-CoV-1 had not become endemic in humans and funding for research in both the public and private sector was diverted to other priorities.

33. SARS-CoV-1 is thought to have resulted from a one-time mutation as the virus reproduced either in the animal host before transmission to humans, or in humans after emergence had occurred. From research conducted during and immediately after the SARS-CoV-1 outbreak, it was shown that workers in live animal markets had a higher prevalence of antibody to SARS-CoV-1 or closely related coronaviruses (13%) than the population served by the market (3%) (Yu, 2003). Antibody in the blood is evidence of previous infection, and it was shown that certain wild animal farms had animals with high levels of a similar antibody (Tu, 2004), and in 2005 a closely-related virus was isolated from civet cats and horseshoe bats. Civet cats, thought to have been infected by horseshoe bats, are thus considered the source of human emergence of SARS-CoV-1 in 2002 (Wang, 2007).

34. The immediate response of the Chinese government after the SARS-CoV-1 outbreak was to order a closing down of wildlife markets and farms, even though wildlife

farming had become a major source of income in many rural areas. These restrictions were not effectively enforced, and wildlife farming and sales have continued in many rural and urban areas (Li, 2020).

35. SARS-CoV-1 did not become endemic in humans because containment, which did not stop virus reproduction in humans, stopped its transmission from person to person. Being unable to transmit to, and thus reproduce in additional humans, the virus disappeared from human populations once the immune system of those persons infected either cleared infection or they died. Serial genetic sequencing showed that SARS-CoV-1 mutated slightly during the short period it was present in humans. The last human infections of SARS-CoV-1 did not occur in nature, but from laboratory accidents in Singapore and Taiwan (2003) and China (2004) (Demaneuf, 2020).

36. MERS-CoV was first identified in the Kingdom of Saudi Arabia in June 2012 in a specimen from a patient who had a pulmonary infection thought by a clinician to be SARS-CoV-1 after having ruled out other known causes of infection. The virus was genetically sequenced and shown to be a novel or newly identified coronavirus in a human: MERS-CoV.

37. Humans become infected from camels that carry MERS-CoV asymptomatically in their nasal passages. Camels are thought to be infected by bats, and may also transmit the virus to other camels in close proximity; and close direct or indirect contact with camels is the risk factor for emergence in humans. The virus remains endemic in camels with periodic infection of humans from camels.

38. MERS-CoV does not transmit easily from person to person except by close human to human contact: to close family contacts who are in contact with body secretions from infected persons; and/or health workers who care for persons with MERS-CoV infection and inadvertently infect other patients because of breaches in infection control such as failure to wash hands and properly clean equipment between patients. MERS-CoV causes outbreaks in health facilities where there is sub-standard infection prevention and control (IPC) and where patients with co-morbidities or immunosuppression are at risk of infection from a person infected with MERS-CoV hospitalised on the same ward, or from a health worker who does not practise effective IPC.

39. Over 2,500 cases of MERS-CoV with 888 associated deaths have been reported since MERS-CoV was first identified, and the majority of cases reported have been from countries in the Middle East. MERS-CoV has spread internationally in travellers, and is known to have entered the UK in infected persons three times, twice in 2012 and once in 2018. As there was not onward transmission to health workers or other patients, it is clear that the routine hospital IPC procedures in place in UK healthcare facilities, and immediate isolation of patients, contributed to the prevention of nosocomial transmission.

40. In May 2015 a major outbreak of MERS-CoV occurred in healthcare facilities in the Republic of Korea when a MERS-CoV infected person returned home from the Middle East. He became ill and was seen at various health facilities with sub-standard infection control practices that amplified transmission. A total of 185 cases and 38 (20%) deaths occurred in the Republic of Korea from mid-May to mid-July 2015 as a result of this importation of MERS-CoV. Those at greatest risk of infection in this hospital-based outbreak were patients with an average age of 55 years, with co-morbidities such as chronic lung disease, high blood pressure, heart disease and diabetes (Kim, 2017).

41. The cause of the outbreak and its spread was a series of factors including weak hospital infection control and patient isolation procedures that led to infection of other patients and family members or friends during hospital visits; a nursing shortage that led to patient hospital-shopping behaviour and dependence on private, less well trained caregivers; and extremely crowded emergency departments without isolation beds. The outbreak was rapidly contained by a change in policies that led to isolation of patients and all close contacts, improved hospital infection control and ventilation, and strengthened national crisis management communication (Kim, 2015).

42. MERS-CoV has not become endemic in humans, but it is endemic in camels and continues to periodically emerge in humans who have close contact with asymptomatically-infected camels.

43. Variants of MERS-CoV have been found in camels on the African continent and no human infections have been clearly documented, though studies of antibodies to MERS-CoV among camel owners in East Africa have suggested that some persons became infected with no symptoms having been reported (Zhou, 2021).

44. During the SARS-CoV-1 and MERS-CoV outbreaks there were superspreading events when multiple contacts of persons at various stages of infection became infected to a larger extent than would be anticipated, or when there were failures in healthcare infection prevention and control.

45. The outbreak in South Korean health facilities was a superspreading event caused by failed infection prevention and control when health workers and their patients became infected by medical procedures that caused the spread of infection by droplet and aerosol. Superspreading events of SARS-CoV-1 were caused by direct face to face droplet transfer and/or transfer of droplets to health workers and other patients by aerosolization during medical procedures, and then spread from some of these infected persons to others, usually in hospital settings but sometimes in communities. The contribution of various superspreading events to the epidemic spread of SARS-CoV-1 has not been fully quantified (Al-Tawfiq, 2020).

46. It is hypothesised that multiple factors may be at the base of superspreading events ranging from immune suppression and/or increased disease severity – both with high viral loads – to extensive social interactions and/or delayed diagnosis in infected hospitalised patients (Al-Tawfiq, 2020; Shen, 2004).

47. A thesis by a postgraduate medical student in 2012 described a novel coronavirus isolated from bats in the Yunnan Province of China in 2021 after an outbreak of severe respiratory disease in six people who had been cleaning the shafts of a copper mine. The thesis states that blood specimens from these patients were negative by PCR for known respiratory viruses including SARS-CoV-1.

48. There were no further cases reported in this outbreak, and studies of bats and rodents in and around the mine shaft identified several coronaviruses and variants from specimens that were then taken to the BSL4[1] laboratory at the Wuhan Institute of Virology where coronavirus strains were identified by genetic sequencing, including one that is closely related to the SARS-CoV-2 virus that was first detected in humans in late 2019.

49. Other coronaviruses have been identified by research in other parts of the world in bats and other animals including pigs, dogs, cats, rodents, cows, horses, camels, Beluga whales, and birds. Some of these viruses have been closely related to SARS-CoV-2, but whether or not they would behave the same as SARS-CoV-2 in human populations, including their ability to mutate as they replicate in humans, cannot be predicted (Alluwaimi, 2020).

[1] Biosafety level 4, the highest level of biosafety precaution

B. SARS-CoV-2 – discovery and epidemiology (matters 4 to 7)

50. There is controversy over the actual origin of the Covid-19 pandemic, caused by SARS-CoV-2. There are two major hypotheses of the origin. One hypothesis postulates that SARS-CoV-2 had its source in wild animals that were being farmed near Wuhan, the capital city of Hubei Province. It is further postulated that the virus either infected humans who transported animals to a market in Wuhan, and/or that it infected market workers and/or persons who purchased wild animals from the market. This hypothesis is based on early cases of Covid-19 which seem to have clustered in Wuhan near the Huanan Seafood Market that, in addition to selling seafood, sold many different varieties of small farmed wild animals.

51. The second hypothesis is that specimens of coronavirus collected at a long-term study site that had been established in Yunnan could have infected humans either during their transport to the Wuhan Institute of Virology BSL4 laboratory for study during the years following the Yunnan outbreak, or that there was a laboratory incident where a laboratory worker was infected with one of these coronaviruses that then mutated into SARS-CoV-2. A variation of this hypothesis is that a coronavirus closely related to SARS-CoV-2 was being manipulated in gain of function research at the laboratory and that it accidentally infected a human. Gain of function research modifies the genetic composition of a virus in order to study its effect on transmission, virulence and other characteristics in laboratory animal models. The hypothesis further suggests that the virus then escaped from the laboratory in an infected human or by another means because of multiple failures in the biosecurity system, or that it was intentionally carried out of the laboratory for some purpose.

52. Both of the hypotheses are considered feasible by many scientists but neither has been proven. As described previously, the uncontested hypothesis of the origin of SARS-CoV-1 epidemic in 2002 was that it was the result of a breach in the species barrier at a live wild animal market; and the last human infections with SARS-CoV-1 in 2003 and 2004 were caused by laboratory accidents.

53. There may never be full understanding of the origins of the Covid-19 pandemic, but the two hypotheses point to the need for decreasing the risk of breaches in the species barrier at live animal markets and in wildlife farming; the need for development and adherence to global standards on safe gain of function research; and the need for stronger biosafety at BSL3 and BSL4 laboratories.

54. There is likewise controversy in the medical literature about when the first human infection with SARS-CoV-2 occurred. Retrospective analysis of genetic sequences of SARS-CoV-2 by virologists and other scientific experts during 2020 suggested that dates of emergence could range anywhere from mid-October 2019, hypothesised by a group of American evolutionary biologists who have done a molecular clock analysis on the first known genetic sequence; to 12 December 2019, as reported

retrospectively by a research group at the Laboratory of Special Pathogens of the Wuhan Institute of Virology in connection with the investigation of a patient from Wuhan with severe respiratory disease who was not in any way linked to the laboratory.

55. It is understood from reports of the World Health Organisation (WHO) that on 31 December 2019 the Wuhan Municipal Health Commission reported a cluster of cases of pneumonia in Wuhan, China; and that on 1 January 2020 WHO, having had this report, set up an incident management support team across the national, regional and global level of the organisation for an outbreak of respiratory infection as a precautionary measure.

56. On 4 January 2020 WHO reported on social media that there was a cluster of pneumonia cases with no deaths in Wuhan, and on 5 January 2020 WHO reported this information in its outbreak news that is widely distributed including through the WHO Event Information System of the International Health Regulations.

57. On 10 January 2020, WHO issued a comprehensive package of technical guidance online on how to detect, test and manage potential cases of respiratory infection based on what it knew at that time, and published it online/distributed it widely within the organisation at its three levels (global, regional and national). This package of technical guidance was based on experience with previous outbreaks of SARS and MERS and known modes of transmission of respiratory viruses. It included infection and prevention control measures to protect health workers caring for patients (droplet and contact precautions), and airborne precautions for aerosol generating procedures conducted by health workers.

58. WHO next reported that on 12 January 2020 China had publicly shared the genetic sequence of a novel coronavirus now known as SARS-CoV-2. There is however still debate as to where and how this genetic sequence information was shared and whether in fact it was shared first on 11 January 2020 by a virologist in Australia who had received the information from a collaborating scientist at a Chinese university (Enserink, 2023).

59. On 14 January 2020 WHO reported in a press briefing there may have been limited human-to-human transmission of the coronavirus among 41 cases that had been confirmed by then, mainly through family members (WHO, 2020a; Wang, 2020).

60. By 24 January 2020 there was a peer reviewed published report in *The Lancet* about the 41 patients infected with this newly identified virus (called at that time 2019 novel coronavirus or 2019-nCoV); and all had a history of exposure to the Huanan Seafood Market in Wuhan (Huang, 2020). *The Lancet* report described disease that included fever in 40 (98%) of the 41 patients, cough in 31 (76%), and myalgia or fatigue in 18 (44%). All 41 patients had pneumonia, 13 (32%) were admitted to the intensive care unit, and six (15%) died with decreased blood oxygen saturation leading to pulmonary failure. Five days later, on 29 January the *New England Journal of Medicine* published the virus' genomic sequence (Zhu, 2020).

61. In addition to reviewing these publications, WHO consulted widely with several different advisory bodies beginning on 5 January 2020. On 30 January, after more information had been obtained about person to person transmission as requested at the first meeting of the Emergency Committee of the International Health Regulations on 23 January 2020, and after the director general had travelled to China, he accepted the recommendation of the Emergency Committee and declared the outbreak to be a public health emergency of international concern (PHEIC). The temporary recommendations that were made by the experts on the Emergency Committee to WHO, after having reviewed all available information at this time, included a statement that the Committee did not recommend any travel or trade restrictions, and referred to guidance on infection prevention and control in healthcare settings and protection of health workers (WHO, 2020b).

62. At a following meeting of the Emergency Committee on 30 April 2020 the Committee recommended that essential travel needed for pandemic response, humanitarian relief, repatriation, and cargo operations be enabled, and that WHO update its recommendations on appropriate travel measures and analyse their effects on international transmission of Covid-19, with a consideration of the balance between benefits and unintended consequences, including entry and exit screening, education of travellers on responsible travel behaviour, case finding, contact tracing, isolation and quarantine (WHO, 2020c).

63. On 31 July 2020, the Emergency Committee made additional recommendations on travel requesting WHO to work with partners to revise the WHO travel guidance in order to reinforce evidence-informed measures that would avoid unnecessary interference with international travel. The Emergency Committee also recommended that WHO Member States proactively and regularly share information with WHO on appropriate and proportionate travel measures and advice, based on risk assessments; to implement necessary measures, including at points of entry, in order to mitigate the potential risks of international transmission of Covid-19; and to facilitate international contact tracing (WHO, 2020d).

64. Many countries in Asia (e.g. Singapore, Japan, Republic of Korea, Singapore, Taiwan, and Hong Kong (China)) had strengthened preparedness after the SARS outbreaks in 2003. Preparedness activities in these countries included cross government pandemic containment simulation exercises; teaching and practising outbreak containment skills with health workers through the implementation of formal training and hospital surge capacity exercises; strengthening infection control measures at health facilities including construction of state of the art patient isolation facilities at hospitals; and strengthening disease detection networks.

65. These countries all had success in slowing the initial domestic spread of SARS-CoV-2, and although their approaches were not identical, rapid investigation of initial outbreaks to identify the source of infection and prevent further spread; identification and isolation of infected individuals with timely isolation of their close contacts; rigorous infection prevention and control in clinical settings with personal

protective equipment for health workers; and simple measures such as hand washing were key components of their response strategy.

66. On 3 February 2020 the Japanese Government reported 10 persons with severe respiratory disease on a cruise ship that had recently taken on passengers in Hong Kong, and by 20 February public health measures such as removal and isolation of ill passengers and isolation of non-ill passengers were being implemented (Rocklöv, 2020). On this same date, a total of 619 of 3,700 passengers were reported with disease demonstrating widespread transmission on the ship.

67. On 11 February 2020, the Coronavirus Study Group (CSG), a specialised group of experts in coronavirus of the International Committee on Taxonomy of Viruses, published the name of the virus as SARS-CoV-2, replacing the provisional designation of 2019-nCoV; and on this same date the director general of WHO announced the name of the disease caused by the virus as Covid-19.

68. By 21 February 2020 it was reported that the virus had spread rapidly within China despite containment measures, and also to 28 other countries, including countries in Europe, with 47 confirmed cases, including 9 from the United Kingdom, where one death had occurred among the 47 (Spiteri, 2020).

69. Since early in the pandemic, researchers around the world have continued to contribute to understanding of the epidemiology of Covid-19 in peer reviewed medical journals, many having first provided their manuscripts to pre-publication websites. Most journals and websites provided free access to publications related to the pandemic, and by 21 December 2022 the Dimensions Database had recorded 1,501,551 peer reviewed publications since the beginning of the pandemic.

70. As with all newly identified respiratory infections there was a great effort to understand its epidemiology – initially by infectious disease modellers and epidemiologists in countries where outbreaks had been detected. Much of the initial understanding was modified as more information became available from peer reviewed epidemiological research. Infectious disease modellers made projections of numbers of persons infected and attempted to suggest when the pandemic might end using parameters that were related to previous experience with respiratory infections including influenza. Data sharing by countries, including genetic sequence information, varied throughout the pandemic with some countries such as the UK freely sharing data nationally and internationally through WHO in a timely manner while others failed to share data, or shared it after variable periods of delay.

71. Researchers addressed major questions about transmission of SARS-CoV-2 during the first months of the pandemic. As this was a new virus in an immunologically naive population, it was not possible early on to calculate an evidence-based secondary attack rate and reproductive number. It was known, however, that the virus spread easily from human to human, especially in indoor and other closed spaces such as the Diamond Princess cruise ship, in what appeared to be superspreading events (Rocklöv, 2020). As a result the question was raised as to whether it was spread by

aerosol particles, or whether infection was transmitted from human to human only by droplets as had occurred in some SARS infections, and as appears to be the predominant means of transmission in MERS; and whether fomites (objects or materials that are contaminated with droplets containing infectious virus) played a role in transmission.

72. Both droplets and aerosol particles contain virus surrounded by moisture – mucus, saliva and/or water. They are produced in the lungs, mouth and nasal cavity, and the virus remains viable as long as the droplets and particles remain moist. Droplets are larger and heavier than aerosol particles, and to infect they must land either directly on a mucus membrane from the infected person, usually from a cough or sneeze; or indirectly from a body part that comes in contact with a mucus membrane such as a hand that has been in contact with a fomite. Aerosol particles however are smaller and lighter than droplets and can travel on air currents farther than droplets before they land on a mucus membrane.

73. It was known for other respiratory infections such as influenza that transmission could occur from an infected person to another when droplets and aerosol particles spread from a cough or sneeze, and also by voice projection such as singing and speaking loudly. And it was understood that the viral load (the number of virus particles) in the nasal passage of infected persons determined the infectivity (ability to infect) of droplets and aerosols.

74. Viral loads in the respiratory passages depend on the titre of the infecting virus in the infected person. They also depend on the immunity in the respiratory passages provided by an antibody that is produced by cells in the respiratory passages (secretory antibody). It is generally understood that the lower the virus titre and the higher the secretory antibody level in the nasal passage, the lower is the infectivity.

75. In the transmission of SARS-CoV-2, as for other respiratory infections, it was assumed that the viral load in the upper respiratory passages of the nose determines infectivity; the greater the viral load, the more virus that can be encapsulated in a droplet or aerosol particle and the greater the transmissibility.

76. Early studies in China had suggested that the SARS-CoV-2 could be transmitted by aerosols as well as by droplets. In one study in January 2020, two buses with religious pilgrims travelled 50 minutes to a common temple site. On one bus a passenger was identified as SARS-CoV-2 PCR positive and presumed to have been infected when travelling on the bus. During a two week period after the event 24 of the 68 passengers on that bus had a positive PCR for SARS-CoV-2 compared to the total of 60 passengers on the other bus who were all PCR negative. The conclusion was that aerosolised transmission was a possibility and this was published in a peer-reviewed medical journal several months after it had been widely reported in the media (Shen, 2020).

77. In another Chinese study in January and February 2020 a total of 10 of 83 customers in a restaurant who were sitting either at table with a person later diagnosed with

SARS-CoV-2 infection, or at adjacent tables, became PCR positive within two weeks of possible exposure, and conclusions were that transmission occurred by aerosolised particles that were circulated by an air conditioning system (Lu, 2020). This information was likewise widely reported in the media prior to peer review and publication.

78. A study in March 2020 in the US found that 53% of 61 persons of a group of singers who had practised together in a closed space had become PCR positive for SARS-CoV-2. The authors concluded that infection was presumably from a member who had symptoms of a cold and was later found to have a positive PCR, and that transmission was likely facilitated by close proximity during practice, augmented by the act of singing (Hamner, 2020).

79. In March 2020 these findings were published online in the US CDC Morbidity and Mortality Weekly Report (MMWR), and recommendations were published including physical distancing of at least 6 feet between persons, avoiding group gatherings and crowded places, and wearing cloth face coverings in public settings where other social distancing measures were difficult to maintain.

80. Respiratory viruses (eg influenza, measles, and respiratory syncytial virus) can infect by droplet and/or aerosol through mucus membranes such as those in the mouth, the nasal passage and the eyes, These initial studies in China and the US provided evidence for both droplet and aerosol transmission, and it was considered urgent to collect more evidence and provide clear definitions of droplet and aerosolization for SARS-CoV-2 as this had a direct bearing on which control measures – including physical distancing, masks, eye protection, and particulate respirators – should be used (Morawska, 2020; Prather, 2020; Greenhalgh, 2021).

81. Medical masks that cover the mouth and nose alone are not fully protective against infection from droplets or aerosols; in order to fully prevent infection particulate respirators (air purifying masks) covering the nose and mouth; and shielding to protect the eyes along with rigorous handwashing have been proven to prevent infection of health workers.

82. Early in the Covid-19 pandemic countries in Asia generally recommended mask wearing to the general public as a precautionary means of preventing transmission from infected persons to others. Mask wearing at the time of a respiratory infection is a long-standing measure of courtesy of persons who have an upper respiratory infection in some Asian countries, and the recommendation was generally accepted. Mask wearing by the general public was one of various measures of control such as handwashing, and was considered a part of public health containment measures.

83. On 29 January 2020 WHO recommended that wearing a medical mask alone during home care and in health care settings in the community offered adequate protection against spread of respiratory infection (transmission from one person to another) if combined with hand hygiene and other infection prevention and control measures such as isolation of persons who were sick. WHO further stated on this date that

wearing medical masks when not indicated could create a false sense of security, and indicated that a medical mask is not required for individuals without respiratory symptoms in a community setting as there was no evidence available on its usefulness to protect non-sick persons (WHO, 2020e). This recommendation and other early guidance by WHO reflect WHO's hesitation to make recommendations when evidence that will justify such recommendations (in this instance evidence of asymptomatic transmission) is not yet available.

84. In the same document WHO identified certain instances when a medical mask should be worn including by persons with respiratory symptoms and by care givers in rooms with persons with respiratory symptoms. If caregivers performed an aerosol generating procedure it was further recommended to use a particulate respirator at least as protective as a US National Institute for Occupational Safety and Health (NIOSH)-certified N95, European Union (EU) standard FFP2, or equivalent. A peer reviewed review article in 2013 supports the WHO recommendations, citing that FFP2 and N95 are approximately equivalent in protecting against airborne infections, and that countries such as the US find N95 respirators acceptable, but that FFP3 is required by the Health and Safety Executive in the UK (Coia, 2013).

85. Medical mask wearing by the general public to prevent others from becoming infected became controversial in some other parts of the world where either public health or political leaders called into question the effectiveness of masks. Many times they cited a lack of definitive scientific evidence about their value in preventing transmission of respiratory infections from an infected person, whereas other peer reviewed sources provided evidence that they did decrease spread (Greenhalgh, 2020; Li 2021).

86. On 1 December 2020 WHO recommended the wearing of non-medical masks by the general public in communities where transmission was known to be occurring in order to prevent community transmission, and maintained its original guidance of medical mask and particulate respirators for patients and healthcare workers to prevent hospital transmission (WHO, 2020f).

87. By December 2022 WHO had unreservedly recommended mask wearing for the general public wherever there was a need to decrease community spread, as by that time more evidence had become available.

88. Though there is still debate about the effectiveness of mask wearing as a means of decreasing community transmission, it became generally accepted in most countries where it was required or recommended in many different public settings. And the current WHO recommendation, that a particulate respirator should be worn by health workers along with other personal protective equipment (PPE) before entering a room with an infected person, is supported by a solid evidence base (WHO, 2022; Coia, 2013).

89. PPE was sought after and used by health workers and others at risk of infection with Covid-19 in most countries as a means of preventing direct exposure to persons with

infection. Countries varied as to what they recommended as PPE, and this often changed over time depending on what medical masks and particulate respirators were available in national stockpiles, and what could be procured on the national and international market. I understand that the issue of face coverings will be examined in the Inquiry's second module.

90. A major question early in the pandemic was whether there was transmission of SARS-CoV-2 from persons who were asymptomatic. This had been a question in both SARS-CoV-1 and MERS-CoV investigations, but as described previously, no conclusions can be drawn from the data that has been collected to date. It is very difficult, if not impossible, to study asymptomatic transmission – especially at the start of a pandemic, at a time when diagnostic testing has yet not been perfected and become widely available, because such a study would require screening and identification of persons who are infected and not symptomatic (eg contacts of persons with known infection), and then determine whether they have transmitted infection to others during the period before they developed early symptoms.

91. Studies to date of seasonal and novel influenza virus transmission provide scant evidence for transmission prior to onset of symptoms (Patrozou, 2009). It is known, however, after years of study that in other respiratory infections such as measles, transmission of virus to others can occur during a period beginning four days before onset of fever and/or rash. Measles is a highly transmissible infection with a reproductive number (R_0) of 12-18 in a population with no previous immunity, R_0 being a reflection of transmissibility for the combination of symptomatic and asymptomatic infections.

92. It is generally believed that the R_0 of seasonal and novel influenza viruses is approximately 1.4, and estimates of the R_0 for SARS-CoV-2 in a non-immune population were between 2.43 to 3.10 during an early Italian outbreak. As with this outbreak and others, there was concern that asymptomatic transmission, in addition to transmission from clinically ill persons, was responsible for much of the SARS-CoV-2 transmission. The current understanding is that the present R_0 of SARS-CoV-2 is approximately 1.0 in the UK where there is a highly immune population.

93. Some of the initial studies that shed light on asymptomatic transmission were in Asia. Research in Singapore for example demonstrated that among 243 cases of Covid-19 reported during the period 23 January to 16 March there were seven clusters of cases in which transmission from asymptomatic persons was the most likely explanation for the occurrence of secondary cases (Wei, 2020). Asymptomatic infection was thus generally accepted as occurring and this study, alongside other publications at the same time (Hu, 2020; Wang, 2020), added more evidence of the need to attempt to prevent transmission by universal mask wearing as a precautionary measure. There is still not a complete understanding about the number of days before onset of signs and symptoms that SARS-CoV-2 can be transmitted from an infected person, and studies are continuing to attempt to provide the evidence necessary for this estimate.

94. There was also concern about indirect transmission of SARS-CoV-2 by fomites – droplet-contaminated exposed surfaces in the home or in public spaces. It was known from influenza and other respiratory infections that fomites could transmit infection if hands of a non-infected person came in contact with a fomite and then touched a mucus membrane such as the eyes, nose or mouth. For measles, it was also understood that virus in droplets and aerosol particles could remain viable on exposed surfaces for up to two hours after an infected person leaves an area, adding to the concern that fomites containing SARS-CoV-2 could create a transmission risk.

95. Early in the pandemic there were studies to determine how long SARS-CoV-2 could survive in a laboratory on a variety of surfaces. The studies suggested that on porous surfaces viable virus was inactivated within minutes to hours, but on non-porous surfaces viable virus could be detected for days to weeks. It was hypothesised that the relatively more rapid inactivation of SARS-CoV-2 on porous compared with non-porous surfaces might be attributable to capillary action within pores that dries and evaporates the moist encapsulation of the fomites.

96. Precautionary measures for the general public including increased hand washing and washing of exposed surfaces were thus recommended by most countries, including the UK, because handwashing by the general public had previously been identified as a means of decreasing transmission of other respiratory viruses (Rabie, 2006).

97. There was speculation that a characteristic of the SARS-CoV-2 virus was that transmission would increase in the winter months as does the influenza virus, despite the fact that high SARS-CoV-2 transmission rates were observed in tropical countries where there was little or no seasonality. These observations suggested that in immunologically naive populations high rates of SARS-CoV-2 transmission could occur in all seasons, and it is hypothesised that in all likelihood SARS-CoV-2 would settle into a seasonal pattern of transmission once population immunity (measured as the number of persons with antibody) had increased.

98. The mean incubation period for SARS-CoV-2 (time from initial infection to onset of signs and symptoms) is 2-14 days as compared to the influenza virus that has an incubation period of 1-4 days. The longer incubation period for SARS-CoV-2 when compared to the incubation period of influenza likely resulted in a slower increase in cases of SARS-CoV-2 at the start of the pandemic, and this is likely one of the reasons that countries in Asia – when the number of cases was small – had success in containing early outbreaks of SARS-CoV-2. As has been demonstrated for influenza, outbreaks cannot be successfully contained at the start of a pandemic. The incubation period of SARS-CoV-2 differs slightly with each variant (Wu, 2022). Vaccination that protects against serious illness and death, and dexamethasone, hydrocortisone, antivirals, and monoclonal antibody preparations have greatly modified infection outcomes.

99. It is currently estimated that up to 33% of those infected in highly vaccinated populations do not develop recognisable signs and symptoms of infection after

vaccination or on reinfection. Except for those with co-morbidities, including obesity, the rest have a broad range of mild to severe signs and symptoms that can include a new and continuous cough, anosmia (loss of smell), ageusia (loss of taste), and a range of non-specific signs and symptoms including shortness of breath, fatigue, loss of appetite, myalgia (muscle ache), sore throat, headache, nasal congestion (stuffy nose), runny nose, diarrhoea, nausea and vomiting.

100. Decreased blood oxygen saturation is a hallmark of serious illness after infection with SARS-CoV-2, and complications include respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism, and/or multi-organ failure, including acute kidney injury and cardiac injury.

101. Infections in the elderly, and in others from deprived areas, and/or from certain non-white ethnic backgrounds have caused more serious illness and death. Underlying health conditions such as diabetes and chronic renal disease, as well as obesity likewise increase the risk of severe disease and death in adults.

102. Care in homes for the elderly was a major risk for infection early in the pandemic, and many times patients in care homes had co-morbidities that are associated with severe illness and death after infection. This is reflected in the reported Covid-19 mortality in the UK when during the first year of the pandemic – to 1 January 2021 – high levels of mortality were known to occur in those persons over the age of 70 years.

103. The severity of illness also differs with each variant and there has been decreased hospitalisation and death with the more recent Delta (the B.1.617.2 variant, first detected in India in October 2020) and Omicron variant (the BA.2 variant, first detected in S Africa in November 2021) when compared with outcomes of infection with the Alpha (the B.1.1.7 variant, first detected in SE England in September 2020) and earlier variants. Increasing levels of vaccination and population immunity are likely contributing to some of these differences in severity of illness.

104. Infants and children generally have mild symptoms after infection, and appear to experience milder symptoms and fewer deaths than adults, except when there are severe co-morbidities such as obesity and chronic respiratory disease including Tuberculosis (Tsankov, 2021; Kapoor, 2021). Rare generalised inflammation has been associated with SARS-CoV-2 infection and continues to be monitored to gain better understanding.

105. Post-Covid Symptoms (long Covid) occur more often in persons who have had severe Covid-19, but anyone who has been infected is at risk of post-Covid conditions. They can include fever, chills, cough, shortness of breath, fatigue, muscle aches, headache, loss of taste or smell, sore throat, nasal congestion or nasal drip, vomiting or diarrhoea, and skin rashes. Post-Covid conditions can last weeks, months, or in some persons for a year or longer. Persons vaccinated against Covid-19 appear to have a lower risk of developing post-Covid conditions compared to persons who are not vaccinated, and continued study is underway.

106. During 2020 many epidemiological modellers attempted to determine the herd immunity threshold. The herd immunity threshold is the percentage of the population that is protected against infection, and is the point at which transmission of the virus cannot be sustained, ie the R_0 is reduced to 1 or less. Some epidemiological modellers suggested that once approximately 75% to 80% of the population had been infected, herd immunity would have developed and transmission could be expected to stop (Kwok, 2020).

107. Modelling was many times based on an understanding of influenza because most modellers had experience in modelling influenza and understood the contact patterns that lead to its transmission; and on the assumption that infection would provide protection against reinfection even though it was known that infection with the endemic coronaviruses that regularly circulate in humans did not provide protection against future infection.

108. This led to debates (before vaccines became available) about letting the virus infect populations in an effort to attain the herd immunity threshold while shielding the elderly and those with co-morbidities, but fortunately these debates could be stopped when vaccines became available.

109. As the pandemic continued, it became clear that vaccines did not fully protect against infection, and that reinfection occurred in persons who had previously been infected with SARS-CoV-2. It therefore became clear that acquired immunity would not be sufficient to lead the population to herd immunity, and that stopping transmission of SARS-CoV-2 by reaching herd immunity could not be attained using current vaccines, or by populations becoming immune through natural infection.

110. As population immunity increases from natural infection and/or vaccination, changes in epidemiology occur for respiratory viruses. The full extent of change cannot be predicted, but hypotheses are that as population immunity increases for SARS-CoV-2, it too will settle into a more regular pattern of transmission that increases during the winter months, and that elderly populations and those with co-morbidities will have the most serious outcomes from infection.

111. Any other differences in epidemiology between SARS-CoV-2 and other respiratory viruses will be better understood as the virus continues its route to endemicity (the point at which the virus persists in the population indefinitely, with a R_0 hovering around or below 1). At present it is not possible to predict the precise epidemiology of SARS-CoV-2: observation is ongoing and evidence is being gathered at many research sites around the world.

112. There is debate about whether the level of antibody titre can be used as a true correlate (measure) of protection and an indication of who is most likely to be protected against serious illness; and there is a continued question as to whether variants in the future will escape vaccine protection against serious illness. If in the future there is a vaccine that protects against infection, it would become a public

health tool that could be used to attain herd immunity and stop transmission in geographic areas with high coverage.

113. Early in the Covid-19 pandemic, studies in Japan traced contacts of persons with Covid-19 forward for isolation and monitoring, and backward to the source of infection. They then shut down those areas where transmission was shown to be occurring, many times in nightclubs, gyms and other public spaces, until preventive measures could be reinforced at those sites.

114. Such precision and short term lock-downs demonstrated that unlike influenza, initial Covid-19 outbreaks could be contained and transmission interrupted. The same was true in Singapore and South Korea in early outbreaks that occurred in religious institutions and nightclubs. Many Asian countries continued to keep transmission at low levels before vaccines became available by outbreak investigation and precision lock-downs at the source, similar to those used in Japan. As of 19 February 2023 Asian countries had reported fewer Covid-19 deaths per million in the population (Japan 566, South Korea 680, Singapore 294; compared to Italy 3,150, USA 3,344, and the UK 3,038) attesting to the effectiveness of their containment strategies, though other factors including the level of co-morbidities and obesity may have also played a role.

115. The strategy of outbreak investigation and precision lockdown was in part possible because of the early response to importations, including travel restrictions and testing of incoming travellers. In areas of the world where early response was not attempted or was ineffective, surges of transmission occurred at many different sites. Other measures such as complete lockdown were then applied in order to attempt to protect healthcare facilities from being overwhelmed by the surge of patients that was foreseen, and to decrease transmission of infection in the community and save lives.

116. There was controversy over border closures during the pandemic, and about testing before travel. Confusion resulted, for example, about the purpose of testing before travel. It was clear that a person who tested positive immediately before travel increased the risk of transmission on the plane or other carrier, and that that person should not travel in order to prevent infection of fellow passengers.

117. At the same time, however, a person who tested negative before travel was permitted to travel, and because virus cannot be detected early in infection by usual testing, this was not a guarantee of freedom of infection and the potential for asymptomatic transmission.

118. It was clearly demonstrated that effective lockdowns within a country could decrease transmission and therefore decrease sickness and death from infection prior to the availability of vaccines. Other results of lockdowns are presently being assessed including the impact on mental health, youth, and education.

119. There was controversy about whether lockdowns at international borders could prevent the entry of virus and variants, and what many epidemiological models have

suggested is that international border lockdowns before widespread transmission (ie very early after the pandemic was identified) likely provided a very short (up to two week) window of opportunity to better understand the epidemiology and to prepare for a pandemic. Retrospective studies at present may help better understand the impact of international border lockdowns on spread of the virus, and also on the impact of international border lockdowns on willingness of countries to freely share data about variants, a necessity for stronger health security in a globalised world.

C. The difference between SARS-type viruses and other viruses

120. The influenza-virus, like the coronavirus, is an RNA virus, and there are four types of influenza virus: A, B, C and D. Types A and B influenza viruses cause seasonal influenza outbreaks each year, and mild mutations regularly occur. Type C influenza virus causes mild disease and does not cause epidemics, and Type D influenza viruses mainly circulate in cattle.

121. The first step of entry of the Influenza virus into human cells is by attachment to the terminal α-sialic acid receptor (Luo, 2012), a receptor that is different from the ACE2 receptor to which the spike protein of SARS-CoV-2 attaches. Minor mutation of the seasonal influenza viruses (A and B) as they reproduce in humans is called antigenic drift, and the virus component of the seasonal influenza vaccine must be changed each year in order to compensate for antigenic drift in order to produce the most effective vaccine for the influenza epidemic season.

122. As for SARS-CoV-2, prevention of influenza is by vaccination. Vaccine composition for seasonal influenza is decided based on the dominant drifted seasonal virus strains as determined from the genetic sequences of viruses collected from laboratories around the world and shared on the Global Initiative on Sharing Avian Influenza Data (GISAID) and other digital platforms.

123. Although vaccine-induced immunity from previous years may provide low levels of cross-protection from the drifted viruses, it is not possible to predict when or what type of drift of the seasonal influenza viruses will occur, nor the level of protection provided by previous vaccines.

124. Antivirals against the influenza virus such as Oseltamivir have been shown in one study to decrease severity of disease in persons with co-morbidity if given within one day after diagnosis (Orzeck, 2007). Most studies conclude that oseltamivir must be given soon after infection in order to have an impact on severity of illness. Oseltamivir has not been shown to clear virus from infected patients, and there remains controversy as to its real effectiveness in decreasing severity of disease and decreasing hospitalisation.

125. Like the endemic coronaviruses including SARS-CoV-2, previous influenza infection does not protect against reinfection, and many of the risk groups for serious outcomes of infection are the same risk groups for influenza – the elderly and those with certain co-morbidities. Long term sequelae of influenza, like coronaviruses, can include fibrosis in the lungs as well as aggravation of existing chronic pulmonary disease (Cipolla, 2020). Healthcare workers are at great risk of infection and are a group recommended for vaccination each year, as are the elderly. In some countries influenza vaccine is now used universally and has been shown to decrease the economic burden of influenza. The pattern of SARS-CoV-2 mutation, and its potential

for drift and shift is not yet fully understood and continued study is underway in the UK and many other countries.

126. Seasonal influenza viruses have emerged in humans from wild birds, in particular wild waterfowl, and from other birds and animals infected with the influenza virus by waterfowl. Novel or new influenza viruses also emerge in humans from birds and animals in nature. A novel influenza virus is created when genetic material from animal and human influenza viruses mix together in the same animal, called reassortment; or when genetic material in an animal influenza virus not exposed to a human virus mutates as it reproduces in that animal.

127. Novel influenza viruses sometimes have multiple mutations that more effectively escape cross protection offered by past seasonal influenza vaccination. When they enter human populations, they have the potential to cause a pandemic and replace other influenza viruses in human populations. The entry and establishment in human populations of a new or novel influenza virus is called antigenic shift. The most recent antigenic shift was in 2009 when a novel H1N1 influenza virus (nH1N1) with multiple mutations appears to have entered human populations from pigs. This virus is now endemic in humans, but could in the future be replaced by a virus with an antigenic shift that leads to greater transmissibility.

128. The nH1N1 virus, colloquially known as swine flu, was first identified In April 2009, in outbreaks in Mexico and the southwestern United States, and on 25 April 2009 the WHO Director General declared that the outbreak was a Public Health Emergency of International Concern (PHEIC), in part based on the initial reports of high mortality among young adults. The nH1N1 virus spread rapidly around the world and WHO declared that containment of the outbreak was not feasible, that countries should implement mitigation measures such as vaccination, and that borders should not be closed nor international travel restricted.

129. In April 2009, mitigation began in the UK with a public health campaign that had the slogan “Catch it, Bin it, Kill it”, and an attempt was made to slow the spread of nH1N1 by isolation of all known contacts and providing them with daily antiviral drugs as prophylaxis in case they had already been infected. Rapid distribution and supply of antivirals proved difficult however, and activities were delayed. Delays were caused by numerous logistics difficulties including multiple outbreak sites with a wide geographic distribution, increased demand on public health workers, and a lack of sufficient transportation required to deliver the drugs.

130. School closures were also undertaken to try to slow the spread of the pandemic influenza virus because it was understood from seasonal influenza outbreaks that transmission occurs at play and primary schools, and that it is the young who take infection home to parents and others living in the household.

131. Studies of the impact of school closures and quarantine of contacts suggested that these measures slowed transmission, but it was not possible to quantify to what extent they slowed transmission, nor to determine the best length and duration of

closure. By slowing the spread of infection they provided a brief time period during which to collect epidemiological information and to organise logistics for procurement of pandemic vaccine and antiviral drugs that were being held in virtual stockpiles (vaccines that are pre-purchased and held in bulk by industry until requested by the purchasing country), and/or in physical stockpiles in the UK.

132. The nH1N1 influenza virus was different from seasonal influenza viruses that were circulating at the time, and few young people had antibody to the H1N1 influenza virus, but nearly one-third of people over 60 years old had antibody against this virus, likely from infection with an H1N1 virus when they were young.

133. It is estimated that between 151,000 and 575,000 persons worldwide died from nH1N1 infection during the first year of the pandemic; and 80% of deaths were estimated to have occurred in those under 65 years of age, primarily among children and young/middle-aged adults; and opposite from the age of deaths that occur during seasonal influenza outbreaks, likely due to the fact that those over 60 had been previously exposed to the H1N1 influenza virus when they were younger. A pandemic influenza vaccine became available 21 October 2009 in the UK, and there were a total of 457 deaths in the UK before the end of the pandemic was declared on 10 August 2010.

134. The impact of the nH1N1 influenza virus on the global population during the 2009 pandemic was less severe than that of previous pandemics. Estimates of pandemic influenza mortality ranged from 0.03% of the world's population during the 1968 pandemic of the H3N2 influenza virus to 1-3% of the world's population during the 1918 H1N1 pandemic. In contrast, it is estimated that 0.001% to 0.007% of the world's population died of respiratory complications associated with the nH1N1 influenza virus infection during the 2009 pandemic.

135. The WHO influenza surveillance network provides information on influenza viruses from around the world from over 120 national laboratories that collect virus specimens from persons with influenza-like illness (ILI). The genetic sequence of each of these viruses is entered into the GISAID or another digital platform, to be used when decisions are made by WHO and influenza experts on the next season's vaccine composition. WHO-convened meetings of the experts occur six months before the seasonal influenza season begins in each hemisphere so that vaccines can be produced on time. The Food and Agriculture Organisation (FAO) monitors influenza viruses in bird and animal populations, helping detect when an influenza virus breaches the species barrier between animals and humans.

136. The UK plays a major role in the WHO influenza network providing genetic sequencing capacity as well as financial support. In addition, seed viruses of new virus strains for vaccine production are developed at no cost to the global community in the UK, and they are then provided to WHO for distribution to vaccine manufacturers interested in producing influenza vaccine.

137. My understanding as to why the UK government prepared for an influenza and not a coronavirus pandemic is conjectural – that a possible influenza pandemic was high on the government risk register, and that there was clear understanding of the importance of influenza and its pandemic potential, whereas the evidence of coronavirus as a pandemic threat was less robust: the outbreaks of SARS-CoV-1 in 2003 and MERS-CoV in 2012 did not cause pandemics and did not lead to endemicity; and the four known human coronaviruses are considered less threatening than the influenza virus, and the cause of the common cold. Coronaviruses were however on the UK radar and guidance was prepared for the management of coronavirus infections after importations of MERS-CoV, and lessons from the influenza pandemic in 2009 led the government to increase the capacity of patient ventilators, and to modify its strategy of attempting to contain early influenza outbreaks to using antivirals to provide early treatment to those who are at risk of serious illness infection.

138. There are additional respiratory viruses that cause human infection including Respiratory Syncytial Virus (RSV), an RNA virus. RSV causes mild upper respiratory infections such as the common cold, and it is spread by droplets and aerosols generated by coughing and/or sneezing, and by fomites that contaminate the hands that then come in contact with mucus membranes.

139. RSV generally causes minor illness but can be serious, especially in infants in whom it can cause inflammation of the small airways in the lung, and pneumonia; and in older adults and those with comorbidities such as congestive heart failure and chronic obstructive pulmonary disease (Ackerson, 2019).

140. RSV reproduces in human cells differently than does the corona- and influenza viruses. It attaches to the cell membrane, not a specific receptor as does SARS-CoV-2, and by fusing with the cell membrane it enters the cell and replicates. RSV is more stable genetically than SARS-CoV-2, though mutations do occur as it replicates.

141. Vaccines and therapeutics are being developed and studied for RSV, and a fully licensed vaccine may become available sometime during 2023.

142. This module is about respiratory viruses that are transmitted from human to human directly by pulmonary droplets or by aerosols and fomites. Other viruses not transmitted by the respiratory route are also important because they have recently caused outbreaks, or continue to do so.

143. Poliovirus, norovirus and rotavirus cause gastro-enteric disease, and the poliovirus also causes neurological disease and/or flaccid paralysis. These viruses are transmitted by the faecal-oral route through water contaminated with human faeces.

144. Ebola, Lassa and Marburg viruses are transmitted by direct contact with body fluids (faeces, vomit, blood) of infected persons and not by the respiratory route. There have been approximately 30 reported outbreaks of Ebola since its discovery in 1976

(CDC, 2023), and most have been caused by amplification of transmission in health facilities with sub-standard infection prevention and control procedures that then spread to other hospitalised patients and then into communities. They have been contained without the use of a vaccine by rigorous protection of health workers, isolation of patients and outbreak containment by contact tracing and identification of cases through surveillance. Between 10% and 75% of persons with clinical illness survive infection, depending on treatment and with which of the four known strains of Ebola virus they have been infected (WHO, 2023b). Some survivors carry the virus for periods of time for up to a year after recovery, and are considered a risk to persons non-infected through sexual intercourse, though the full implication of carriage of the Ebola virus is not yet understood.

145. Ebola outbreaks occurred in three West African countries – Guinea, Liberia and Sierra Leone – in 2013 to 2016 and were amplified in transmission first in health facilities and then spread from person to person in communities, either to persons caring for family members or preparing the dead for burial. The outbreaks were stopped by the same measures used to stop previous outbreaks as listed above. Persons with infection travelled to European and North American countries, as well as to Nigeria, Mali and Senegal, and rapid detection and isolation with contact tracing stopped these infections from causing major outbreaks. Towards the end of the West African outbreaks a vaccine that had been developed for biodefence purposes with US funding through the US Biomedical Advanced Research and Development Authority (BARDA) was shown to be effective in preventing infection, and several monoclonal antibody preparations were shown to be effective in decreasing mortality. The vaccine, which requires storage until use at −80°C to −60°C, is stockpiled by Gavi (The Global Alliance for Vaccines and Immunization), and now used to protect health workers and contact of contacts of infected persons as a part of control measures, though by the time the logistics can be set up for vaccination many outbreaks have been successfully stopped by routine containment measures alone.

146. Lessons from the West African outbreak, where more deaths from malaria than from Ebola were reported to WHO during the period of the outbreak, included understanding that when health systems are unable to accommodate an epidemic-related surge of patients, routine health problems cannot be managed either.

147. It is not possible to predict when an outbreak of Ebola will occur, nor which of the four strains of the Ebola virus will be the cause. Aerosol transmission of the Ebola virus has never been documented, and the virus does not have the potential to cause a pandemic because of its short incubation period (3 to 5 days) before the onset of illness that rapidly incapacitates and immobilises patients when they are most infectious.

148. The Zika virus is transmitted to humans by the bite of an infected mosquito, and illness after infection is mild and rarely fatal. Outbreaks of Zika virus infection in 2015 were linked to neurological symptoms including Guillain Barre Syndrome in Pacific Islands (Cao-Lormeau, 2016), islands in the Mediterranean and in Latin American

countries including Brazil (Plourde, 2016). Some of these outbreaks were linked to microcephaly, but the causative pathway is not understood and no outbreaks with microcephaly have occurred since then. The Zika virus is not transmitted by the respiratory route, and vector borne infections do not become pandemic though outbreaks can occur periodically, especially during rainy seasons in the tropics when mosquito vector breeding sites in standing water are increased.

149. Human monkeypox (Mpox) virus is transmitted from person to person by direct contact with skin lesions, and studies to determine if respiratory transmission also occurs are ongoing, but to date they have not provided conclusive results.

150. The control of the current outbreaks of Mpox in men who have sex with men has been facilitated by behaviour change and vaccination using a non-replicating smallpox vaccine that, unlike previous smallpox vaccines, is safe to use in HIV-infected persons.

151. Mpox continues to periodically emerge in sub-Saharan Africa and research must be increased to understand its potential to cause sustained outbreaks in unvaccinated populations. Such research is especially urgent because the population without smallpox vaccination continues to increase worldwide since routine vaccination was stopped in the 1980s, and populations everywhere are susceptible to infection (Adetifa, 2023).

152. Other viruses such as the Nipah virus are transmitted directly or indirectly to humans from infected bats, and transmitted rarely from human to human directly, though they can be transmitted indirectly and cause outbreaks by failed infection prevention and control in healthcare facilities.

D. Description of certain UK bodies concerned with threats (matter 8)

153. The Human Animal Infections and Risk Surveillance Group (HAIRS) is an innovative platform for monitoring infections occurring in animals in the UK and world wide, and for conducting a risk assessment of the potential of these infections to emerge and spread in humans in the UK. The HAIRS group consists of technical experts of the UK government sectors in animal and plant health, the environment, food and rural affairs, food safety, and human health protection in England. The devolved administrations and the Republic of Ireland are also members of the HAIRS group.

154. The HAIRS group has been meeting each month virtually, and face to face at least once each quarter, since 2004 when the group was first established. At each meeting the HAIRS experts follow a standardised process to assess new, potentially emerging or other infectious hazards, including zoonotic agents, that are identified from surveillance and other less formal networks in the UK and globally, including those managed by WHO and the Food and Agriculture Organisation (FAO).

155. Once information on new and potential emerging infectious hazards has been assimilated, the hazards are reviewed, and if further information is required in order to fully assess the risk it is sought by assigned experts. Once all the information is available, an assessment of the risk or probability of infection in the UK population and its potential impact on human health is conducted using a fixed set of questions. Risk management options are then identified by the HAIRS experts using standard algorithms within the HAIRS guidelines, and they are recommended to groups such as the UK Health Security Agency (UKHSA), the NHS and their veterinary equivalents, As a final step, the risks are communicated within government and placed in the public domain on the HAIRS website and in annual reports.

156. Infectious hazards that are assessed as potential risk to human populations in the UK and the Republic of Ireland are included in the *Infectious Disease Surveillance and Monitoring System for Animal and Human Health: Summary of notable events and incidents of public health significance*, which is produced and distributed monthly across government.

157. Major hazards listed in the most recent HAIRS annual Report (2017) identified eight major risks to the UK and Irish population including vectors of infection such as imported mosquitoes and ticks, avian influenza, several infections of dogs including brucella and oriental eye worm infection, chronic wasting disease in Norwegian deer, Mycobacterium bovis in cattle, and psittacosis in parrots. Current infectious hazards that are being followed by the HAIRS experts include human Mpox, and avian influenza has again been registered at the top of the current list.

158. The UK Health Protection Agency (HPA) was a statutory body with a mandate of protecting the UK population against all hazards including infectious disease,

chemical, nuclear and biological threats. Its role was to provide an integrated approach to protecting UK public health through the provision of support and advice to the NHS, local authorities, emergency services, other Arms Length Bodies, the Department of Health and the others.

159. As a statutory body, HPA worked independently, but in close alignment with the UK government through the chief medical officer. It was governed by a board of non-executive directors that included representatives from the devolved administrations, and staff included technical experts in public health; disease detection, surveillance and risk assessment; laboratory science; chemical, biological, radiological and nuclear response; and other hazards such as flooding and heatwaves.

160. HPA functions included public health surveillance (the ongoing systematic collection, analysis, and interpretation of data collected for target hazards such as ILI surveillance for influenza); and response including outbreak investigation, reference laboratory support to the NHS, training and risk assessment, public health research, collecting and analysing data to improve understanding of public health challenges, and using scientific evidence to provide answers to public health problems.

161. In addition to detecting disease outbreaks through public health surveillance, the agency responded to outbreaks by investigation and containment by local public health teams; and responded to hazards such as child infections at petting farms, measles outbreaks, flooding, and heatwaves by coordinated actions led by HPA experts. In addition to these core activities that prevented, detected and mitigated national public health emergencies, HPA effectively led the high profile public health investigation of the Litvinenko polonium-210 attack in 2006; and led the response to the H1N1 influenza pandemic of 2009.

162. Lessons learned from the influenza H1N1 pandemic included the need for more coordinated actions across government, and a series of more inclusive desktop and field exercises for pandemic influenza were developed and implemented as a means of preparing for future pandemics.

163. In 2013 HPA became an executive agency in the Department for Health and Social Care (DHSC) and served as the nidus for the creation of Public Health England (PHE). PHE brought together health protection and health promotion (also called health improvement) with a mandate of making the public healthier; and of reducing differences between the health of different groups by promoting healthier lifestyles, advising government and supporting action by local government, the NHS and the public.

164. My view at the time of the merger, and afterwards, was positive, and the general consensus of the DHSC board, to which I was seconded as an observer during the transition period, was that the move was beneficial to public health because of the synergies created that enabled leadership and technical staff working in non-communicable and communicable disease control to share knowledge and skills.

As an example, the social marketing skills used in the Stoptober anti-smoking campaigns were adapted for use in communicable disease screening programmes as well.

165. By bringing together health protection and health promotion, synergies were created within PHE, especially where the vulnerable are concerned, with increased emphasis on infections such as tuberculosis and hepatitis that are especially prevalent in the homeless and those in relative poverty with substandard housing; and increased emphasis on prevention of smoking and poor diet and obesity, also more prevalent in disenfranchised populations that are living in poverty. Examples of synergy include: the use of social marketing that had been developed and used for health promotion that provided lessons for increasing participation in tuberculosis screening programmes, and more active campaigns to decrease obesity that has negative impacts on infection because of type 2 diabetes.

166. During the time when I was a staff member of the Centers for Disease Control and Prevention a similar merger had occurred, and the general belief was that by bringing together both communicable and non-communicable disease control activities under one leadership, US public health had been strengthened.

167. The mandate of PHE was laid out in a 2013 framework agreement that articulated the respective roles and responsibilities of PHE and DHSC, and this framework was republished in 2018 after a satisfactory Cabinet Office-led review of PHE. PHE's work was conducted by dedicated PHE local health protection teams in conjunction with new directors of public health in local government.

168. Approximately 130 Directors of Public Health covering 150 local authorities were appointed by PHE, working at times in conjunction with the NHS. They successfully managed infectious disease outbreaks in schools, nursing and care homes, and food businesses as had HPA, and also significant national events including the Manchester bombings, the Grenfell Fire, the Salisbury poisonings, and numerous flooding events. PHE also created a national focal point for the wider determinants of health to work with local government as they developed better housing and clean air, and as they attempted to ensure economic development by the creation of new jobs.

169. PHE continued a health protection role in England to protect against public health hazards, to prepare for and respond to public health emergencies, and to use its information and expertise to ensure foresight for future public health challenges. One of its most important contributions to preparedness was the co-designing and implementation, with the Cabinet Office Civil Contingencies Secretariat and the DHSC / Chief Medical Officer, of simulation exercises to respond to public health risks on the national risk register, including pandemic planning.

170. Cross government simulation exercises were initially designed, with input from HPA, for preparedness and response to pandemic influenza. They were aimed at strengthening cross government collaboration and preparedness for pandemic response, and a national influenza preparedness plan was developed and regularly

updated based on outcomes of these exercises. The value of the preparedness plan, which had created awareness across government of essential response measures, was demonstrated during the response to the 2009 pandemic of H1N1 influenza.

171. After a PHE mission to the Kingdom of Saudi Arabia by a team from PHE to investigate an outbreak caused by a newly identified coronavirus (now named Middle East Respiratory Syndrome Coronavirus) in 2016, recommendations were provided by the team leader and used for MERS planning and to help develop the national MERS exercise conducted in 2015.

172. The exercises included participation of all parts of HPA and then PHE as well as local authorities, but I was not directly involved in the implementation of the exercises and am unable to describe the response of other government agencies such as the Health and Safety Executive, nor of other non-governmental bodies such as unions.

173. PHE also supported local authorities and the NHS in planning and providing health and social care services such as immunisation, and cancer and infection (hepatitis C) screening programmes. As was in its mandate, PHE was a principal agency involved in the initial response to the Covid-19 pandemic despite a 40% budget reduction in real terms between its inception in 2013 and 2020.

174. Failure to obtain an increase in the PHE budget during the period that I was chair placed more responsibility on local government authorities who were expected to lead and manage public health activities on decreasing budget allocations. As funds were not provided by PHE to local government through a budget justification process for specific public health interventions, there was a decreased ability to reserve and use funding under central command and control for specific activities such as contact tracing at the time when they were needed.

175. After the Ebola outbreaks in West Africa that began in 2013 PHE created the UK Public Health Rapid Support Team (UK-PHRST), a UK aid-funded project operated by Public Health England and the London School of Hygiene and Tropical Medicine. UK-PHRST rapidly deploys specialist experts to outbreaks of infectious diseases overseas to prevent them from becoming global threats, either after a request from WHO or a bilateral request from countries, and conducts outbreak related research that helps build capacity for local outbreak prevention and control activities with overseas partners.

176. PHE was widely recognized in Europe and worldwide as a comprehensive public health agency, and it served as an example to other countries including France where Sante Publique France was recently established with a similar organisational structure to PHE. It also responded to calls from WHO for support to the 2014-2016 Ebola outbreak in DRC, and to outbreaks of Zika and MERS. In 2017, an external peer review by experts from a group of public health institutions from around the world concluded that PHE met and exceeded its role as outlined in the framework agreement with DHSC.

177. In August 2020, as the SARS-CoV-2 pandemic continued, a decision was made to dissolve PHE without preceding review and consultation, and the health promotion component became the Office of Health Improvement and Disparities (OHID) in the Department of Health and Social Care, while the health protection functions were moved into a new agency, the UKHSA with the remit letter specifying that UKHSA must work in coordination with other bits of Government and within the health family to address the inequalities in health that put populations at greater risk of infectious diseases.

178. Specific examples of how working with OHID, NHS England (NHSE) and NHS public health teams will contribute to the government's 'levelling up' agenda include focusing on reducing inequalities in communities impacted by infectious disease environmental hazards, and other threats by targeting action towards disproportionately affected groups; and working with local partners, local authorities and the NHS to take action to reduce inequalities from the impact of Covid-19 on different communities so that all are more equally protected from the disease (UK Government, 2022).

179. I have been asked to address other key threat agencies such as NERVTAG, SAGE or HSE but I have not done so because I do not have the knowledge to comment on them.

E. The pros and cons of the creation and divergence of threat agencies

180. The Covid-19 pandemic has demonstrated that preparedness for mitigating and containing threats to health security cannot be accomplished by strong health protection (public health) capacities alone. Preparedness requires resilient and robust health care so that a surge of patients can be accommodated while routine health services are continued; and healthy populations able to resist serious illness after infection. Preparedness for infectious disease threats also requires understanding and mitigation of risks of infectious disease emergence at the animal/human interface.

181. Threat agencies that concentrate on public health and health protection in the human health sector alone, without taking into account the need for understanding infections and risks from animal populations; and threat agencies that fail to understand the need for resilience of health care and effective health promotion that leads to more healthy populations, will not provide the health security required to rapidly contain future pandemics and other public health emergencies.

182. PHE was a threat reduction agency that was highly suited for this challenge because of synergies that were developed between public health and health promotion. These functions were in fact integrated within PHE under the same management, and at the same time links with the NHS and across government were assured by DHSC, permitting an opportunity for a better understanding that investment in public health and healthy populations decreases demand on emergency and other clinical needs in the NHS.

183. Because infectious disease outbreaks and pandemics are currently detected in human populations that inadvertently serve as sentinel populations for emergence, emergence is often not detected early enough to effectively respond to and contain early outbreaks. There is a need to shift the paradigm from detection and response in humans that costs lives and economies, to prevention at the source – prevention at the animal/human interface. This can be accomplished by collaborative foresight and risk assessment as done by the HAIRS group, a group that was visionary when established, and that continues to work in an innovative One Health environment (an approach recognising the interaction between the health of humans, animals, and the environment).

184. The strength of the HAIRS group is that it works informally at a technical and not a political level, creating trust and a partnership that is accustomed to sharing and discussing information and data concerning potential biological threats from each individual agency partner. HAIRS is an excellent example of pandemic preparedness that requires strong cross government working, in partnership with the devolved administrations, and the HAIRS model has been adopted by WHO for promotion in its One Health activities, and the quadripartite of FAO, WHO, the World Organisation for

Animal Health (WOAH, formerly known as OIE), and the UN Environment Programme (UNEP) is an emulation of the HAIRS group at the global level.

185. New threat agencies that are solely focussed on health protection through preparedness, disease detection and outbreak response fail to incorporate lessons from recent outbreaks and pandemics. These lessons include an understanding that preparedness must include surge capacity in health care that can accommodate a surge of patients affected by a pandemic, as well as continuing to provide for routine health care needs; and healthy populations that have fewer co-morbidities and obesity and can therefore better resist serious outcomes from infection.

186. In addition to broadening their understanding of preparedness, new threat agencies must also understand the importance of prevention, including that the harsh economic impact from outbreaks and pandemics can be prevented if effective cross government and international partnerships address not only human health, but animal health and the environment as well.

F. International organisations and their assessment of and response to the risks of a public health emergency and the risks of a coronavirus pandemic

187. The European Centre for Disease Prevention and Control (ECDC) is a public health agency of the European Union (EU), operational since 2005. ECDC's ambition is to protect over 500 million EU citizens from infectious diseases that are mainly caused by parasites, viruses, bacteria and fungi. ECDC is headquartered in Stockholm, Sweden and employs around 300 professional and administrative staff.

188. ECDC is not an implementing agency, but rather collects, analyses and shares data from EU surveillance networks on more than 50 infectious disease topics such as Covid-19, influenza, HIV/AIDS, hepatitis, measles, tuberculosis, antimicrobial resistance and vaccination. ECDC experts assess biological risks, including the risk of epidemics and pandemics, to Europe; and provide guidance to help countries in the prevention and control of infectious diseases including preparedness for outbreaks and other public health threats including pandemics.

189. When an outbreak or pandemic spreads within Europe, ECDC regularly collects data and information from all EU countries and conducts risk assessments and standardised information that permits it to formulate and provide real time technical guidance to EU countries through its web pages and direct communications. Many countries outside the EU look to the ECDC for guidance during internationally spreading outbreaks and pandemics; and it is valued, as is the US CDC, as an international centre of excellence.

190. UKHSA and the European Centre for Disease Prevention and Control (ECDC), signed a memorandum of understanding (MoU) on 1 December 2021 to strengthen the collaboration on communicable disease prevention and control between the two organisations, with UKHSA acting on behalf of the UK.

191. Likewise, UKHSA, as a UK Focal Point of the UK-EU Trade and Cooperation Agreement (TCA) continues to share information on serious cross-border health threats, including most recently on monkeypox and hepatitis cases of unknown origin.

192. The Health Emergency Preparedness and Response Agency (HERA) is a newly established directorate-general of the European Commission created in September 2021 to better prepare the EU for a future pandemic based on lessons learned during the EU's response to the Covid-19 pandemic. Its mission is to prevent, detect, and rapidly respond to health emergencies; and it anticipates threats and potential health crises through most up-to-date intelligence gathering, and then prepares by building the necessary response capacities

193. During the pandemic preparedness phase, HERA works closely with EU Member States to analyse, identify, and prioritise possible health threats. Based on the priorities identified, HERA coordinates and co-funds, with Member Countries, the research and development of medical countermeasures required; and attempts to ensure the industrial capacity to produce and supply these countermeasures, including vaccines, medicines and diagnostic tests, for stockpiling and during actual pandemics.

194. HERA is developing and will deploy, during a public health emergency, an overall management system within the EU to ensure the continued development, production and distribution of medicines, vaccines, diagnostic tests and other countermeasures.

195. The UK does not have formal links with HERA as it does with ECDC.

196. The World Health Organisation (WHO) was established in 1948 as the United Nations agency with a mission to connect nations and its partners in promoting good health, keeping the world safe and serving the vulnerable so that everyone, everywhere can attain the highest level of health. WHO currently has three strategic priorities: to increase global efforts to expand universal health coverage; to direct and coordinate the world's response to health emergencies; and to promote healthier lives using science-based policies and programmes.

197. WHO has a political arm, the World Health Assembly, that provides for its governance. Decisions on WHO strategic directions and its budget are made, often using resolutions, and sometimes international regulations and/or treaties, at the World Health Assembly by ministers of health from all its member countries.

198. The WHO technical arm sets global norms and standards and provides technical and capacity strengthening guidance to countries on request, and is widely solicited by lower and middle income countries around the world.

199. There are six WHO regional offices that follow WHO strategic directions and coordinate activities to implement these, and other priorities as determined by their own regional governance body, the Regional Committee, that likewise often works through resolutions.

200. Within WHO there are several global threat/risk assessment and management mechanisms. Four of the most important, and supported either currently or in the past by the United Kingdom financially and/or by in kind provision of services and experts, are the Global Outbreak and Response Network (GOARN), the Global Influenza Surveillance and Response Network (GISRS), the Global Polio Laboratory Network (GPLN), and the *ad hoc* Emergency Committee (EC) of the International Health Regulations (IHR).

201. GOARN was begun in the late 1990s in partnership with Health Canada that had developed a web crawling mechanism that uses keywords to identify outbreaks and other public health hazards. The Global Public Health Intelligence Network (GPHIN)

collects information in the seven official languages of WHO and at the end of each day cleans and organises the data collected that day and sends it on to WHO for verification and risk assessment.

202. GOARN was formalised in 2000 and continues to receive information about potential global hazards from GPHIN, and from over 270 technical partner institutions and networks (and their members) across the globe including international networks of laboratories, United Nations organisations (eg UNICEF, UNHCR), the Red Cross and Red Crescent Societies (ICRC, IFRC), international humanitarian non-governmental organisations (eg Médecins Sans Frontières, International Rescue Committee, Epicentre), and national public health institutions including members of the International Association of National Public Health Institutes (IANPHI).

203. The information about public health hazards provided to GOARN is verified daily and risk assessment conducted. A summary of the risk assessment is provided to IHR focal points so that all countries are aware of the assessment and any control measures recommended by WHO.

204. During an internationally spreading epidemic or pandemic GOARN actively seeks information from countries for its daily risk assessments, and supports the collection of standardised information that is provided to the appropriate WHO disease control programme that prepare and provide real time guidance to Member States for epidemic and pandemic control.

205. Another activity of GOARN is to provide technical support to WHO Member States experiencing a human health emergency due to various threats including disease outbreaks, food safety, chemical toxins, zoonosis, natural and manmade disasters. All GOARN technical partners have agreed to pool their technical resources rapidly to assist affected countries seeking support or outbreak response from WHO.

206. When there is a need, GOARN partner institutions are solicited by the GOARN electronic communication system to provide technical support in outbreak response to countries that have requested support from WHO. For those partners that can provide support, their entry to countries is facilitated by WHO.

207. Since its inception, in addition to its daily risk assessment activities, GOARN has conducted over 160 operations and deployed over 3,500 technical experts to support more than 100 countries seeking international assistance. The GOARN steering committee is currently chaired by a UK public health expert, and the UK-PHRST is a leading partner of GOARN.

208. GISRS is an informal network of over 120 national laboratories around the world that regularly provides information on the incidence of influenza and genetic sequence data and/or influenza virus specimens to WHO through the GISAID and other data platforms. GISAID was formalised by WHO in May 2008 as a public domain for the deposit of genetic sequence information collected and shared by and among laboratory scientists.

209. Sequence data from GISAID and other sources is used by WHO for risk assessment of influenza twice each year – in February in the northern hemisphere, and in August in the southern hemisphere.

210. Influenza A and B viruses provided to WHO by countries are prepared to serve as vaccine seed viruses by the UK National Institute for Biological Standards and Control (NIBSC), an in kind contribution of the UK to WHO, and by other institutions in the USA, Japan and Australia. Seed viruses are then provided to manufacturers of flu vaccine by WHO. Influenza viruses are also used by laboratories in the UK and the US to prepare diagnostic tests that are distributed to the laboratory network, another in kind contribution to WHO.

211. When GISRS identifies a novel or new influenza virus in humans the same procedures for risk assessment are followed, and seed influenza virus provided to vaccine producers for a pandemic vaccine.

212. In 2007 as the novel avian influenza virus (H5N1) spread in Asian countries, the government of Indonesia, that regularly provided influenza viruses through GISRS, was unable to obtain a vaccine containing the H5N1 strains from the vaccine producer that had received the seed virus made from the Indonesia strain. As a result, a movement of equal sharing of virus and equal sharing of benefits was begun by the Indonesian Minister of Health.

213. Through a series of intergovernmental meetings at WHO the movement for sharing of virus and equal sharing of benefits resulted in the Pandemic Influenza Preparedness (PIP) framework, an agreement with vaccine producers that they would voluntarily provide to WHO a proportion of the pandemic vaccine they develop for distribution to Member States; and that they would contribute financially each year to GISRS. The PIP framework continues to date, and some vaccine producers are voluntarily contributing financial support to GISRS, and have signed agreements to provide pandemic vaccines. GSK (formerly GlaxoSmithKline) in the UK is one of the vaccine producers that is voluntarily adhering to the PIP framework with signed agreements on vaccine donation and financial contributions to GISRS.

214. GPLN is a laboratory network for global surveillance of polio, linked to WHO and the polio eradication initiative. Similar to GISRS, GPLN collects polio virus specimens from the stool of children with acute flaccid paralysis who have been identified by national surveillance officers. Virus is either genetically sequenced in national or global reference laboratories linked to GPLN. Genetic sequence information is used to confirm the type of polio virus isolated so that an appropriate national response can be mounted, and the sequence information is also used as a genetic fingerprint to trace the geographic origin of the infection so that vaccination can be provided where needed.

215. The GPLN has also established environmental surveillance systems that search for polio virus in sewage. Environmental surveillance is a very powerful system that

isolates polio virus from human waste and provides it to laboratories for genetic sequencing that helps identify where polio transmission is occurring, and provides important information for the certification of eradication. It is the environmental surveillance system managed by NIBSC that recently detected a vaccine-derived polio virus in the London Sewage system.

216. Environmental surveillance systems in many countries, including the UK, have also played a major role in monitoring SARS-CoV-2 in human waste by identifying which variants are circulating, acting as an early warning system of viral circulation and/or mutation.

217. GPLN is overseen by the Global Polio Eradication Initiative, and also independently by groups such as the independent polio monitoring board, the chairman of which is a former UK chief medical officer.

218. The Global Early Warning System (GLEWS) gathers information on infectious hazards from the surveillance and verification channels of the quadripartite organisations FAO, WOAH, WHO and the UNEP on a web-based electronic platform. Joint risk assessment is then conducted by the One Health quadripartite and early warning messages are sent out to Member States of each organisation through the risk communication process of each of the four agencies.

219. GLEWS was established in 2006 and has since evolved into GLEWS+ which is currently developing a more formal and standardised process for joint risk assessment in order to provide a more robust and timely threat/risk assessment. As it further develops, it is planned that GLEWS+ will more systematically link to areas such as wildlife health, food and biological threats; drive more advanced and cross-sectoral risk assessment; and provide more opportunities for participation by a broader range of stakeholders.

G. Perceived or actual deficiencies in international forecasting

220. The effectiveness of international risk assessment and forecasting is only as strong as the national public health systems that provide information on public health hazards to global mechanisms of the international organisations such as those described in Section F. International organisations generally do not have recurrent funding in their core budgets to fund these mechanisms, and most (eg GPLN and GSIS) are supported on a yearly basis by interested donors who provide funding in a competitive fund-raising environment. National funding requires government commitment and budgeting, and in lower and middle income countries (LMIC), often depends on supplementary funding from multilateral and bilateral donors, and loans from the World Bank and regional bank mechanisms.

221. The Global Health Security Agenda (GHSA) partnership was an attempt to increase bilateral funding arrangements from donor countries to strengthen public health capacity in LMIC partners, but it was unsuccessful in mobilising un-earmarked funding for surveillance and detection systems based on LMIC national planning. Rather, donor partners in the GHSA provided funding for areas of their own national interest (eg the US government provided funding and technical support for the establishment of One Health platforms through USAID, and the UK provided funding for strengthening surveillance for AMR through the Fleming Fund), leaving gaps in national public health surveillance and disease detection systems.

222. Deficiencies in the quality of forecasting require that increased investment and funding be provided to LMICs that are at present a weak source of information to the global mechanisms. Global mechanisms are heavily funded by donors, one reason being that donors have more oversight of how the funding is spent. However, more investment in LMICs is required as it will increase the quality of the information the global mechanisms receive. There is also a need for many LMIC governments to better understand the value proposition of strengthening and budgeting for their own national capacity development.

223. Other deficiencies in international forecasting are the lack of global consensus on which information from countries should be mandatorily provided to global forecasting and other mechanisms, and the lack of an ethical information sharing framework that includes sharing of benefits, though mechanisms such as the PIP framework have made advances, as have later innovative mechanism discussed in sections below. Global consensus on these issues must be developed if international forecasting is to be more effective.

H. Explanation of the status of the WHO within the exchange of information relating to global health risks and the International Health Regulations

224. The International Health Regulations (IHR) were agreed in 1969 by the World Health Assembly, an agreement with its roots in the 14th century response to plague as it spread throughout the world. The city state of Venice at that time adopted a new measure – quarantine – requiring all ships to remain anchored away from port for 40 days before being permitted to dock. Though the aetiology of plague was not understood, observations had linked it to rats. Quarantine, as the 40 days came to be known, was a means of ensuring that if plague was on board a ship, at the end of the 40 day period rats and human passengers would have become sick and died.

225. Quarantine at international borders remained the major tool to attempt to prevent the international spread of plague, and as time went on quarantine was required for three other diseases as well – smallpox, cholera and yellow fever. A series of treaties between countries in the Americas and Europe in the 19th century required individual country reporting when one of these diseases was detected within its national borders. Other countries could then attempt to stop infection at their international borders by quarantine of persons travelling from that country.

226. These treaties and other global agreements in the early 20th century were consolidated within the IHR of 1969. The objective of the IHR was to prevent the international spread of these four diseases by measures at borders described in the IHR 1969 (e.g. a vaccination requirement for passengers arriving from a country that had reported yellow fever to WHO). In addition all ports were required to eliminate breeding sites for mosquitoes, rats and other vectors.

227. The specific objective of the IHR was preventing the international spread of these four infections (plague, cholera, smallpox and yellow fever) with minimal interruption of travel and trade. By 2003, it was understood that actions at borders could not alone prevent the international spread of infections, and that the limited scope of the IHR to four infectious diseases was no longer valid as other infectious diseases and hazards had come to play a more important role in a globalised world. The IHR were therefore renegotiated and revised taking into account needs in a globalised world, and the technical innovations in communication that were occurring in the late 20th and early 21st century.

228. The revised IHR (IHR 2005) place primary emphasis on a requirement for countries to develop and/or sustain the capacity to rapidly detect, identify and respond to all disease hazards as a means of limiting national morbidity and mortality, and preventing national and international spread. WHO attempts to hold countries accountable to developing and strengthening their core public health capacities by requesting a progress report each year.

229. The IHR 2005 also provide a safety net that includes a decision tree for countries to use in order to determine whether a public health event is a potential public health emergency of international concern (PHEIC) and should therefore be reported immediately to WHO. Reporting of a potential PHEIC to WHO is required by the IHR 2005, followed by risk assessment by an Emergency Committee (EC) convened by the director general. There is, however, no means of ensuring that countries report, even though they agree to adhere to the IHR.

230. Once the EC has met, it makes a recommendation to the director general as to whether or not it considers the potential PHEIC to be a PHEIC, and if so a series of temporary recommendations, including recommendations on international travel, are made to ensure a unified national and global response. The EC recommendation is then considered by the director general along with other risk assessments from WHO advisory bodies or external experts, and he/she decides whether to declare a PHEIC with follow up as recommended by the EC.

231. In January 2020 the Director General convened an EC to assess the risk from Covid-19, and based on its recommendation and that of other experts who were consulted formally and informally, the director general declared that Covid-19 was a PHEIC. The global response to the announcement did not result in a unified global response as was expected under the IHR 2005. Rather than adhering to the WHO risk assessment and recommendations for international travel and trade as stipulated by the IHR, countries showed a preference to conduct their own risk assessment and management at international borders causing confusion and disorder in international travel and trade. It was possible for countries to do their own risk assessment in part because of abundant scientific and technical information being rapidly published and peer reviewed, and freely shared by medical journals in front of their usual paywalls. A series of reviews of the IHR 2005 is underway to determine how they might be modified and strengthened based on lessons learned from the Covid-19 response.

232. Though one requirement under the IHR 2005 is to develop core capacities in public health, there is no agreement within the IHR on more equitable access of the goods required for public health response to outbreaks and for capacity development. As of February 2023, an international pandemic treaty is currently being negotiated at WHO which, if successfully negotiated, will likely be complementary to the IHR and provide for some of the IHR deficiencies, for example by a requirement for equitable sharing in benefits and stronger preparedness across government including the environmental and animal health sectors. There is also continuing discussion about a means of better enforcing the IHR requirement to report as soon as a potential PHEIC is identified.

I. Description and explanation of other international coordinating bodies, operation and interaction with the UK government

233. After the development of the PIP framework in 2011 to ensure more equitable access to pandemic influenza vaccine, and based on lessons learned during the 2013 to 2014 Ebola outbreak in West Africa and the Covid-19 pandemic, additional innovative international coordinating mechanisms were established for more equitable access to technical support and goods required during outbreak and pandemic response, and for preparedness. These mechanisms include the GHSA, the Global Preparedness Monitoring Board (GPMB), the Pandemic Emergency Financing Facility (PEF), the Coalition for Epidemic Preparedness Innovations (CEPI), the Access to Covid-19 Tools (ACT) Accelerator, and The Pandemic Fund (Financial Intermediary Fund for pandemic prevention, preparedness and response [FIF-PPR]).

234. The Global Health Security Agenda (GHSA) is a global partnership of over 100 countries with a goal of strengthening LMIC capacity to prevent, detect, and respond to infectious disease threats. Since its inception in 2014, the GHSA has supported voluntary joint external evaluations (JEEs) of core capacity in public health in its partner countries. JEEs help countries identify the most critical gaps within their human and animal public health systems so that they can prioritise and identify opportunities for filling and strengthening these gaps and thus enhance their preparedness and response capacities.

235. The target of the GHSA is for countries to take greater ownership of global health security efforts by 2024, and to strengthen health security related technical areas within five years by completing the Joint External Evaluation (JEE), measured by reaching a level of demonstrated capacity in at least five technical areas required for preparedness and response.

236. Many partner countries of the GHSA and other countries voluntarily undertake an evaluation of the Performance of Veterinary Services (PVS) Pathway in order to assess their current strengths and gaps in providing sustainable improvement of national Veterinary Services. As for the JEE, PVS assessment reports lead to national capacity strengthening with support from the World Organisation for Animal Health (WOAH).

237. The Global Preparedness Monitoring Board (GPMB) is an independent monitoring and accountability board established in 2018 to better ensure preparedness for global public health crises. It is co-convened by the director general of WHO and the president of the World Bank, and its members include globally recognized leaders and experts from a wide range of sectors including clinical medicine, global health, veterinary epidemiology, environment, human rights, economics, law, gender and development.

238. The GPMB provides an independent and comprehensive appraisal for policy makers and the world about progress towards increased preparedness and response capacity for disease outbreaks and other emergencies with public health consequences, and is considered to be a roadmap for a safer world.

239. Recommendations from its most recent report (2021) are to strengthen global governance (including providing WHO greater resources, authority, and accountability); to adopt an international agreement on health emergency preparedness and response that addresses issues such as equitable access to common public health goods; to create a financing mechanism for preparedness, and empowerment communities, civil society and the private sector; to strengthen independent monitoring of preparedness and response and create a mechanism for mutual accountability.

240. The Pandemic Emergency Financing Facility (PEF), created in 2016, was a financing mechanism that was housed at the World Bank. It was designed to provide financing to help the world's poorest countries respond to cross-border, large-scale outbreaks by providing immediate funding from a standing cash fund, and by providing additional funding from an insurance fund once an outbreak had met the required criteria.

241. PEF payments could go directly to governments, or to pre-approved frontline responder organisations such as WHO and UNICEF. The first financial commitment approved by the PEF was a $12 million grant of the government of the Democratic Republic of the Congo (DRC) for response to an Ebola outbreak occurring in an area of civil disturbance.

242. When SARS-CoV-2 was identified in 2020, Covid-19 was determined by the PEF advisory body to have met the criteria for PEF support from the insurance fund, and in April 2020 the $195.84 million in the insurance fund was provided to lower and middle income countries; and to fragile and conflict affected countries. In April 2021, after the insurance funds had been transferred to the beneficiary countries, the PEF was officially closed. The UK government was a donor to the PEF.

243. The Coalition for Epidemic Preparedness Innovations (CEPI) was created in 2017 to accelerate the development of vaccines and other biologic countermeasures against epidemic and pandemic threats, and to facilitate more equitable accessibility to vaccines. CEPI creates public/private partnerships to support the development of vaccines and new vaccine platforms to protect against known viral infections with epidemic or pandemic potential as identified by WHO.

244. Currently CEPI is supporting partnerships necessary to develop vaccines to protect against disease caused by viruses such as Nipah, Lassa, and MERS. CEPI is also supporting epidemiological research that is required to better understand the best strategies for delivering vaccines to contain outbreaks caused by viruses with epidemic potential such as the monkeypox virus.

245. CEPI co-leads the COVAX facility to make Covid-19 vaccines more accessible in LMICs, and is now a partner in the 100 Days Mission. The 100 Days mission fulfils a UK challenge to the G7 to make available safe, effective and affordable diagnostics, vaccines and therapeutics in a future health crisis

246. The 100 Days Mission is a global public-private effort to harness scientific innovations for diagnostics, vaccines and therapeutics so that they are ready to be adapted and deployed within the first 100 days of a future pandemic threat. As a partner in the Mission, CEPI has committed to facilitating development of vaccines against newly emerged pathogens within 100 days of their identification by supporting the newer vaccine platforms that were developed during the Covid-19 pandemic. As of 22 March 2022 the government of the United Kingdom had contributed $356 million to CEPI since its inception in 2017.

247. The Access to Covid-19 Tools Accelerator (ACT Accelerator) was created in 2020 to bring together governments, health organisations, scientists, businesses, civil society, and philanthropists to accelerate the development, production, and equitable allocation and access to Covid-19 diagnostic tests, therapeutics, and vaccines. Accelerator activities are concentrated in four different pillars or areas of work described in the following paragraphs.

248. The Diagnostics pillar of the ACT accelerator is led by the Foundation for Innovative New Diagnostics (FIND) and the Global Fund on AIDS, TB and Malaria. It rapidly identifies and validates new diagnostic tests for Covid-19, provides guidance to countries on their use, and negotiates prices for bulk purchase. The diagnostics pillar has negotiated prices to make over 500 million diagnostic tests for Covid-19 affordable for purchase by LMICs, and by the end of 2022 has delivered 164 million diagnostic tests to LMICs. FIND is also a partner in the 100 Days Mission.

249. The Therapeutics pillar of the ACT accelerator is led by Unitaid and the Wellcome Trust and has mobilised and delivered $276 million worth of medical oxygen and therapeutics to LMICs by the end of 2022.

250. The Vaccines pillar – also known as the COVAX facility – is led by CEPI, the Global Alliance for Vaccines and Immunizations (Gavi) and WHO. The COVAX facility is meant to negotiate the best possible price for vaccines and make them available to all COVAX partner countries at this negotiated price. Working through Gavi, WHO, and UNICEF it has delivered 1.87 billion doses of Covid-19 vaccine to LMICs by the end of 2022.

251. Under the ACT-accelerator WHO works with the World Bank and the Global Fund to strengthen health systems and community networks that are working to contain Covid-19. By the end of 2022, $736 million worth of Personal Protective Equipment (PPE) had been delivered to LMICs for the protection of frontline workers.

252. The ACT-Accelerator launched a transition plan in October 2022 with changes required to move from managing Covid-19 as an acute emergency to integration into longer term disease control programmes. The UK investment in the Act Accelerator has been $1.2 billion of a total ACT-Accelerator budget of $23.8 billion.

253. The Pandemic Fund is a financial intermediary fund (FIF) of the World Bank for pandemic prevention, preparedness, and response. It was established in September 2022 with a goal of providing a dedicated stream of long term financing to strengthen prevention, preparedness and response capacities in LMICs. In addition to providing funding, the Pandemic Fund hopes to improve coordination for capacity strengthening among its partners and incentivise increased bilateral funding by its partners. Over $1 billion in financial commitments to the Pandemic Fund were announced by countries at the G20 summit in November 2022, including the United Kingdom.

254. The first call for proposals for investments to be funded by the Pandemic Fund was opened at the end of January 2023, and proposals will be reviewed by a newly formed technical advisory panel.

J. High level comparative examination of international structures referred to in sections E to I above and UK structures

255. There are many innovative mechanisms for assessing and managing infectious disease threats. These include global and national mechanisms for data collection and risk assessment; for supporting outbreak and pandemic preparedness and response; and for facilitating more equitable access to goods needed for strong public health.

256. Many of these mechanisms are vertical, and for some, such as the One Health quadripartite, collaboration is bringing them closer together with the potential for creating synergy and decreasing duplication that could result in stronger outcomes and cost savings.

257. For other vertical mechanisms potential opportunities for synergy and cost saving are missed. The PIP framework for example, created for increasing access to pandemic influenza vaccine, was not considered for ensuring more equitable access to Covid-19 vaccine, and a new mechanism within the ACT accelerator was established.

258. Finally, strong national public health capacity with comprehensive surveillance, timely disease detection and rapid reporting is necessary for success in decreasing the risks from global threats. There therefore needs to be greater focus on helping LMIC governments better engage in preparedness by including recurrent line items and funding in national budgets, with donors providing supplemental funding with strict donor phase out planning and assumption of full funding by government. The value proposition of strong public health capacity must be understood by all governments.

259. Some of these issues could be addressed through the upcoming IHR revision process and the negotiations leading to a pandemic treaty.

260. The following table lists the international structures described in sections E to I above, and provides a comparison to UK structures that currently exist and/or the UK relationship to them:

Table 1: International and UK structures involved in the assessment of and response to public health emergencies

International structure	UK structure	Comparison
ECDC	UKHSA	UKHSA proactively collaborates across the public health system in order to prepare for, respond to and recover from all health hazards including building and sustaining strong local and national government collaboration including with agencies in Scotland, Wales, Northern Ireland, the Crown dependencies, local authorities and other system partners to ensure threats are effectively identified, mitigated and addressed at home and abroad.
HERA	UK Vaccine Network and National Institute of Biological Standards and Control (NIBSC)	The UK Vaccine Network brings together industry, academia and relevant funding bodies to make targeted investments in specific vaccines and vaccine technology for infectious diseases with the potential to cause an epidemic. NIBSC develops new vaccines and assures the quality of biological medicines and diagnostics. Their value could be increased by strong collaboration with HERA and other international vaccine development groups.
WHO and regional offices	Department of Health and Social Care	The UK government is represented by DHSC at both the World Health Assembly and the WHO European Regional Office Regional Committee and contributes both technically and financially to their activities, thus increasing the possibility that all countries can detect and rapidly stop outbreaks where and when they occur, and prevent national, regional and global spread.
GOARN	UK-PHRST	UK-PHRST is a specialist team ready to respond to disease outbreaks around the world before they develop into health emergencies. The team also conducts rigorous operational research to improve epidemic preparedness. UK-PHRST adds value to GOARN, of which it is a partner, and this relationship will continue and could be strengthened by increased funding to provide a greater contribution to national and global health security.

International structure	UK structure	Comparison
GISRS/GISAID	UK Influenza-Like Illness (ILI) Surveillance	The UK regularly submits genetic sequence data of influenza to GISRS and SARS-CoV-2 to WHO through the GISAID platform and provides genetic sequencing to countries on the request of WHO and bilaterally. Increased funding would strengthen this unique capacity and provide a greater contribution to national and global health security.
GPLN	NIBSC	The UK maintains environmental surveillance for polio in certain parts of the UK and has recently identified an imported polio virus in the London sewage system. NIBSC is also working with WHO on research for new polio vaccines that decrease the risk of vaccine-derived polio and serves as a WHO Collaborating Centre for polio. Increased funding would strengthen this capacity and provide greater contribution to national and global health security.
GLEWS	HAIRS	HAIRS conducts risk assessment at the animal/human interface by bringing together government sectors in human, animal and environmental sectors in England and the devolved administrations. Close collaboration with GLEWS would increase UK and international health security.
IHR	UKHSA and DHSC	The UK IHR focal point is located with UKHSA and DHSC represents the UK at the World Health Assembly which is currently reviewing the effectiveness of the IHR during Covid-19. Continuing UK input to an eventual amendment process to the IHR, and to the pandemic treaty currently being developed by WHO will increase national and global health security.
PIP Framework	GSK and DHSC	DHSC has participated in the intergovernmental body that led to the PIP framework and GSK has signed an agreement with WHO to provide pandemic influenza vaccine through PIP. Continued association with the PIP framework by DHSC will increase global equity in public health.

International structure	UK structure	Comparison
GHSA	DHSC	DHSC is a member of GHSA and provides much of its contribution through the Fleming Fund that supports surveillance in antimicrobial resistance in GHSA partner countries. Non-earmarked contributions to national public health strengthening in LMICs would increase their ability to rapidly detect and respond to outbreaks, thus preventing international spread.
GPMB	University College London	Currently a faculty member of University College London is a member in his own capacity. Continued association with the GPMB by the UK government could heighten national health security.
PEF	UK former financial contributor through the World Bank	This fund has now been closed.
CEPI	UK Vaccine Network and NIBSC	Both the Vaccine Network and NIBSC work on vaccine development for epidemic or pandemic disease threats and close association is occurring. Increased funding to the activities of the Network and NIBSC vaccine development activities would increase health security globally.
ACT Accelerator	DHSC	The ACT-Accelerator is in a final phase and questions remain about its continuation. The UK provided great support to the CoVax facility with contributions of its AstraZeneca vaccine.
Pandemic Fund	DHSC	A medical epidemiologist of UKHSA is a member of the expert panel that makes funding decisions. He is on the panel in his own personal capacity, and increased UK funding of the Fund would permit an increase in public health capacity development in LMICs.

K. Conclusions and recommendations

Conclusion 1

261. UK research during the pandemic has been cutting edge, and has benefited from funding by government, private foundations and research councils. It has answered many questions nationally, and placed the UK among the nations that have early on understood the dynamics and means of managing and controlling the pandemic. This includes achieving one of the highest vaccination rates in the world, with trust in the health system being one of the major reasons. The UK has also been strong in genetic sequencing which has been of importance to vaccine manufacturers, and has shared results and offered sequencing support to the rest of the world. Though genetic sequencing will likely continue to be important in selection of Covid-19 vaccine components, and in contributing to understanding of the effectiveness of therapeutics in the future, it is not likely to be of use in contact tracing. When a new genetic sequence is identified, because of its ease of human to human transmission and rapid international spread, it is not possible to determine where that variant genetic sequence has first developed. Likewise, excellence in clinical trials has shown best possible medical management of patients with Covid-19 and saved uncountable lives around the world. By answering pandemic-related questions within a very short period of time, the UK was able to move, during late summer/early autumn 2022, from pandemic response mode to one of control with comprehensive surveillance to ensure that modifications to control could be made as necessary. This way forward has been understood and adopted by many other countries, in advance of guidance coming from international organisations.

Recommendation 1

262. Funding for research should continue in order to answer questions related to the pandemic strategy adopted by the UK, including total population lockdowns, and the impact the strategy has had on sickness and death, and on surge capacity and resilience to continue routine healthcare. Funding should also be made available for analysis of long term outcomes including better understanding of long Covid and other sequelae, and for better understanding of the impact of pandemic control measures on mental health, on youth, and on industry and business in the travel sector. By joining the Horizon research programme of the EU, in which the UK was a leader in the past, increased funding would become available to supplement that provided nationally.

Conclusion 2

263. The UK has been one of the most respected major donors to international activities that help better prepare the world for epidemics and pandemics, whether these international activities are based in the UK or elsewhere. It has understood that protecting the UK requires strengthening capacities around the world to prevent or

more rapidly detect and respond to outbreaks and pandemics. UK donor support has reflected this and is both technical – sharing the high level understanding of its science and public health by making UK scientists and public health experts available to international advisory bodies and for capacity strengthening in epidemic and pandemic preparedness in lower and middle income countries as described in this report; and financially – the UK has previously been one of the donor countries to reach the UN recommended overseas development spend of at least 0.7% of gross national income.

Recommendation 2

264. Funding should continue to be made available to national academic and technical experts so that they are able to support international activities that strengthen epidemic and pandemic preparedness and response activities, including support for funds at academic institutions and within government that permit replacement of skills nationally when UK experts are responding to overseas needs. Official Development Assistance (ODA) support should also continue to be provided both to public-private and other pandemic preparedness activities, as well as to international organisations that provide global guidance and support epidemic and pandemic prevention, preparedness and response capacity development. This should include continued active participation of the UK government in negotiations around the revised international health regulations and the pandemic treaty, using its soft diplomatic power when needed.

Conclusion 3

265. The UK has demonstrated the value of cross-government working in epidemic and pandemic preparedness by such organisations as the HAIRS group, bringing together those government sectors that are concerned with human and animal health and the environment. Private sector, including pharma, agribusiness and travel, has often been excluded from this cross-sectoral working, including on advisory groups for pandemic control, because of fear of conflict of interest, many times justified. Private sector has a role to play, however, in decisions made regarding such issues as international border controls and diagnostic testing, and at the same time large corporations develop many epidemic and pandemic control measures within their organisation that might be useful more widely if shared with government advisory bodies.

Recommendation 3

266. Continue to make permanent cross-government interaction in activities that lead to stronger epidemic prevention, preparedness and response, and identify means of including the private sector in such activities by ensuring that conflict of interest – whether perceived or real – is understood and respected in decision making.

Conclusion 4

267. The cross government and devolved administration involvement in HAIRS has created a One Health environment in the UK – One Health defined by many as an approach that recognises and works on the interconnection between the health of people, animals, plants, and the environment. Such an environment can help shift the current paradigm of rapid epidemic and pandemic detection and response to prevention at the source, thus saving lives in both the animal and human health sectors and preventing negative impact on the economy.

Recommendation 4

268. Cross government working in a One Health mode – without ceding to the temptation to create a separate One Health ministry or agency – should be formalised and permanent. Cross government work in a One Health mode for epidemic prevention, preparedness and response should continue, and include all economic sectors, both public and private, so that a shift can be made to prevention at the source. Such a shift might be partially accomplished, for example, by increased use of cost-effective vaccines in humans and animals, cleaner agriculture, and cross sector joint risk assessment, analysis and action.

Conclusion 5

269. Some of the failures in epidemic and pandemic preparedness could have been prevented by focussing on preparedness activities that include, but are not limited to, the public health system. These activities include ensuring a surge capacity within the NHS that is available from the start of an epidemic or pandemic, and more effectively encouraging healthy lifestyles that prevent obesity and co-morbidities that make people more susceptible to serious illness and death after infection.

Recommendation 5

270. Increase DHSC oversight of the partnership between the government agencies responsible for health improvement, medical management and health protection/public health with a focus on better epidemic and pandemic preparedness in the future.

Annex 1: References

Literature and other materials relied on to make this report were accessed between 1 December 2022 and 17 April 2023.

Ackerson, B. *et al.* (2019) 'Severe Morbidity and Mortality Associated With Respiratory Syncytial Virus Versus Influenza Infection in Hospitalized Older Adults', *Clinical Infectious Diseases*, 69(2), pp. 197–203. Available at: https://doi.org/10.1093/cid/ciy991.

Adetifa, I. *et al.* (2023) 'Mpox neglect and the smallpox niche: a problem for Africa, a problem for the world', *The Lancet*, p. S0140673623005883. Available at: https://doi.org/10.1016/S0140-6736(23)00588-3.

Alluwaimi, A.M. *et al.* (2020) 'The Coronaviruses of Animals and Birds: Their Zoonosis, Vaccines, and Models for SARS-CoV and SARS-CoV2', *Frontiers in Veterinary Science*, 7, p. 582287. Available at: https://doi.org/10.3389/fvets.2020.582287.

Al-Tawfiq, J.A. and Rodriguez-Morales, A.J. (2020) 'Super-spreading events and contribution to transmission of MERS, SARS, and SARS-CoV-2 (COVID-19)', *Journal of Hospital Infection*, 105(2), pp. 111–112. Available at: https://doi.org/10.1016/j.jhin.2020.04.002.

Cao-Lormeau, V.-M. *et al.* (2016) 'Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study', *The Lancet*, 387(10027), pp. 1531–1539. Available at: https://doi.org/10.1016/S0140-6736(16)00562-6.

Centers for Disease Control and Prevention (2023) *History of Ebola Virus Disease*, *Viral Hemorrhagic Fevers (VHFs), Ebola Disease*. Available at: https://www.cdc.gov/vhf/ebola/history/summaries.html.

Cipolla, E.M., Huckestein, B.R. and Alcorn, J.F. (2020) 'Influenza sequelae: from immune modulation to persistent alveolitis', *Clinical Science*, 134(13), pp. 1697–1714. Available at: https://doi.org/10.1042/CS20200050.

Coia, J.E. *et al.* (2013) 'Guidance on the use of respiratory and facial protection equipment', *Journal of Hospital Infection*, 85(3), pp. 170–182. Available at: https://doi.org/10.1016/j.jhin.2013.06.020.

Corman, V.M. *et al.* (2018) 'Hosts and Sources of Endemic Human Coronaviruses', *Advances in Virus Research*, 100, pp. 163–188. Available at: https://doi.org/10.1016/bs.aivir.2018.01.001.

Demaneuf, G. (2020) 'The Good, the Bad and the Ugly: a review of SARS Lab Escapes'. Available at: https://doi.org/10.5281/ZENODO.4293256.

Department of Health and Social Care and UK Health Security Agency (2022) *Letter from Maggie Throup to Professor Dame Jenny Harries, UKHSA chief executive*, *Correspondence - Letter from Maggie Throup to Professor Dame Jenny Harries, UKHSA chief executive*. Available at: https://www.gov.uk/government/publications/ukhsa-priorities-in-2022-to-2023/letter-from-maggie-throup-to-professor-dame-jenny-harries-ukhsa-chief-executive.

Enserink, M. (2023) 'Dispute simmers over who first shared SARS-CoV-2's genome', *Science*, 380(6640), pp. 16–17. Available at: https://doi.org/10.1126/science.adi1218.

Galanti, M. and Shaman, J. (2021) 'Direct Observation of Repeated Infections With Endemic Coronaviruses', *The Journal of Infectious Diseases*, 223(3), pp. 409–415. Available at: https://doi.org/10.1093/infdis/jiaa392.

Grant, R. *et al.* (2019) 'A Review of Asymptomatic and Subclinical Middle East Respiratory Syndrome Coronavirus Infections', *Epidemiologic Reviews*, 41(1), pp. 69–81. Available at: https://doi.org/10.1093/epirev/mxz009.

Greenhalgh, T. *et al.* (2020) 'Face masks for the public during the covid-19 crisis', *BMJ*, p. m1435. Available at: https://doi.org/10.1136/bmj.m1435.

Greenhalgh, T. *et al.* (2021) 'Ten scientific reasons in support of airborne transmission of SARS-CoV-2', *The Lancet*, 397(10285), pp. 1603–1605. Available at: https://doi.org/10.1016/S0140-6736(21)00869-2.

Hamner, L. *et al.* (2020) 'High SARS-CoV-2 Attack Rate Following Exposure at a Choir Practice — Skagit County, Washington, March 2020', *Morbidity and Mortality Weekly Report (MMWR)*, 69(19), pp. 606–610. Available at: https://doi.org/10.15585/mmwr.mm6919e6.

Hamre, D. and Procknow, J.J. (1966) 'A New Virus Isolated from the Human Respiratory Tract.', *Experimental Biology and Medicine*, 121(1), pp. 190–193. Available at: https://doi.org/10.3181/00379727-121-30734.

Heymann, D.L. (2004) 'The international response to the outbreak of SARS in 2003', *Philosophical Transactions of the Royal Society of London*. Edited by R.M. May et al., 359(1447), pp. 1127–1129. Available at: https://doi.org/10.1098/rstb.2004.1484.

Hu, Zhiliang *et al.* (2020) 'Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China', *Science China. Life Sciences*, 63(5), pp. 706–711. Available at: https://doi.org/10.1007/s11427-020-1661-4.

Huang, C. *et al.* (2020) 'Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China', *The Lancet*, 395(10223), pp. 497–506. Available at: https://doi.org/10.1016/S0140-6736(20)30183-5.

Kapoor, D. *et al.* (2021) 'Impact of Comorbidities on Outcome in Children With COVID-19 at a Tertiary Care Pediatric Hospital', *Indian Pediatrics*, 58(6), pp. 572–575. Available at: https://doi.org/10.1007/s13312-021-2244-0.

Kim, K.H. *et al.* (2017) 'Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in South Korea, 2015: epidemiology, characteristics and public health implications', *Journal of Hospital Infection*, 95(2), pp. 207–213. Available at: https://doi.org/10.1016/j.jhin.2016.10.008.

Kim, Y. (2015) 'Healthcare policy and healthcare utilization behavior to improve hospital infection control after the Middle East respiratory syndrome outbreak', *Journal of the Korean Medical Association*, 58(7), p. 598. Available at: https://doi.org/10.5124/jkma.2015.58.7.598.

Kwok, K.O. *et al.* (2020) 'Herd immunity – estimating the level required to halt the COVID-19 epidemics in affected countries', *Journal of Infection*, 80(6), pp. e32–e33. Available at: https://doi.org/10.1016/j.jinf.2020.03.027.

Li, P. (2020) 'Reopening the Trade after SARS: China's Wildlife Industry and the Fateful Policy Reversal', *Environmental Policy & Law*, 50, pp. 1–17. Available at: https://doi.org/10.3233/EPL-201008.

Li, Y. *et al.* (2021) 'Face masks to prevent transmission of COVID-19: A systematic review and meta-analysis', *American Journal of Infection Control*, 49(7), pp. 900–906. Available at: https://doi.org/10.1016/j.ajic.2020.12.007.

Lu, J. *et al.* (2020) 'COVID-19 Outbreak Associated with Air Conditioning in Restaurant, Guangzhou, China, 2020', *Emerging Infectious Diseases*, 26(7), pp. 1628–1631. Available at: https://doi.org/10.3201/eid2607.200764.

Luo, M. (2012) 'Influenza Virus Entry', *Advances in Experimental Medicine and Biology*. Edited by M.G. Rossmann and V.B. Rao, 726, pp. 201–221. Available at: https://doi.org/10.1007/978-1-4614-0980-9_9.

Markov, P.V., Katzourakis, A. and Stilianakis, N.I. (2022) 'Antigenic evolution will lead to new SARS-CoV-2 variants with unpredictable severity', *Nature Reviews Microbiology*, 20(5), pp. 251–252. Available at: https://doi.org/10.1038/s41579-022-00722-z.

McKinney, K.R., Gong, Y.Y. and Lewis, T.G. (2006) 'Environmental transmission of SARS at Amoy Gardens', *Journal of Environmental Health*, 68(9), pp. 26–31. Available at: https://go.gale.com/ps/i.do?p=AONE&sw=w&issn=00220892&v=2.1&it=r&id=GALE%7CA145934763&sid=googleScholar&linkaccess=abs (Accessed: 20 April 2023).

Morawska, L. and Milton, D.K. (2020) 'It Is Time to Address Airborne Transmission of Coronavirus Disease 2019 (COVID-19)', *Clinical Infectious Diseases*, 71(9), pp. 2311–2313. Available at: https://doi.org/10.1093/cid/ciaa939.

Orzeck, E.A., Shi, N. and Blumentals, W.A. (2007) 'Oseltamivir and the risk of influenza-related complications and hospitalizations in patients with diabetes', *Clinical Therapeutics*, 29(10), pp. 2246–2255. Available at: https://doi.org/10.1016/j.clinthera.2007.10.001.

Parashar, U.D. and Anderson, L.J. (2004) 'Severe acute respiratory syndrome: review and lessons of the 2003 outbreak', *International Journal of Epidemiology*, 33(4), pp. 628–634. Available at: https://doi.org/10.1093/ije/dyh198.

Patrozou, E. and Mermel, L.A. (2009) 'Does Influenza Transmission Occur from Asymptomatic Infection or Prior to Symptom Onset?', *Public Health Reports*, 124(2), pp. 193–196. Available at: https://doi.org/10.1177/003335490912400205.

Peiris, J. *et al.* (2003) 'Coronavirus as a possible cause of severe acute respiratory syndrome', *The Lancet*, 361(9366), pp. 1319–1325. Available at: https://doi.org/10.1016/S0140-6736(03)13077-2.

Peiris, J.S.M. *et al.* (2003) 'The Severe Acute Respiratory Syndrome', *New England Journal of Medicine*, 349(25), pp. 2431–2441. Available at: https://doi.org/10.1056/NEJMra032498.

Plourde, A.R. and Bloch, E.M. (2016) 'A Literature Review of Zika Virus', *Emerging Infectious Diseases*, 22(7), pp. 1185–1192. Available at: https://doi.org/10.3201/eid2207.151990.

Prather, K.A. *et al.* (2020) 'Airborne transmission of SARS-CoV-2', *Science*. Edited by J. Sills, 370(6514), p. 303.2-304. Available at: https://doi.org/10.1126/science.abf0521.

Primarolo, D., Malloch-Brown, M. and Lewis, I. (2009) 'Health is global: a UK Government strategy for 2008–13', *The Lancet*, 373(9662), pp. 443–445. Available at: https://doi.org/10.1016/S0140-6736(08)61820-6.

Public Health England (2018) 'Framework Agreement between the Department of Health and Social Care and Public Health England'. PHE publications. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/677457/Framework_agreement_between_DHSC_and_PHE_2018.pdf (Accessed: 16 April 2023).

Rabie, T. and Curtis, V. (2006) 'Handwashing and risk of respiratory infections: a quantitative systematic review', *Tropical Medicine and International Health*, 11(3), pp. 258–267. Available at: https://doi.org/10.1111/j.1365-3156.2006.01568.x.

Rocklöv, J., Sjödin, H. and Wilder-Smith, A. (2020) 'COVID-19 outbreak on the Diamond Princess cruise ship: estimating the epidemic potential and effectiveness of public health countermeasures', *Journal of Travel Medicine*, 27(3), p. taaa030. Available at: https://doi.org/10.1093/jtm/taaa030.

Salzberger, B. *et al.* (2021) 'Epidemiology of SARS-CoV-2', *Infection*, 49(2), pp. 233–239. Available at: https://doi.org/10.1007/s15010-020-01531-3.

Shen, Y. *et al.* (2020) 'Community Outbreak Investigation of SARS-CoV-2 Transmission Among Bus Riders in Eastern China', *JAMA Internal Medicine*, 180(12), pp. 1665–1671. Available at: https://doi.org/10.1001/jamainternmed.2020.5225.

Shen, Z. *et al.* (2004) 'Superspreading SARS Events, Beijing, 2003', *Emerging Infectious Diseases*, 10(2), pp. 256–260. Available at: https://doi.org/10.3201/eid1002.030732.

Spiteri, G. *et al.* (2020) 'First cases of coronavirus disease 2019 (COVID-19) in the WHO European Region, 24 January to 21 February 2020', *Eurosurveillance*, 25(9). Available at: https://doi.org/10.2807/1560-7917.ES.2020.25.9.2000178.

Tsankov, B.K. *et al.* (2021) 'Severe COVID-19 Infection and Pediatric Comorbidities: A Systematic Review and Meta-Analysis', *International Journal of Infectious Diseases*, 103, pp. 246–256. Available at: https://doi.org/10.1016/j.ijid.2020.11.163.

Tu, C. *et al.* (2004) 'Antibodies to SARS Coronavirus in Civets', *Emerging Infectious Diseases*, 10(12), pp. 2244–2248. Available at: https://doi.org/10.3201/eid1012.040520.

Vijgen, L. *et al.* (2005) 'Complete Genomic Sequence of Human Coronavirus OC43: Molecular Clock Analysis Suggests a Relatively Recent Zoonotic Coronavirus Transmission Event', *Journal of Virology*, 79(3), pp. 1595–1604. Available at: https://doi.org/10.1128/JVI.79.3.1595-1604.2005.

V'kovski, P. *et al.* (2020) 'Coronavirus biology and replication: implications for SARS-CoV-2', *Nature Reviews Microbiology*, 19, pp. 155–170. Available at: https://doi.org/10.1038/s41579-020-00468-6.

Wang, H. *et al.* (2020) 'The genetic sequence, origin, and diagnosis of SARS-CoV-2', *European Journal of Clinical Microbiology & Infectious Diseases*, 39(9), pp. 1629–1635. Available at: https://doi.org/10.1007/s10096-020-03899-4.

Wang, L.-F. and Eaton, B.T. (2007) 'Bats, Civets and the Emergence of SARS', in J.E. Childs, J.S. Mackenzie, and J.A. Richt (eds) *Wildlife and Emerging Zoonotic Diseases: The Biology, Circumstances and Consequences of Cross-Species Transmission*. Berlin, Heidelberg: Springer Berlin Heidelberg, pp. 325–344. Available at: https://doi.org/10.1007/978-3-540-70962-6_13.

Wang, Y. *et al.* (2020) 'Clinical Outcomes in 55 Patients With Severe Acute Respiratory Syndrome Coronavirus 2 Who Were Asymptomatic at Hospital Admission in Shenzhen, China', *The Journal of Infectious Diseases*, 221(11), pp. 1770–1774. Available at: https://doi.org/10.1093/infdis/jiaa119.

Wei, W.E. *et al.* (2020) 'Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020', *Morbidity and Mortality Weekly Report*, 69(14), pp. 411–415. Available at: https://doi.org/10.15585/mmwr.mm6914e1.

Wilder-Smith, A. *et al.* (2005) 'Asymptomatic SARS Coronavirus Infection among Healthcare Workers, Singapore', *Emerging Infectious Diseases*, 11(7), pp. 1142–1145. Available at: https://doi.org/10.3201/eid1107.041165.

World Health Organisation (2003) *Severe Acute Respiratory Syndrome (SARS), Health Topics - Severe Acute Respiratory Syndrome (SARS)*. Available at: https://www.who.int/health-topics/severe-acute-respiratory-syndrome.

World Health Organisation (2020a) United Nations Geneva - press conference video, Twitter. Available at: https://twitter.com/UNGeneva/status/1217146107957932032 (Accessed: 16 May 2023).

World Health Organisation (2020b) *Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV), Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV)*. Available at: https://www.who.int/news/item/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov).

World Health Organisation (2020c) *Statement on the third meeting of the IHR (2005) Emergency Committee regarding the outbreak of coronavirus disease (COVID-19), Statement on the third meeting of the IHR (2005) Emergency Committee regarding the outbreak of coronavirus disease (COVID-19)*. Available at: https://www.who.int/news/item/01-05-2020-statement-on-the-third-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-coronavirus-disease-(covid-19).

World Health Organisation (2020d) *Statement on the fourth meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of coronavirus disease (COVID-19)*. Available at: https://www.who.int/news/item/01-08-2020-statement-on-the-fourth-meeting-of-the-internatio

nal-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-coronavirus-disease-(covid-19).

World Health Organisation (2020e) 'Advice on the use of masks the community, during home care and in health care settings in the context of the novel coronavirus (2019-nCoV) outbreak'. World Health Organisation. Available at: who.int/docs/default-source/documents/advice-on-the-use-of-masks-2019-ncov.pdf.

World Health Organisation (2020f) *Mask use in the context of COVID-19: interim guidance, 1 December 2020*. WHO/2019-nCoV/IPC_Masks/2020.5. World Health Organisation, p. 22. Available at: https://apps.who.int/iris/handle/10665/337199.

World Health Organisation (2022) *Questions and answers: Coronavirus disease (COVID-19): Masks*, *Questions and answers: Coronavirus disease (COVID-19): Masks*. Available at: https://web.archive.org/web/20221228233749/https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-covid-19-masks.

World Health Organisation (2023a) *Coronavirus disease (COVID-19): Masks*, *Questions and answers / Coronavirus disease (COVID-19): Masks*. Available at: https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-covid-19-masks.

World Health Organisation (2023b) *Ebola virus disease*, *Fact Sheets / Ebola virus disease*. Available at: https://www.who.int/news-room/fact-sheets/detail/ebola-virus-disease.

Wu, Y. *et al.* (2022) 'Incubation Period of COVID-19 Caused by Unique SARS-CoV-2 Strains: A Systematic Review and Meta-analysis', *JAMA Network Open*, 5(8), p. e2228008. Available at: https://doi.org/10.1001/jamanetworkopen.2022.28008.

Yu, D. *et al.* (2003) 'Prevalence of IgG Antibody to SARS-Associated Coronavirus in Animal Traders --- Guangdong Province, China, 2003', *Maridity and Mortality Weekly Report Weekly*, 52(41), pp. 986–987. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5241a2.htm.

Zhou, Z. *et al.* (2021) 'Phenotypic and genetic characterization of MERS coronaviruses from Africa to understand their zoonotic potential', *Proceedings of the National Academy of Sciences*, 118(25), p. e2103984118. Available at: https://doi.org/10.1073/pnas.2103984118.

Zhu, N. et al. (2020) 'A Novel Coronavirus from Patients with Pneumonia in China, 2019', New England Journal of Medicine, 382(8), pp. 727–733. Available at: https://doi.org/10.1056/NEJMoa2001017.

Additional background references:

Britton, T., Ball, F. and Trapman, P. (2020) 'A mathematical model reveals the influence of population heterogeneity on herd immunity to SARS-CoV-2', *Science (New York, N.Y.)*, 369(6505), pp. 846–849. Available at: https://doi.org/10.1126/science.abc6810.

Cabrera Martimbianco, A.L. *et al.* (2021) 'Frequency, signs and symptoms, and criteria adopted for long COVID-19: A systematic review', *International Journal of Clinical Practice*, 75(10), p. e14357. Available at: https://doi.org/10.1111/ijcp.14357.

CDC (2023) *Respiratory Syncytial Virus Infection (RSV)*, *Centers for Disease Control and Prevention, About RSV*. Available at: https://www.cdc.gov/rsv/index.html.

CDC COVID-19 Response (2019) 'Covid-19 Science Update', *CDC COVID-19 Response*, 77. Available at: https://www.cdc.gov/library/covid19/pdf/public_pdfs/2021-02-19-Science-Update_Final_Public_v2.pdf.

Centers for Disease Control and Prevention (2022) *Types of Influenza Viruses*, *Influenza (Flu)*. Available at: https://www.cdc.gov/flu/about/viruses/types.htm (Accessed: 24 March 2023).

Centres for Disease Control and Prevention (2019) *Joint External Evaluations (JEE) for Improved Health Security*, *Advancing the Global Health Security Agenda: CDC Achievements & Impact*. Available at: https://www.cdc.gov/globalhealth/security/ghsareport/2018/jee.html.

Centres for Disease Control and Prevention (2022a) *Influenza Historic Timeline*, *Influenza Historic Timeline*. Available at: https://www.cdc.gov/flu/pandemic-resources/pandemic-timeline-1930-and-beyond.htm.

Centres for Disease Control and Prevention (2022b) *Symptoms of COVID-19*, *Symptoms of COVID-19*. Available at: https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html.

Centres for Disease Control and Prevention (2022c) *What is the Global Health Security Agenda?*, *Global Health - CDC and the Global Health Security Agenda*. Available at: https://www.cdc.gov/globalhealth/security/what-is-ghsa.htm.

Centres for Disease Control and Prevention, Division of Viral Diseases and National Center for Immunization and Respiratory Diseases (2021) *Science Brief: SARS-CoV-2 and Surface (Fomite) Transmission for Indoor Community Environments*, *CDC COVID-19*. Available at:

https://www.cdc.gov/coronavirus/2019-ncov/more/science-and-research/surface-transmission.html.

Chan-Yeung, M. (2004) 'Severe acute respiratory syndrome (SARS) and healthcare workers', *International Journal of Occupational and Environmental Health*, 10(4), pp. 421–427. Available at: https://doi.org/10.1179/oeh.2004.10.4.421.

Chaudhuri, S. *et al.* (2020) 'Modeling the role of respiratory droplets in Covid-19 type pandemics', *Physics of Fluids*, 32(6). Available at: https://doi.org/10.1063/5.0015984.

Chung, Y.-S. *et al.* (2018) 'Genetic Characterization of Middle East Respiratory Syndrome Coronavirus, South Korea, 2018', *Emerging Infectious Diseases*, 25(5), pp. 958–962. Available at: https://doi.org/10.3201/eid2505.181534.

Coalition for Epidemic Preparedness Innovations (2022) 'CEPI Investment Overview'. Coalition for Epidemic Preparedness Innovations. Available at: https://100days.cepi.net/wp-content/uploads/2022/03/250322_CEPI_Investment-Overview.pdf.

Cohen, P. *et al.* (2020) 'The Early Natural History of SARS-CoV-2 Infection: Clinical Observations From an Urban, Ambulatory COVID-19 Clinic', *Perspectives and Controversies, Mayo Clinic*, 96(6), pp. 1124–26. Available at: https://doi.org/10.1016/j.mayocp.2020.04.010.

Corman, V. *et al.* (2018) 'Hosts and Sources of Endemic Human Coronaviruses', *Advances in Journal Research*, 100, pp. 163–188. Available at: https://doi.org/10.1016/bs.aivir.2018.01.001.

Coronaviridae Study Group of the International Committee on Taxonomy of Viruses (2020) 'The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2', *Nature Microbiology*, 5, pp. 536–544. Available at: https://doi.org/10.1038/s41564-020-0695-z.

D'Arienzo, M. and Coniglio, A. (2020) 'Assessment of the SARS-CoV-2 basic reproduction number, R0, based on the early phase of COVID-19 outbreak in Italy', *Biosaf Health*, 2(2), pp. 57–59. Available at: https://doi.org/10.1016/j.bsheal.2020.03.004.

Dimensions (2023) *COVID-19 Report: Publications, Clinical Trials, Funding*. Automatic Data Summary. Digital Science & Research Solutions, Inc. Available at: https://covid-19.dimensions.ai.

Drexler, J.F., Drosten, C. and Jo, W.K. (2021) 'The evolutionary dynamics of endemic human coronaviruses', *Virus Evolution*, 7(1). Available at: https://doi.org/10.1093/ve/veab020.

Dunning, J. and Openshaw, P. (2010) 'Impact of the 2009 influenza pandemic', *Thorax*, 65, pp. 471–472. Available at: https://doi.org/10.1136/thx.2010.142398.

Esper, F. *et al.* (2023) 'Alpha to Omicron: Disease Severity and Clinical Outcomes of Major SARS-CoV-2 Variants', *The Journal of Infectious Diseases*, 227(3), pp. 344–352. Available at: https://doi.org/10.1093/infdis/jiac411.

Gao, Z. *et al.* (2021) 'A systematic review of asymptomatic infections with COVID-19', *Journal of Microbiology, Immunology and Infection*, 54(1), pp. 12–16. Available at: https://doi.org/10.1016/j.jmii.2020.05.001.

Global Early Warning System (no date) *GLEWS — The Global Early Warning System*, *ABOUT GLEWS+*. Available at: http://www.glews.net/.

Global Outbreak Alert and Response Network (no date) *GOARN*, *About GOARN*. Available at: https://goarn.who.int/ (Accessed: 15 May 2023).

Global Polio Eradication Initiative (no date) *GPEI-The Global Polio Laboratory Network*, *The Global Polio Laboratory Network*. Available at: https://polioeradication.org/polio-today/polio-now/surveillance-indicators/the-global-polio-laboratory-network-gpln/.

Global Preparedness Monitoring Board (no date) *About us - GPMB*, *About Us - What is the GPMB?* Available at: https://www.gpmb.org/about-us (Accessed: 15 May 2023).

Government of Canada (2022) *About - GPHIN - Canada.ca*, *About the Global Public Health Intelligence Network (GPHIN)*. Available at: https://gphin.canada.ca/cepr/aboutgphin-rmispenbref.jsp?language=en_CA.

GOV.UK (2023) *Human Animal Infections and Risk Surveillance group*, *Human Animal Infections and Risk Surveillance group*. Available at: https://www.gov.uk/government/groups/human-animal-infections-and-risk-surveillance-group.

Hodgson, D. *et al.* (2021) 'The potential for vaccination-induced herd immunity against the SARS-CoV-2 B.1.1.7 variant', *Eurosurveillance*, 26(20), p. 2100428. Available at: https://doi.org/10.2807/1560-7917.ES.2021.26.20.2100428.

Jackson, C. *et al.* (2013) 'School closures and influenza: systematic review of epidemiological studies', *BMJ Open*, 3(2), p. e002149. Available at: https://doi.org/10.1136/bmjopen-2012-002149.

Jayaweera, M. *et al.* (2020) 'Transmission of COVID-19 virus by droplets and aerosols: A critical review on the unresolved dichotomy', *Environmental Research*, 188. Available at: https://doi.org/10.1016/j.envres.2020.109819.

Lalchhandama, K. (2020) 'The chronicles of coronaviruses: the bronchitis, the hepatitis and the common cold', *Science Vision*, 20(1), pp. 43–53. Available at: https://doi.org/10.33493/scivis.20.01.04.

Lin, R.J., Lee, T.H. and Lye, D.C. (2021) 'From SARS to COVID-19: the Singapore journey', *The Medical journal of Australia*, 212(11), pp. 497–502. Available at: https://doi.org/10.5694/mja2.50623.

Muñoz-Escalante, J.C. *et al.* (2021) 'Respiratory syncytial virus B sequence analysis reveals a novel early genotype', *Scientific Reports*, 11(1), p. 3452. Available at: https://doi.org/10.1038/s41598-021-83079-2.

Padfield, S. *et al.* (2020) 'A practical review of "containment" during the influenza A (H1N1): an audit of the flu response centre in Yorkshire and the Humber', *Journal of Public Health (Oxford, England)*, 34(2), pp. 203–208. Available at: https://doi.org/10.1093/pubmed/fdr117.

Pekar, J. *et al.* (2021) 'Timing the SARS-CoV-2 index case in Hubei province', *Science (New York, N.Y.)*, 372(6540), pp. 412–417. Available at: https://doi.org/10.1126/science.abf8003.

Pung, R. *et al.* (2021) 'Effectiveness of Containment Measures Against COVID-19 in Singapore', *Epidemiology*, 32(1), pp. 79–86. Available at: https://doi.org/10.1097/EDE.0000000000001257.

The World Bank (no date) *Pandemic Emergency Financing Facility*, *Pandemic Emergency Financing Facility*. Available at: https://www.worldbank.org/en/topic/pandemics/brief/pandemic-emergency-financing-facility.

Usher, A.D. (2021) 'ACT Accelerator strains donors' aid budgets', *Lancet (London, England)*, 397(10290), p. 2137. Available at: https://doi.org/10.1016/S0140-6736(21)01284-8.

Wang, L.-F. *et al.* (2006) 'Review of Bats and SARS', *Emerging Infectious Diseases*, 12(12), pp. 1834–1840. Available at: https://doi.org/10.3201/eid1212.060401.

World Health Organisation (2008) *International Health Regulations (2005)*. Second. World Health Organisation. Available at: https://www.who.int/publications-detail-redirect/9789241580410.

World Health Organisation (2020g) *WHO Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020.* Available at: https://www.who.int/director-general/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020 (Accessed: 24 March 2023).

World Health Organisation (2020h) *Listings of WHO's response to COVID-19*, *Listings of WHO's response to COVID-19 - Timeline.* Available at: https://www.who.int/news/item/29-06-2020-covidtimeline.

World Health Organisation (2023) *Access to COVID-19 tools funding commitment tracker Snapshot*. Publication. Available at: https://www.who.int/publications/m/item/access-to-covid-19-tools-tracker.

World Health Organisation (no date a) *COVID-19 IHR Emergency Committee*, *COVID-19 IHR Emergency Committee*. Available at: https://www.who.int/groups/covid-19-ihr-emergency-committee (Accessed: 8 February 2023).

World Health Organisation (no date b) *Pandemic Influenza Preparedness (PIP) Framework*, *enza Preparedness (PIP) Framework*. Available at: https://www.who.int/initiatives/pandemic-influenza-preparedness-framework.

World Organisation for Animal Health, (2019) 'OIE Tool for the Evaluation of Performance of Veterinary Services, Seventh Edition, 2019'. Available at: https://www.woah.org/app/uploads/2021/03/2019-pvs-tool-final.pdf.

Zhou, P. *et al.* (2020a) 'A pneumonia outbreak associated with a new coronavirus of probable bat origin', *Nature*, 579, pp. 270–273. Available at: https://doi.org/10.1038/s41586-020-2012-7.

Zhou, P. *et al.* (2020b) 'Addendum: A pneumonia outbreak associated with a new coronavirus of probable bat origin', *Nature*, 579, pp. 270–273. Available at: https://doi.org/10.1038/s41586-020-2951-z.

Annex 2: Matters to be addressed from Letter of Instruction

Virology

1. Coronavirus viruses:
    a. A description and summary of the extent of scientific knowledge about such viruses both prior to the discovery of SARS CoV-2 virus and since;
    b. An explanation of the genetic link between SARS CoV-2 and other viruses; variations in the strain;
    c. An explanation of the predictability of the SARS CoV-2 virus including but not limited to; its emergence, its likely effects and the probability of mutations and the effects of any mutations.

2. An explanation of the difference between SARS-type viruses and other viruses, including influenza.

3. Details of the first discovery of the virus and its recognised effects at that time.

Epidemiology

4. A description of the epidemiology of the SARS CoV-2 virus. This should include, but not necessarily be limited to:
    a. its likely source;
    b. zoonotic origin;
    c. The first infections;
    d. The first detection;
    e. Its naming;
    f. Notification by WHO.

5. An explanation of the method by which SARS CoV-2 is transmitted, and how understanding of this has changed over time. This should include, but not necessarliy limited to:
    a. transmission methods - droplet and aerosol;
    b. transmission risks, including risks from indirect transmission;
    c. contact patterns;
    d. viral loads;
    e. environmental factors.

6. An explanation of the likelihood of infection, including the risk of infection from those who are pre-symptomatic and asymptomatic. Please include an explanation of how the understanding of pre-symptomatic and asymptomatic infection has changed over time.

7. The course of the disease and its clinical features.

Threats

8. Identification and brief description and role of the UK bodies concerned with threats. This should include, but are not limited to:
    a. The now abolished Threats, Hazards, Resilience and Contingency Committee (THRCC);
    b. the Human Animal Infections and Risk Surveillance ('HAIRS') Group;
    c. Cabinet Office's Horizon Scanning Programme team;
    d. The New and Emerging Respiratory Virus Threats Advisory Group ('NERVTAG')
    e. the transfer of HPA to the PHE;
    f. the transfer of health protection duties from Public Health England to the UK Health Security Agency in October 2021.

9. An explanation of the pros and cons of the creation and/or divergence of threat agencies.

International organisations and comparison

10. Examples of the global assessment of:
    a. the risks of a public health emergency;
    b. the risks of a coronavirus pandemic;
    c. the response to a and b.

11. An explanation of any perceived or actual deficiencies in international forecasting.

12. An explanation of the status of WHO within the exchange of information relating to global health risks and the International Health Regulations.

13. A description and explanation of other international 'co-ordinating' bodies. Please provide examples of their design, operation and interaction with the UK government.

14. A high level comparative examination of international structures referred to in your answers to question 10-14 and UK structures.