Witness Name: Professor Sir Christopher Whitty

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UK COVID-19 INQUIRY

MODULE 4

SIXTH WITNESS STATEMENT OF PROFESSOR SIR CHRISTOPHER WHITTY

Contents

I, PROFESSOR SIR CHRISTOPHER JOHN MACRAE WHITTY will say as follows:

Section 1: Introduction

1.1 I am the current Chief Medical Officer ("CMO") for England. This is the sixth witness statement that I have submitted to the UK COVID-19 Inquiry ("the Inquiry") and is made in response to a Rule 9 request dated 5 October 2023. I have previously submitted corporate statements on behalf of the Office of the Chief Medical Officer ("OCMO") and personal statements to Modules 1, 2 and 3.

1.2 This corporate statement explains the role of the OCMO in relation to the development, procurement, approval and delivery of COVID-19 vaccines and therapeutics. It has been produced with the assistance of a team within the OCMO (as well as some former OCMO staff) and so covers areas that are beyond my direct involvement. For several issues I have relied on records and will address issues of which I did not have first-hand experience.

1.3 The gradual move from social measures, also known as non-pharmaceutical interventions ("NPIs") to much more effective, and much less socially disruptive, clinical interventions (drugs, vaccines, diagnostics) was essential to the UK's response to COVID-19. When measured against realistic timelines it was achieved rapidly. This depended on a large scientific effort internationally, in which the UK played a major part.

1.4 Science is an international endeavour, depending on many thousands of scientists co-operating over time and space. Once clinical studies are undertaken, and in particular clinical trials, it also depends on volunteers. Both the scientific effort and the volunteering spirit of UK citizens were remarkable; over 1 million citizens in England volunteered to be part of clinical studies, this included research which helped to develop, test and determine the place of the vaccines and therapeutics covered in this Module of the Inquiry. We all owe both the scientists and the volunteers a great debt of gratitude; without them the mortality, burden of illness and social and economic disruption of the pandemic would have been still greater, and very possibly a lot greater. The same volunteer spirit, which cannot be taken for granted, is again likely to be critical in the response to future pandemics.

1.5 The OCMO played a part in this effort which we describe below. We would however like to emphasise that what was achieved in the scientific response to COVID-19 was

based on the collective effort of very large numbers of people, and scientific discoveries going back over decades.

Section 2: Overview of the role of the CMO for England and the OCMO

2.1 As CMO for England, I act as the UK Government's principal medical adviser. I am also the professional head of the public health profession and the medical profession in Government in England. I provide public health and clinical advice to the Prime Minister, Ministers in the Department of Health and Social Care ("DHSC"), and Ministers and senior officials across Government (restricted to England where responsibility is a devolved power). Responsibility for health is largely a devolved matter so Scotland, Wales and Northern Ireland have their own CMOs. From October 2019 until August 2021 I was concurrently the Chief Scientific Adviser to DHSC and Head (CEO equivalent) of the National Institute for Health Research ("NIHR") (now the National Institute for Health and Care Research), the UK's leading government research funder for applied medical research, and for this Module this dual role was important practically.

2.2 My roles have also included several senior positions in medical research and my academic background is as a clinical epidemiologist and clinical trialist in infectious diseases. Prior to becoming CMO, I was Professor of Public and International Health at the London School of Hygiene & Tropical Medicine. I was Head of the NIHR from January 2016 to August 2021 when this role passed to Professor Lucy Chappell. I have also been Chief Scientific Adviser and director of the extensive and multidisciplinary Department for International Development research programme. These roles equipped me with an understanding of how clinical research can be set up and conducted rapidly and safely including in emergencies. When I was not in Government, I had chaired the National Expert Panel on New and Emerging Infections ("NEPNEI") and briefly the Advisory Committee on Dangerous Pathogens ("ACDP"). When in a Government role, I chaired the UK Vaccines Network ("UKVN") from its inception in 2015 (both in and out of Government) and the UK Clinical Research Collaboration (UKCRC), among other bodies.

2.3 I am a Fellow of the Royal Society, the Academy of Medical Sciences, the Royal College of Physicians, the Faculty of Public Health and honorary Fellow of the Faculty of Pharmaceutical Medicine, the Royal College of Paediatrics and Child Health and

the Royal College of General Practitioners among other learned bodies. I remain a National Health Service ("NHS") consultant physician in infectious diseases at University College London Hospitals and have practical experience of research in the NHS.

2.4 The CMO is a professionally independent position at Permanent Secretary level. Since the position was first established in 1855, the CMO has always had an advisory role in Government, a leadership role for the public health and medical professions, a public facing role to inform the public of health issues and a scientific role. The professionally independent nature of the position and that of the Deputy Chief Medical Officers ("DCMO") is demonstrated by the fact that the CMO can write reports and make public statements which do not accord with Government policy when relevant to public health. I sit on the Executive Committee and the Board of the Department of Health and Social Care. The CMO currently reports to the DHSC Permanent Secretary.

2.5 The DCMOs support the CMO but, as senior medical advisers, can also act on their own behalf. The DCMOs provide advice as senior clinical or public health experts in their own right. Usually, there is a principal DCMO for health improvement (mainly focused on non-communicable diseases such as cancer and heart disease) and one for health protection (e.g. infectious diseases and other emergencies). During most of the pandemic, all the DCMOs in post worked, at least in part, as part of the COVID-19 response.

2.6 I was appointed CMO on 1 October 2019 and remain in post. Three full-time DCMOs were in post during the pandemic period relevant to this Module. Professor Sir Jonathan Van-Tam took on the role of DCMO for health protection in 2017 and relinquished it upon taking up a senior position in academia in March 2022. Professor Dame Jenny Harries became DCMO for health improvement in 2019 and continued in that role until taking up the position of CEO of the UK Health Security Agency ("UKHSA") in April 2021. Professor Thomas Waite was appointed as an interim DCMO covering COVID-19 in July 2021. He subsequently succeeded Professor Van-Tam as DCMO for health protection and remains in post. In addition, Dr Aidan Fowler, whose main role is as the National Director of Patient Safety in NHS England ("NHSE"), has the title of DCMO and was seconded as a DCMO from March 2020.

2.7 Professor Van-Tam was the lead DCMO for most of the activities covered by this Module. He has a background in pharmaceutical studies (from both an academic and an industry perspective) and the public health aspects of communicable diseases. He

has specialised in respiratory viruses for over 30 years, especially influenza, and previously chaired NERVTAG from 2014-2017. His professional background will be further laid out in his personal witness statement in response to a Rule 9 request for this Module from the Inquiry. We (the DCMOs and I) also worked very closely on drugs and vaccines with the Government Chief Scientific Adviser ("GCSA") Sir Patrick Vallance who is an eminent clinical pharmacologist and was President of R&D in the pharmaceutical company, Glaxo Smith Kline ("GSK"), and a Professor of Medicine among other roles prior to becoming GCSA. We also worked closely with Professor Sir Stephen Powis, the National Medical Director of NHSE and a distinguished clinician-scientist.

2.8 Collectively, the DCMOs and I are supported by a single private office (a small team that support senior civil servants or Ministers). Two senior private secretaries (Grade 7) led this team and were responsible for ensuring that we were supported in our roles; the senior private secretaries led on science and policy respectively. In addition to the traditional make up of a private office (private secretaries and diary managers) the team includes public health speciality registrars - trainees in public health - who edit the annual reports issued by the OCMO and provide additional clinical and public health input if appropriate. At its largest size the OCMO was 19 people, including the CMO and DCMOs; its current size is 12.

Section 3: Glossary of Terms

3.1 In this statement I refer to a number of acronyms, committees and groups which it may be helpful to summarise at the beginning so they can be easily understood when reading the statement in isolation.

- ACDP: The Advisory Committee on Dangerous Pathogens. The ACDP is an expert advisory committee of DHSC. It is chaired by Professor Thomas Evans and provides scientific advice on the risks of exposure to pathogens.
- CHM: The Commission on Human Medicines. See paragraph 6.12 below.
- COG-UK: COVID-19 Genomics UK Consortium. COG-UK was a group of academic institutions and public health agencies that was created in April 2020 to collect, sequence, and analyse genomes of SARS-CoV-2 as part of the UK pandemic response.

- CRN: The NIHR Clinical Research Network. The CRN is funded by DHSC via the NIHR to improve national health through research. It works in partnership with the NHS, universities, local government, and other research funders to fund health and social care research.

- CSA: Chief Scientific Adviser to a Government department. CSAs provide independent scientific advice to their main department, and individually and collectively give scientific advice across Government in their specialist areas.

- HRA: The Health Research Authority. See paragraph 6.13 below.

- JCVI: The Joint Committee on Vaccination and Immunisation. See paragraphs 6.6 to 6.10 below.

- MHRA: The Medicines and Healthcare Products Regulatory Agency. See paragraph 6.11 below.

- MRC: The Medical Research Council. MRC is part of UK Research and Innovation ("UKRI"). It is responsible for coordinating and funding medical research to prevent illness, develop therapies and improve human health. It concentrates on basic research through to translational and complements the work of NIHR.

- NEPNEI: The National Expert Panel on New and Emerging Infections. NEPNEI was established to provide independent expert advice to the CMO on public health risk from new and emerging infections.

- NERVTAG: The New and Emerging Respiratory Virus Threats Advisory Group. NERVTAG is a standing committee of DHSC. It advises the CMO and DHSC on the threat posed by new and emerging respiratory viruses. The NERVTAG COVID-19 Therapeutics Sub-Committee was established early in 2020 to provide initial advice on therapeutics.

- NHSE: NHS England. NHSE leads the NHS in England.

- NIHR: The National Institute for Health Research (the National Institute for Health and Social Care Research since April 2022). NIHR is the main Government funder of applied research in health and social care, and one of the largest government funders of medical, public health and care research in Europe. It supports a major network of research in the NHS as well as in universities. It concentrates on translational and applied research and complements the work of MRC. As CSA in

DHSC I was the head (CEO equivalent) of NIHR for the early part of the pandemic until August 2021.

- OSCHR: The Office for Strategic Coordination of Health Research. OSCHR is a forum operating across the NHS designed to bring together public funders of health research work with other stakeholders, especially NIHR and MRC.

- PHE: Public Health England. PHE was the forerunner to UKHSA on health protection. It also had responsibility for health improvement (primarily non-communicable diseases). The functions of PHE were separated in 2021, when UKHSA and the Office for Health Improvement and Disparities ("OHID") were established.

- SAGE: The Scientific Advisory Group for Emergencies. SAGE is an independent advisory group, convened to provide scientific advice to support decision-making in COBR in the event of a national emergency.

- UKCRC: The UK Clinical Research Collaboration. UKCRC is a partnership that brings together the main UK research funding bodies, academia, the NHS, regulatory bodies, the bioscience, healthcare and pharmaceutical industries, and patients, with the aim of improving the way clinical research is conducted in the UK.

- UKHSA: The UK Health Security Agency. Established in name in April 2021 and formally operational from October 2021, UKHSA is responsible for protecting the public from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats.

- UKRI: UK Research and Innovation. UKRI is the umbrella body of the seven research councils, including the MRC.

- UKVN: The UK Vaccine Network. See paragraph 6.14 below.

- VTF: The Vaccines Taskforce. See paragraph 6.15 below.

Section 4: Overview of the OCMO's role in the UK's research response to COVID-19

4.1 The development and dissemination of medical countermeasures to COVID-19 can be broken down into four elements:

i. Research

ii. Procurement

iii. Regulatory Approval

iv. Delivery

4.2 I discuss each of these elements, in relation to both vaccines and therapeutics, in more detail in the sections below. However, in broad terms, the OCMO played a significant role in supporting research, a more limited role in advising others about technical aspects of science or medicine relevant to procurement and delivery, and a minimal role in approvals that did not extend to having any influence over actual regulatory decisions taken by the MHRA. Outside of a severe public health crisis, the accepted and most practical sequential 'running order' for the elements above is: Research – Regulatory Approval – Procurement – Delivery. As will become apparent during this witness statement and many others, when faced with a severe pandemic and very substantial international competition for initially scarce vaccines and therapeutics, it was not always possible nor even advisable to follow a normal running order and some activities ran in parallel. Furthermore, for some of the therapeutics described, these were repurposed already-licenced medicines (e.g. dexamethasone) so there was no need for a 'Regulatory Approval' stage.

4.3 Given the OCMO's significant role in the research stage, I first set out here a general overview of the UK's research structures and the OCMO's involvement in the UK's research response to COVID-19.

4.4 The OCMO played a part in preparing the UK to respond to COVID-19 and to move from NPIs to medical countermeasures by taking action to set up research from the earliest stage of the pandemic. As a team, we were involved in ensuring early research happened through setting up early research calls, directing research panels on priorities, funding research and facilitating quick progress from that research. We also strongly encouraged clinicians to take part in research and ensured that research was

built into the national response from the start (i.e., in the "contain, delay, research, mitigate" strategy). There was some surprise by some in government that we put such heavy emphasis on research from January 2020 before the UK had had any domestic transmission or any deaths and before the World Health Organization ("WHO") had declared a Public Health Emergency of International Concern. We (the OCMO), and the GCSA, were however certain that if a pandemic occurred it was only by moving to medical countermeasures of drugs, vaccines and diagnostics that COVID-19 would eventually be de-risked.

4.5 NPIs are essential for any major infectious threat before there are medical countermeasures but they are invariably less well targeted, less effective and more destructive socially and economically than medical countermeasures such as drugs and vaccines. They can reduce and delay transmission if applied thoroughly, but once an individual is infected, the severity of the organism (in this case SARS-CoV-2) is unmodified unless medical countermeasures are in place. For that reason, transitioning from an NPI-led response to a medical countermeasure-led response needs to happen at the earliest practical and safe opportunity. Generally, this transition will be a phased one. The combination of which medical countermeasures would be effective, and the order in which a breakthrough or other significant discovery might occur, was not predictable at the start of the pandemic. Although vaccines proved the most effective in COVID-19, at the start of the pandemic this was far from a given. For the last major pandemic, HIV, we still do not have a vaccine despite a massive scientific effort to produce one, and it was therapeutics (drugs) which have eventually largely de-risked the HIV pandemic. The first major clinically important change was not in fact a vaccine, but the discovery by UK clinician-scientists that dexamethasone would reduce mortality in hospitalised patients in June 2020. This remarkably fast discovery would not have occurred so early unless the UK had focused resources on prioritised research on COVID-19 from late January 2020.

4.6 The UK CMOs, DCMOs, GCSA and NHS National Medical Director jointly with several distinguished scientists wrote a 'Technical Report on the COVID-19 Pandemic in the UK' for our successors. This contains significant technical information relevant to this Module, especially Chapters 1, 3 and 9. As we observe in the introduction to Chapter 3 of the Technical Report published on 1 December 2022:

"In all pandemics and major epidemics the initial response depends on sparse information, and in the case of a new pandemic such as COVID-19 there will often be no proven medical countermeasures. The key purpose of research is to understand

the disease itself, to improve information for policy and clinical decision making, to optimise existing clinical treatment and to provide the tools to move from social to medical countermeasures. The central role of research in supporting the response is sometimes underestimated by non-medical planners and policymakers. Since the mid-19th century science has always been, and will almost always be, the exit strategy from pandemics and epidemics" **(CJMW6/001 – INQ000203933)**.

4.7 My contribution to COVID-19 research cut across my roles as CMO, DHSC CSA and head of NIHR. Disentangling retrospectively when I was acting as CMO and when as CSA or head of NIHR is not always straightforward, and in reality the roles were complementary. The OCMO set up research calls and provided a bridge between researchers and Government to ensure the most useful research was carried out to inform policy. Professor Van-Tam also took a leading role in this area and the GCSA was involved. Our greatest concerns were that research would not be fast enough (as was generally the case during the influenza pandemic in 2009), or that multiple, underpowered, studies would be launched which competed locally for patient volunteers, failed to reach their endpoints, and so yielded inconclusive findings. Our actions were intended to reduce those risks and harness the substantial research excellence in the UK.

4.8 The UK has a centralised health delivery system through the NHS, and two major Government funders of clinical research: NIHR which I led, and MRC, part of UKRI with which we worked very closely and often jointly funded. Additionally, the UK has a strong research charity sector including the Wellcome Trust as well as several other major research charities. There is good co-ordination under normal circumstances between these funders including through OSCHR and UKCRC. It was therefore well situated for the Government funders of research, NIHR and MRC, to coordinate which research was prioritised. It was important to the UK's research response that we had previously existing clinical funders, with significant budgets, well-established ways of working, effective national ethical review (the HRA) and regulation (the MHRA), and a strong clinical research culture.

4.9 The NHS in England and the other nations of the UK has a long history of conducting clinical research. Relatively few countries have a single dominant government-supported health system and this makes (or can make) rapid coordination of health research much easier. The NIHR has an extensive infrastructure embedded in the NHS in England to conduct clinical research, including research space, clinical

academics and research nurses. This infrastructure can be used to conduct clinical research funded via any route - so includes MRC, charity and industry funded studies.

4.10 In addition to the public funders the UK also has a vibrant life sciences industry. This relies on the government research ethics system (the HRA), the regulatory system (the MHRA) and, to conduct trials, NIHR infrastructure and NHS clinicians. In turn, academic scientists funded with public money did much of the testing of vaccines and therapeutics developed in the private sector. The private and public systems should therefore be seen as complementary and, in our view, in this emergency they generally worked well together, particularly on Phase 3 and Phase 4 studies.

4.11 The UK also had the UKVN, which was established in 2015 after the Ebola crisis in West Africa to address the perceived lack of incentive for the pharmaceutical industry to investigate the development of vaccines for intermittent infectious disease outbreaks and epidemics in low-income countries. I have chaired the UKVN in a personal capacity since its inception and continue to do so.

4.12 In early January 2020 it was still unclear what the impact of COVID-19 would be, but it was clear to the OCMO that if it did become a pandemic, research of multiple forms would be key to the response over the course of the pandemic. The OCMO team worked with the UKVN team in DHSC, NIHR and UKRI to launch a rapid response research call **(CJMW6/002-004 – INQ000047636, INQ000047637 & INQ000047587)**. Speed was important so the research call went live on 4 February 2020 **(CJMW6/005 & 006 – INQ000047670 & INQ000047676)**. For context the first official UK case of COVID-19 was announced on 31 January 2020 and the first death from COVID-19 in the UK was on 5 March 2020. The deadline for the first part of the research call (vaccines and treatments) was 13 February. The deadline for the second part (any other COVID-19 research) was 27 February **(CJMW6/007 – INQ000047681)**. Professor Van-Tam briefed the adjudication panel on the epidemiological situation and what kind of research (policy relevant research which would yield timely results) was needed so that the research chosen would be the most likely to help **(CJMW6/008 – INQ000047784)**, but the independent panel, not Professor Van-Tam, selected the studies in priority order. This first call funded the RECOVERY trial and the Oxford/AstraZeneca vaccine **(23 March 2020 – CJMW6/009 – INQ000203986)**. A total of 26 projects were funded at a cost of approximately £26 million. After the initial call a second rolling research call was opened, where applications were made and decided upon in a rolling fashion. Four highlight notices on ethnicity, mental health, seroprevalence and transmission were issued to seek proposals on these specific

topics, aimed at research for public health benefit within 12 months. Overall, the rolling call led to the commission of approximately 50 studies at a cost of approximately £50 million.

4.13 Many of these studies proved central to the UK and international response. Examples include:

i. The RECOVERY trial – studying treatments for hospitalised patients.

ii. The PRINCIPLE trial – studying treatments in primary care.

iii. The PANORAMIC trial – studying new antiviral treatments in the community.

iv. The REMAP-CAP trial – studying treatments for patients with severe community-acquired pneumonia.

v. Preclinical and clinical trials of the Oxford/AstraZeneca vaccine and developing manufacturing processes at scale.

vi. PHOSP-COVID – a national consortium to understand and improve long-term health outcomes from COVID-19.

vii. Research and surveillance on COVID-19 using the OpenSAFELY platform, which also looked at vaccine coverage and effectiveness.

viii. UK-REACH – studying ethnicity and COVID-19 outcomes in healthcare workers.

4.14 The OCMO also readied the research system to respond across the board by ensuring that the existing infrastructure was pivoted to respond to COVID-19 **(CJMW6/010 – INQ000047546)**. One way in which this was done was that NIHR set up a prioritisation process. Trials, observational studies and other research studies we considered of particular importance for clinical practice, public health or policy were designated Urgent Public Health badged ("UPH") by an independent expert panel, which I signed off as CMO/CSA. This focused the research workforce on a smaller number of trials and other studies and resulted in larger recruitment across a narrower remit; therefore ensuring that key trials and other studies were able to achieve end points which were adequately statistically powered rapidly. UPH badging also meant HRA and MHRA regulatory approval was expedited. About 1,600 applications in total were received, with 101 studies UPH approved. Targeted support from NIHR research infrastructure was important for partially or wholly commercial trials, such as the Novavax vaccine,

as well as for entirely publicly funded ones. The CRN supported recruitment of over a million patients from all across the UK into UPH studies (March 2020 – March 2021). The UPH process did, by necessity, mean that other COVID-19 studies received less support from NIHR sources, and important non-COVID-19 research had to be deprioritised.

4.15 Following a review of the 2009 pandemic influenza outbreak, the NIHR commissioned a portfolio of projects, put on standby in a maintenance-only state and awaiting activation in the event of a new influenza pandemic. The portfolio included studies covering surveillance, communications, triage, and clinical management. Some of those sleeping contracts were stood up and repurposed for COVID-19. This included:

i. Evaluating and improving communication with the public during a pandemic, using rapid turnaround telephone surveys.

ii. Pandemic Respiratory Infection Emergency System Triage.

iii. Maternal and perinatal outcomes of pandemic influenza in pregnancy.

iv. Real time refinement and validation of criteria and tools used in primary care to aid hospital referral decisions for patients of all ages in the event of surge during an influenza pandemic.

v. The ASAP trial (a double-blinded randomised controlled trial of early low dose steroids in patients admitted to hospital with influenza infection during a pandemic), which was not activated but the study protocol was used to inform the dexamethasone arm of the RECOVERY trial.

4.16 Professor Van-Tam who had worked on FLU-CIN, a network of hospital surveillance for flu, set in train work to stand up CO-CIN, a network of hospital surveillance for COVID-19. Over the course of the pandemic before standing down it recruited over 300,000 patients. It provided the first UK open-access comprehensive clinical-epidemiological data at scale in the pandemic, reporting weekly to DHSC and SAGE. CO-CIN reports and papers fed into 80 SAGE meetings, 72 NERVTAG meetings, and many subgroups. UK nation's public health agencies were given direct access to the raw data. Aggregate data was shared with the WHO, US CDC and ECDC in Europe. This helped inform clinical management, therapeutic and vaccine decisions.

4.17 In the March 2020 Budget, Her Majesty's Treasury ("HMT") provided the NIHR with £30 million of new funding to enable further rapid research into COVID-19. This was

colloquially known as the 'fighting fund'. This could be spent with joint agreement from me and the GCSA. The idea was that given the health emergency there would be some discrete pieces of research or related work that needed to be done so rapidly that it was not possible to fund them through the normal mechanisms, so this alternative funding was used. Work funded through this route included:

i. £9.9 million for clinical trials phase 1 and 2 of the Oxford/AstraZeneca vaccine.

ii. £9.5 million for CO-CIN to collect data for hospitalised COVID-19 patients.

iii. £8.5 million for COG-UK to deliver large scale, rapid sequencing of the disease to monitor changes in the virus to give early warning of the emergence of new variants.

Section 5: Chronology of key dates in respect of vaccines and therapeutics

5.1 I set out below a chronology of what we perceive to be some key dates in respect of vaccines and therapeutics from the start of 2020, concentrating on the earlier period in particular. As with all science the development of vaccines and therapeutics built on decisions taken, and research undertaken, over many previous years and in many countries. The sections below focus on UK science, and particularly that in England, as that was our area of responsibility. We have included some important negative results (the drug did not work) because these can be as important for changing or confirming clinical practice as positive ones (the drug does work). This chronology concentrates on trials, but many UK observational studies or platforms such as SIREN and OPENSafely also gave essential information on safety and efficacy of drugs and vaccines. Although the speed of the outputs may look normal to those not used to clinical research it was very rapid compared to any previous emergency we are aware of, and exceptionally rapid compared to non-emergency situations.

2020

- **Mid-January** onwards - Oxford University scientists under Professor Dame Sarah Gilbert pivoted a MERS coronavirus research programme (funded by the UKVN) over to SARS-Cov-2.

- **27 January** – GCSA, DCMOs and I met with research funders (UKRI, MRC, the Wellcome Trust and NIHR) to discuss setting up the rapid response research call.

- **4 February** – Rapid response research call with funding from NIHR and UKRI went live (Deadline for the first part – 13 February. Deadline for the second part – 27 February).

- **2 March** – NIHR-UKRI Rapid response research call assessment panel met for the first part of the call (vaccines and therapeutics).

- **16 March** - Professor Powis and I wrote to all NHS Trusts asking for their full support in implementing the RECOVERY trial of drugs for hospitalised patients with COVID-19 **(CJMW6/011 – INQ000048103)**.

- **17 March** – NIHR-UKRI Rapid response research call assessment panel met for the second part of the call (wider research).

- **19 March** – First patients recruited to the RECOVERY trial of drugs for hospitalised patients with COVID-19.

- **23 March** – NIHR-UKRI Rapid response research call – first six projects formally announced (note that researchers were told before this date and started the research). Including £2.1 million for RECOVERY and £2.6 million for the Oxford/AstraZeneca vaccine.

- **24 March** – 10th patient recruited to the RECOVERY trial.

- **27 March** – 100th patient recruited to the RECOVERY trial.

- **27 March** – Human volunteers started to be screened for the Oxford virus-vectored vaccine (what later became the Oxford/AstraZeneca vaccine).

- **1 April** – Vaccines Taskforce Programme Board met for the first time.

- **1 April** – UK CMOs and Professor Powis sent letter to clinicians asking for every effort to be made to enrol COVID-19 patients in clinical trials, not to use novel or off-label treatments outside of a trial **(CJMW6/012 – INQ000068589)**.

- **3 April** – 1,000th patient recruited to the RECOVERY trial.

- **17 April** – Rapid response research call – second wave of projects announced (note that researchers were told before this date and started the research).

- **17 April** – The PRINCIPLE trial of therapeutics in primary care (early disease) opened.

- **23 April** – Phase 1/2 trial of the Oxford/AstraZeneca vaccine started.

- **6 May** – the UK CMOs and Professor Powis wrote to clinicians to encourage enrolment by mobilising the NIHR and equivalent workforce in devolved nations **(CJMW6/013 – INQ000069095)**.

- **10 May** – 10,000th patient recruited to the RECOVERY trial.

- **28 May** – Phase 2/3 trial of the Oxford/AstraZeneca vaccine started in the UK. (Parallel trials started subsequently in Brazil and South Africa).

- **5 June** – The RECOVERY trial demonstrated no clinical benefit from hydroxychloroquine.

- **16 June** – The RECOVERY trial demonstrated that dexamethasone reduces deaths by up to one third in the sickest patients. The UK CMOs and Professor Powis wrote out to the NHS on the same day so NHS patients were able to receive the treatment immediately if attending clinicians thought it relevant to their care **(CJMW6/014 – INQ000069714)**. This is discussed in more detail at paragraphs 7.12 to 7.14.

- **20 June** – The SIREN study led by PHE launched. It would go on to give many insights into immunity following infection and vaccination.

- **29 June** – The RECOVERY trial showed no clinical benefit from Lopinavir-ritonavir.

- **2 September** – REMAP-CAP results showed corticosteroids may be an effective treatment.

- **19 November** – REMAP-CAP initial results showed tocilizumab may have some benefit.

- **2 December** – Government authorised the Pfizer/BioNTech vaccine for emergency use in the UK on the advice of the MHRA.

- **2 December –** JCVI published its first advice on vaccine prioritisation.
- **8 December** – First UK citizen vaccinated outside of a clinical trial.
- **8 December** - Oxford/AstraZeneca trial results first published showing vaccine efficacy and safety.
- **9 December** – MHRA announced a 15-minute observation period following vaccination. Anyone with a history of anaphylaxis to vaccine, medicine or food should not receive the Pfizer/BioNTech vaccine.
- **14 December** – The RECOVERY trial showed no clinical benefit from azithromycin.
- **30 December** – Government authorised the Oxford/AstraZeneca vaccine for emergency use in the UK on the advice of the MHRA.
- **30 December** – UK CMOs published their clinical advice on extending the interval between the first and second vaccine doses.
- **31 December** – UK CMOs and Professor Van-Tam issued a letter to the medical profession explaining the scientific and public health rationale for extending the interval between the first and second vaccine doses.

2021

- **4 January** – Deployment of the Oxford/AstraZeneca vaccine began in the UK.
- **7 January** – REMAP-CAP preprint showed that tocilizumab and sarilumab are likely to reduce the risk of death.
- **8 January** – Government authorised the Moderna vaccine for emergency use in the UK on the advice of MHRA.
- **15 January** – The RECOVERY trial showed no clinical benefit from convalescent plasma from people previously infected. This was considered a surprising negative result.

- **19 January** – The SIREN study found that antibodies from past COVID-19 infection provide 83% protection against reinfection for at least 5 months, but that some people with antibodies may still carry and transmit the virus.

- **25 January** - The PRINCIPLE trial showed that doxycycline and azithromycin were not effective in primary care (early disease).

- **28 January** - Interim results of the Novavax vaccine phase 3 trial carried out in the UK with more than 15,000 participants were published showing good efficacy.

- **11 February** – The RECOVERY trial showed that tocilizumab reduces the risk of death when given to hospitalised patients with severe COVID-19.

- **5 March** – The colchicine arm of the RECOVERY trial was closed on the basis that there was sufficient data to show the drug was not effective.

- **1 April** - The PRINCIPLE trial showed that the asthma drug Budesonide reduced the period of illness in COVID-19 in primary care (early use in milder disease).

- **7 April** – Deployment of the Moderna vaccine began in the UK.

- **7 April** – JCVI advised that there is a preference for people under 30 to be offered Pfizer/BioNTech or Moderna vaccines as an alternative to the Oxford/AstraZeneca vaccine, where available, due to extremely rare adverse events related to blood clots. This advice was predicated on there being another vaccine available.

- **14 April** – Government launched consultation on making vaccination a condition of deployment in care homes with older adults.

- **16 April** – JCVI advised that pregnant women should be offered the vaccine at the same time as the rest of the population, based on their age and clinical risk group with a preference for the Pfizer/BioNTech or Moderna vaccines, where available.

- **7 May** – JCVI advised that people under 40 should be offered an alternative to the Oxford/AstraZeneca vaccine, where available, due to extremely rare blood clots with greater prevalence in that age group. This advice was predicated on there being another vaccine available.

- **18 May** – The results of the colchicine arm of the RECOVERY trial were published, confirming that the drug was not effective.

- **26 May** - The PRINCIPLE trial showed that colchicine was not effective in primary care.

- **27 May** – a preliminary report by the ComFluCOV study found that almost all reactions to receiving a combination of 'flu and COVID-19 vaccines were reported as mild to moderate and that, with the exception of the co-administration of Oxford/AstraZeneca and FluAd vaccines, giving COVID-19 vaccines and influenza vaccines together was non-inferior to giving the COVID-19 vaccine alone.

- **28 May** – MHRA approved the Janssen single-dose vaccine for use in the UK (it was never deployed).

- **4 June** – MHRA concluded that the Pfizer/BioNTech vaccine was safe and effective for use in children aged 12 to 15 years old.

- **7 June** – data from the Com-COV2 study (looking at the effects of a Moderna or Novavax second dose in people primed with Oxford/AstraZeneca or Pfizer/BioNTech, with an 8-12 week interval) indicated an increase in reactogenicity in recipients of Moderna as a second dose, but similar patterns of reactogenicity were observed in recipients of Novavax as a second dose, compared to those who received an homologous schedule.

- **8 June** – The RECOVERY trial showed that Aspirin does not improve survival for patients hospitalised with COVID-19.

- **28 June** – data from the Com-COV study indicated that both mixed schedules (Oxford/AstraZeneca followed by Pfizer/BioNTech, and Pfizer/BioNTech followed by Oxford/AstraZeneca) induced high concentrations of antibodies against the SARS-CoV-2 spike IgG protein when doses were administered 4 weeks apart.

- **4 August** – JCVI issued advice on vaccination of under-18s (see paragraph 6.48 below).

- **17 August** – MHRA approved the Moderna vaccine for use in 12- to 17-year olds.

- **3 September** - JCVI issued further advice on vaccination of 12- to 15-year-olds and recommended that further advice be sought from the UK CMOs.

- **13 September** – UK CMOs issued advice on the vaccination of 12- to 15-year-olds.

- **2 December** – data from the COV-BOOST study were published, confirming that all study vaccines (Oxford/AstraZeneca, Pfizer/BioNTech, Moderna, Novavax, Valneva, Janssen and Curevac) boosted antibody and neutralising responses following an initial two doses of either Oxford/AstraZeneca or Pfizer/BioNTech, with no safety concerns.

- **8 December** - The PANORAMIC trial of novel antiviral COVID-19 treatments for use early on in the illness by people in the community with COVID-19 began.

- **14 December** – With MHRA and CHM support, the UK CMOs advised a temporary suspension of the 15-minute observation time following administration of Pfizer and Moderna vaccines, to allow for increased speed of vaccination and booster programmes in response to the spread of the Omicron variant.

- **22 December** – JCVI issued further advice on vaccination of children and young people, recommending primary vaccination of 5- to 11-year-olds in a clinical risk group or who are a household contact of someone who is immunosuppressed, and booster vaccination of 12- to 17-year-olds.

- **22 December** – data from the Com-COV study indicated a greater increase in antibodies in participants immunised at a 12-week interval versus participants immunised at a 4-week interval.

2022

From the beginning of 2022, the volume of output from trials and other studies in the UK and internationally was very large and cannot easily be summarised.

- **16 February** – JCVI issued advice on vaccination of 5- to 11-year-olds, recommending non-urgent vaccination of those who are not in a clinical risk group.

- **3 March** - The RECOVERY trial showed that Baricitinib (an anti-inflammatory treatment for rheumatoid arthritis) reduced mortality by around $^{1}/_{5}$.

- **22 December** – The PANORAMIC study shows Molnupiravir (an antiviral) did not reduce hospitalisation or deaths in vaccinated people at high risk **(CJMW6/014a – INQ000391271**.

Section 6: Vaccines

Key individuals, government and non-government bodies

6.1 I am asked by the Inquiry to provide details of the individuals, government and non-government bodies with whom the OCMO worked in relation to matters relevant to COVID-19 vaccines. I do so here.

Individuals

6.2 Professor Van-Tam had an extensive history in vaccine development and respiratory infections, and he therefore took the lead in the vaccine work including that with the JCVI, and NERVTAG (which he had previously chaired). He was later joined in this work by Professor Thomas Waite, who has a background in infectious disease epidemiology, and who was therefore able to take on some of the responsibilities of Professor Van-Tam.

6.3 In our view the UK was very fortunate that Sir Patrick Vallance was GCSA during this pandemic. As a distinguished clinical pharmacologist and physician and previous Professor of Medicine and President of GSK he had a really strong understanding of the medical as well as the scientific concepts involved in the development of vaccines and therapeutics. He was consistently exceptionally collegiate to the OCMO over the prolonged period of stress of the pandemic and had a deep understanding of the UK science environment, both academic and in industry. It therefore made the OCMO-GCSA interactions extremely easy at a technical and personal level. This was far from a given. Sir Patrick and I also benefitted greatly from the advice of the CSA network across Government in addition to the scientific committee structure.

6.4 We were also fortunate to be working with Professor Powis. A distinguished clinical academic in renal medicine and immunology as well as a previous NHS physician he has a very good understanding of the realities of clinical research and practice in the NHS, and the working relationship was close and effective.

6.5 The other key individuals that I, and others within the OCMO, worked with in relation to vaccines were:

i. Professor Wei Shen Lim – Chair of the JCVI (for the purposes of advising on COVID-19).

ii. Dame June Raine – CEO of the MHRA.

iii. Dame Emily Lawson – Senior Responsible Officer for the NHS COVID-19 vaccine deployment at NHSE.

iv. Steve Russell – Chief Delivery Officer of NHSE.

v. Professor Sir Munir Pirmohamed – Chair of the CHM.

vi. Dr Louise Wood – Director of the Science, Research and Evidence Division of DHSC and de facto the operational head of NIHR.

vii. Professor Fiona Watt and Professor John Iredale – successively Executive Directors of MRC.

Government bodies

6.6 **JCVI:** the JCVI is an independent Departmental Expert Committee ("DEC") and Scientific Advisory Committee ("SAC") and, unlike most other DECs/SACs, has a statutory basis in England and Wales. It is formed of a main committee with subject specific sub committees. It was originally an advisory board for polio immunisation that became the JCVI in 1963. It was put on a statutory footing when it became a SAC, established in England and Wales under the NHS Act 1977. The NHS (Standing Advisory Committees) Order 1981[1] established the JCVI in its current form. That order specifies that it is constituted for the purpose of advising on *"The provision of vaccination and immunisation services being facilities for the prevention of illness".*

6.7 Appointments to the JCVI committee are made on merit and in accordance with the principles of the Code of Practice for Scientific Advisory Committees and the Cabinet Office's Governance Code for Public Appointments, which is regulated by the Commissioner for Public Appointments. New member appointments are routinely made through an open competition.

6.8 The JCVI provides advice and recommendations for all UK Health Departments based on consideration of scientific and other evidence that is used by Government to inform, develop and make policy. All four nations have observers on the JCVI and while it has no statutory basis in Scotland or Northern Ireland, on most vaccine programmes JCVI advice is adopted.

[1] SI 1981/597

6.9 The JCVI, when providing advice on COVID-19, was chaired by Professor Wei Shen Lim, standing in for Professor Sir Andrew Pollard who had a perceived conflict of interest arising from involvement with what became the Oxford/AstraZeneca vaccine.

6.10 The JCVI advice on COVID-19 is public and was widely publicised at the time with the Chair briefing the public, often alongside Professor Van-Tam.

6.11 **MHRA:** the MHRA is an executive department of DHSC and is the independent expert body that regulates medicines, medical devices and blood components for transfusion in the UK. It was responsible for approving COVID-19 vaccines for use in the UK and continually monitoring their safety once the rollout was underway. The MHRA is led by Chief Executive Officer, Dr June Raine.

6.12 **CHM**: the CHM is an advisory non-departmental public body sponsored by DHSC. It advises ministers on the safety, efficacy and quality of medicinal products. It worked in collaboration with the MHRA to monitor and advise on the safety of the COVID-19 vaccines. It is chaired by Professor Sir Munir Pirmohamed.

6.13 **HRA:** the HRA provides ethical and organisational permissions for clinical or other studies including human subjects, with independent ethics committees. All trials undertaken in England have to be authorised by the HRA following ethical review.

6.14 **UKVN:** as explained above, the UKVN was established in 2015 to support the development of vaccines and vaccine technology for infectious disease with the potential to cause an epidemic in low and low-middle income countries ("LMICs"). It brings together expertise from across industry, academia and relevant funding bodies to advise DHSC on research and development investment. I am the Chair of the UKVN and have been since its inception. I discuss its role in relation to the development of COVID-19 vaccines below.

6.15 **VTF:** the VTF was set up in March 2020 and formally established in April to coordinate and drive forward the UK's efforts to develop and procure an effective vaccine against COVID-19. It brought together expertise from across government and the private sector in pursuit of that objective. Dame Kate Bingham was appointed as Chair in May 2020, reporting directly to the Prime Minister and working within the Department for Business, Energy and Industrial Strategy ("BEIS"). Professor Van-Tam was a member of, and Clinical and Public Health Adviser to, the VTF.

Non-government bodies

6.16 The University of Oxford played a key role in developing the Oxford/AstraZeneca vaccine. Imperial College was also funded to develop a vaccine, although in the end that did not progress to deployment. Pfizer, Moderna, AstraZeneca were the key vaccine manufacturers in relation to the UK's response, other vaccine manufacturers were involved in clinical studies in the UK but did not make the same material difference to the UK response.

Research

Development

6.17 The development of vaccines for COVID-19 built on decades of global research and preparation, benefitting from previous work to develop prototype vaccines for SARS and MERS. Decades of research also went into developing mRNA vaccines, many of which were/are planned as cancer vaccines. It was also supported by pre-existing protocols for rapid vaccine implementation in the face of a new global pandemic, and existing networks such as the UKVN.

6.18 As explained above, I chair the UKVN, and have done so since its inception. Recognising the risk posed by coronaviruses in 2016, the UKVN funded Oxford University with a grant of £1.87m to develop a vaccine for MERS. It was this technology that was used to develop the Oxford/AstraZeneca vaccine for COVID-19. The UKVN also provided funding to support Imperial College London's work to develop an RNA vaccine against Ebola, Lassa and Marburg, which began in 2017 and was pivoted to COVID-19 in 2020. Once the VTF was established the UKVN, which was set up principally to fund vaccines for Overseas Development Assistance ("ODA") eligible countries, did not play a major role in the domestic response.

6.19 The NIHR/UKRI rapid research call released in February 2020 provided funding for the Oxford University and Imperial College London vaccine development work. NIHR infrastructure also supported clinical trials in the UK of several vaccines developed in the private sector in other nations, including: Novavax, Janssen, Valneva and Medicago/GSK.

6.20 The trials of the COVID-19 vaccines were independently led by the relevant pharmaceutical companies and their academic and NHS partners. The OCMO retained some oversight of the process so that we could update Ministers on progress.

To that end, Professor Van-Tam had regular calls with senior figures at the major pharmaceutical companies. He also occupied one of two seats that were assigned for UK Government representatives on the Oxford/AstraZeneca vaccine steering group (the other being occupied by Dame Kate Bingham) and was briefed on the latest developments as part of his role on the VTF.

Efficacy and scheduling

6.21 Once the UK had obtained data on relatively safe and effective vaccines, a second strand of research continued to: a) monitor vaccine efficacy and safety; and b) inform how the vaccines could be most effectively used.

6.22 Observational studies to monitor vaccine efficacy were led by PHE (and later UKHSA) and included SIREN funded by UKRI (which monitored infection in healthcare workers), VIVALDI jointly funded by UKHSA and NIHR (which monitored infection in care home staff and residents), CONSENSUS funded by UKHSA and DHSC (which compared the immunity response of those who had received the vaccine with the authorised dosing schedule with those who had it with the extended dosing schedule).

6.23 Trials aimed at assessing how best to use the vaccines were conducted through the National Immunisation Schedule Evaluation Consortium ("NISEC"). NISEC funded by NIHR, was formed in 2017 in response to a DHSC research call for vaccine evaluation to inform policy and decision-making for the national immunisation programme. The programme pivoted to COVID-19, establishing several national multicentre trials. Studies included:

i. Com-COV / Com-COV 2 / Com-COV 3 – the Oxford Vaccine Group's Com-COV studies looked at the consequences of administering a mixed dosing schedule (for example giving the Oxford/AstraZeneca vaccine as a first dose and the Pfizer/BioNTech vaccine as a second dose).

ii. ComFluCOV – this study, run by the Bristol Trials Centre, looked at the safety and immune responses when administering a COVID-19 vaccine and influenza vaccine at the same time.

iii. Preg-CoV – this study, run by St George's Vaccine Institute, University of London, was set up to identify the optimal time to administer COVID-19 vaccines in pregnancy to best protect women against COVID-19.

iv. COV-Boost – this study, run by University Hospital Southampton NHS Foundation Trust, was set up to assess which vaccines were most effective as a booster vaccination.

6.24 Professor Van-Tam often acted as the link between the research community, the VTF and the JCVI to ensure that the system was joined up, the studies were useful and the results were taken into account when policy decisions were being made. The NISEC studies played an important role in the JCVI's considerations.

Procurement

6.25 The procurement of vaccines was led by the VTF under Dame Kate Bingham and subsequently Sir Richard Sykes. The OCMO was represented on the VTF by Professor Van-Tam. The OCMO role was purely advisory. For most issues on procurement the best information will be given by the VTF.

6.26 The role of Professor Van-Tam in advising on quantities of vaccines and some technical aspects of vaccine strategy will be covered in his personal witness statement for this Module so is not repeated here.

Approval

6.27 The approvals process for both drugs and vaccines is statutorily and necessarily independent of government. It is conducted by the MHRA, led by Dr Raine, with clinical advice from the CHM, led by Professor Pirmohamed. The OCMO were very respectful of that independence (and indeed on occasion reiterated to Dr Raine that we would strongly support the independence if needed) **(CJMW6/015 – INQ000071886)**. Professor Van-Tam and I had communications with Dr Raine and Professor Pirmohamed to understand the process and timelines, and to give forewarning of upcoming decisions. We did not however give advice or voice opinions to the MHRA or the CHM on regulatory and safety matters, a highly technical field in which they have acknowledged international expertise. The MHRA had a difficult technical job which it conducted in our view in an exemplary and rapid fashion whilst maintaining rigour and independence, at a time of great pressure and public expectation on the organisation. Further information on the approvals process is best sought from the MHRA and the CHM.

Delivery

6.28 The delivery of the COVID-19 vaccines can be thought of in two parts: the clinical and the operational (with some overlap between the two). The clinical delivery encompasses matters such as vaccine prioritisation, vaccine safety and decisions around dosing. Operational delivery comprises all the logistics involved in physically administering the vaccines to the public. The operational side of the delivery was led by NHSE and PHE, in collaboration with their counterparts in the devolved administrations. Some OCMO staff volunteered at the vaccination clinics. The OCMO did not have a prominent role to play in the operational aspects of vaccine delivery, although we did occasionally advise where there was some clinical and operational overlap. For example, in December 2021 the UK CMOs and lead DCMOs for vaccination jointly advised their respective health ministers that the precautionary 15-minute waiting/observation time following receipt of certain mRNA vaccines should be temporarily suspended in view of the upswing of the Omicron variant, the consequential need to accelerate the vaccine programme, and the relatively small number of serious anaphylactic reactions that had been seen by that time **(CJMW6/016 & 017 – INQ000074502 & INQ000438682)**. It was also important that we monitored the progress of the rollout as it had obvious consequences for the wider response to COVID-19, including the gradual transition away from non-pharmaceutical interventions. Professor Van-Tam, in particular, kept abreast of the operational rollout to help ensure that it went as smoothly and expeditiously as possible.

6.29 The primary advisory body for the clinical side of the rollout was the JCVI. However, the OCMO worked with the JCVI, through its Chair to ensure that delivery was as effective as possible and that it was coordinated with the wider response. Professor Van-Tam and I discussed issues with Professor Lim, whilst respecting the independence of JCVI advice (which Professor Lim was, entirely rightly, very determined to ensure was never infringed).

6.30 Professor Van-Tam attended JCVI meetings to provide context for the decisions that needed to be taken and to contribute his expertise to discussions when appropriate. He emphasised to its members, on multiple occasions, that he had no decision-making power within JCVI and Professor Lim ensured he was never included in any voting. Professor Harries occasionally attended JCVI meetings when Professor Van-Tam was unavailable. Having received advice from the JCVI, it was not uncommon for the

Secretary of State for Health and Social Care to seek additional views from the OCMO, including to explain their thinking when this was not clear to him.

Prioritisation

6.31 The decisions on vaccine prioritisation were taken by the Government on the advice of the JCVI. The JCVI first formally considered the question of vaccine prioritisation at its meeting on 7 May 2020. The minutes of that meeting provide a summary of the committee's discussion on the matter **(CJMW6/018 – INQ000279774)**. On 18 June 2020, the JCVI published its preliminary advice that the following groups should be prioritised for vaccination:

i. frontline health and social care workers; and

ii. those at increased risk of serious disease and death from COVID-19 infection stratified according to age and risk factors **(CJMW6/019 – INQ000106485)**.

6.32 On 25 September 2020, the JCVI updated its advice on prioritisation and published an interim prioritisation list **(CJMW6/020 – INQ000416170)**, stratified according to age and risk factors as then understood. That advice was considered by ministers at a COVID-O meeting on 13 November 2020 **(CJMW6/021 – INQ000091132)**. In advance of that meeting a paper summarising and discussing the JCVI's advice was prepared by DHSC, with input from Professor Van-Tam **(CJMW6/022 – INQ000090908)**. Professor Van-Tam then advised the committee in the following terms:

"[Professor Van-Tam said] *The recommendation in the paper was provisional, while JCVI awaited further data from vaccine manufacturers. The JCVI reserved the right to alter these recommendations where clinical data showed them to be inappropriate, for example, if the elderly reacted poorly, or MHRA authorisation imposed specific license conditions.*

Continuing, [Professor Van-Tam said] *that the principle was to prevent death and serious illness in the first instance through inoculating those most at risk. This would be the approach taken internationally. While it would be possible to apply this principle at an individual level to achieve the optimal ordering, this over engineering would be too challenging to implement. Given the need to move at speed, cohorts should be easy to identify and deliver. The assessment made by the JCVI was that age was the largest risk factor, larger than comorbidities used to identify the CEV. Moreover, the majority of the CEV were picked up within the age cohorting, and would have priority*

access. This would be picked up by the Chief Medical Officer's office and the JCVI secretariat." **(CJMW6/021 – INQ000091132)**

6.33 The minutes of that COVID-O meeting record concern that people classified as Clinically Extremely Vulnerable ("CEV") were not going to be sufficiently prioritised for vaccination. They note the following as part of the Chancellor of the Duchy of Lancaster's summing up, *"The Government should deploy the vaccine efficiently, at speed and at scale, which was reflected in the JCVI's work. This was subject to a further discussion between the Deputy Chief Medical Officer and the JCVI relaying the committee's concerns around the Clinically Extremely Vulnerable"* **(CJMW6/021 – INQ000091132)**.

6.34 Discussions around when to call the CEV for vaccination and how best to define that group were already ongoing prior to the COVID-O meeting on 13 November and they were picked up again by Professor Van-Tam following that meeting. On 17 November, Professor Van-Tam updated the OCMO team on the matter by email: *"JCVI will almost certainly move a little further in next 1-2 days on the CEV (for which we will need one very clear lay definition and description of how this group will be contacted please Jenny and Nisha). I anticipate that when 70-74s are called, the CEV will be called at the same time"* **(CJMW6/023 – INQ000153225)**. On 18 November, at a 'daily vaccines catch-up', he updated the Secretary of State on the matter, noting that there would be *"a potential resolution early next week"* **(CJMW6/024 – INQ000153242)**. The JCVI met on 19 November, with Professors Van-Tam and Harries in attendance, and the issue of vaccine prioritisation for the CEV was discussed. The minutes of that meeting record the following:

"DHSC has now updated the clinically extremely vulnerable (CEV) list; they have been identified by work commissioned by DCMO with UK senior clinicians. There would be a transition over to the QCOVID risk stratification tool method, but this would not happen within the next few weeks. NHS Digital had confirmed that 'call and recall' of this group would be possible and DHSC indicated that they would be flagged with a code and could be reached.

The request was for JCVI to consider advice for the CEV group separately against the other priority groups. It was noted that some considerations on this had been underway prior to the request.

DHSC noted that there was an expectation from COVID-O that an update of the prioritisation would reconsider the position of the CEV. It was suggested that the absolute lowest they should sit is above the general 'at risk' group.

There was a discussion of the numbers in the CEV group. It was noted that many in the CEV list would be included in groups 3,4,5 (persons aged 65 to 80 years) and that they were otherwise in JCVI's existing high-risk at-risk group with the exception of pregnant women with congenital heart disease.

…

***Summary** – It was agreed that, based on the absolute risk data from QCOVID, persons who are clinically extremely vulnerable CEV should be offered immunisation alongside those aged 70-75 years.* **(CJMW6/025 – INQ000416139)**

6.35 On 30 November 2020, the JCVI's final advice on prioritisation was sent to the Secretary of State for Health and Social Care and the Minister for Covid Vaccine Deployment for their approval. On 1 December 2020, the Secretary of State for Health and Social Care confirmed he was happy to accept the JCVI's advice and asked that I liaise with devolved administrations via the UK CMOs to ensure there was technical agreement across the UK **(CJMW6/026 –INQ000071966)**. I convened a call with my counterparts in the devolved administrations and our unanimous agreement with JCVI's advice was conveyed to the Secretary of State on the same day **(CJMW6/027 – INQ000071965)**.

6.36 Following the MHRA's authorisation of the Pfizer/BioNTech vaccine for use in the UK on 2 December 2020, the JCVI published its advice **(CJMW6/028 – INQ000234638)** on vaccine prioritisation and its priority list as follows:

i. Residents in a care home for older adults and their carers

ii. All those 80 years of age and over and frontline health and social care workers

iii. All those 75 years of age and over

iv. All those 70 years of age and over and clinically extremely vulnerable individuals

v. All those 65 years of age and over

vi. All individuals aged 16 years to 64 years with underlying health conditions which put them at higher risk of serious disease and mortality

vii. All those 60 years of age and over

viii. All those 55 years of age and over

ix. All those 50 years of age and over

6.37 The JCVI published further advice on 30 December 2020 **(CJMW6/029 – INQ000256950)**. It reiterated that the first priorities for the vaccination programme should be the prevention of mortality and the maintenance of the health and social care systems. It did not make any changes to the priority list set out in its advice of 2 December but did explain that *"The order of priority for each group in the population corresponds with data on the number of individuals who would need to be vaccinated to prevent one death, estimated from UK data obtained March to June 2020"*. That metric remained a key consideration throughout the initial rollout. The JCVI also indicated that prioritisation in the next phase of the programme once these initial groups were protected would be informed by data from the first phase, but that priority could be given to the following groups based on their occupational risk or the societal need to maintain their effective operations: first responders, the military, those involved in the justice system, teachers, transport workers, and public servants essential to the pandemic response. However, it also noted that priority occupations for vaccination were considered an issue of policy for DHSC to consider in collaboration with other government departments, rather than for JCVI to advise on as it was not a direct clinical prioritisation.

6.38 The JCVI's views on prioritisation were supported by independent academics. For example, the COVID-19 Actuaries Response Group note – 'How logical is the UK's vaccine priority ordering' – 5 December 2020, shows how the advice worked in principle using the actuarial assessment of lifetime risk (**CJMW6/030 – INQ000257328**). The Inquiry may find their table helpful:

The table below shows the estimated COVIDs deaths in each group, cumulative percentage of total COVID deaths, approximate population of each group and the vaccinations required to prevent one COVID death.

Vaccination Group		COVID deaths	Cumulative % of total COVID deaths	Additional Population	Vaccinations to prevent one death
1	residents in a care home for older adults	22,800	36%	0.5m	20
	their carers	<100	36%	0.5m*	
2	everyone aged 80 and over	18,900	66%	3.0m	160
	frontline health and social care workers	900	68%	2.5m	
3	everyone aged 75 and over	6,300	78%	2.2m	350
4	everyone aged 70 and over	5,600	86%	3.3m	600
	clinically extremely vulnerable	1,000	88%	1.4m	
5	everyone aged 65 and over	3,100	93%	3.3m	1,000
6	age 16-64 with underlying health conditions; at higher risk	600	94%		
7	everyone aged 60 and over	2,000	97%	3.8m	2,000
8	everyone aged 55 and over	900	98%	4.4m	4,000
9	everyone aged 50 and over	500	99%	4.7m	8,000
10	All the rest	600	100%	37m	47,000
		63,200			*Assume 1:1 ratio for carers

6.39 As the vaccine programme progressed, the OCMO was occasionally called on to advise on matters relating to prioritisation. For example, on several occasions the OCMO advised in relation to the vaccination of health and social care workers as part of the JCVI's second priority group:

i. It was agreed that the UK CMOs should decide on the definition of "frontline health and social care workers" **(CJMW6/031-033 – INQ000463990, INQ000448409 & INQ000416129)**.

ii. On 6 January 2021, the Secretary of State requested OCMO advice on the rationale for prioritising healthcare workers as part of the second priority group. Our advice was that the JCVI's advice was logical and rooted in good public health principles and we saw no reason to depart from it **(CJMW6/034 – INQ000072434)**.

iii. In mid-January 2021, the OCMO was asked to advise on whether workers at vaccine manufacturing sites could be considered frontline healthcare workers **(CJMW6/035 – INQ000153602)**. Professor Van-Tam and I provided advice to the Secretary of State that supported vaccinating this group as part of the second priority group but also noted that this was ultimately a policy decision, rather than a clinical one **(CJMW6/036 – INQ000153609)**.

iv. On 25 January 2021, the OCMO advised on a draft submission for the Secretary of State that recommended certain roles within the funeral sector should be considered frontline healthcare workers for the purposes of vaccine prioritisation **(CJMW6/037 & 038 – INQ000072538 & INQ000072539)**.

6.40 Additionally, in the early weeks and months of the vaccine rollout, the OCMO had a role to play in helping protect the integrity of the JCVI prioritisation when it came under pressure from some parts of Government. Our view was that it was very easy to make a case for the importance of large numbers of essential workers in the public and private sector, but given the shortage of vaccine supply and deployment capacity every low-risk person prioritised and vaccinated meant a high-risk individual who had a much higher chance of coming to harm was not vaccinated. For example, in late January and early February 2021 there was a question from within DHSC about whether to prioritise the vaccination of staff at COVID-19 testing sites and laboratories. My advice was conveyed to DHSC officials by OCMO members in the following terms:

"the JCVI priority list is based on protecting those who are vulnerable to COVID-19, meaning likely to die from COVID-19. This is either directly through prioritising those likely to die e.g. 80+ or indirectly e.g. vaccinating care home workers in older adult care homes. He (CMO) has consistently said groups that are not interacting with those who are vulnerable to COVID-19 should not be added to the JCVI priority list." **(CJMW6/039 & 040 – INQ000072577 & INQ000072578)**.

6.41 Similarly, throughout January and February 2021, there was significant pressure from MPs, Unions and certain parts of the press to extend vaccine prioritisation to more public sector workers (including teachers and police). The OCMO advice was consistent with that set out in the paragraph above. OCMO's position was summarised by Professor Harries in response to a suggestion about piloting vaccine prioritisation for teachers (a summary that was endorsed by Professor Van-Tam):

"…I am afraid I would not support the proposal you set out below and know that Professor Van-Tam, my DCMO colleague who leads on the vaccine work, would be in a similar position.

…

My logic would be broadly as follows:

1. *The agreed prioritisation of vaccination has been to save lives*

2. *As you have noted mortality and morbidity rates amongst school teachers are either lower than or similar to relevant comparator occupational groups*

3. *Children themselves rarely get seriously ill either and therefore there is no strong argument for direct protection of people teachers are coming into regular contact with (assuming transmission is reduced by vaccination tbc)*

4. *All teachers who are clinically extremely vulnerable should have been vaccinated by now as will all those in households to which children might return*

5. *All teachers with underlying health conditions are being vaccinated and those with further associated multiple risk factors including some personal ones eg ethnicity, area of deprivation, are being pulled to the top of the Group 6 vaccination programme. This also applies to households to which children might return so risk to household members is lowered.*

6. *My understanding of the data on parental views is that they are increasingly content for schools to be open and confidence is higher than in the previous big return to school*

7. *Therefore vaccination in your study would be for confidence in the teachers only*

8. *By vaccinating healthy teachers, particularly the younger ones, we will be lengthening the time that people with acknowledge* [sic] *causal risks for mortality, including specifically age, have to wait before receiving a potentially lifesaving intervention*

9. *If there are hospital slots available they should be offered by the local health system to those who will benefit most from vaccination.*

10. *Stepping outside the JCVI guidance means you would be actively choosing to respond to a subjective assessment of one group's confidence levels above an objective and very real risk of death in others.*

I cannot see how such an approach could or would gain ethics approval.

Quite apart from this more logical discussion, such a move would inevitably open the flood gates to every other group of workers who may feel they lack confidence in the current pandemic – for example shop workers, bus drivers etc – all public facing and essential for our current ability to maintain a relatively normal [sic] *and probably all meeting a higher number of new social interactions through their workplaces than teachers.*

Finally having a really clear and simple roll out programme for the UK has enabled delivery of vaccine to huge numbers of individuals at unprecedented pace in a way which will almost certainly save lives. Whilst you will know I am usually hugely in favour of local variations and process adaptations this is one where I think outcomes could well be very different – because cutting across JCVI guidance as you have suggested in a way which is not compliant with the national vaccination programme will mean other areas will feel there are flexibilities to amend and adjust in their own delivery to different groups in a way which might build local confidence – and potentially slow down the overarching programme.

I recognise that you will need local flexible delivery models to get some of your least vaccine confident communities – but these should still be centred on mortality risk." **(CJMW6/041 – INQ000072914)**

6.42 In May 2021, when asked for advice on prioritising elite UK athletes for vaccinations, Professor Van-Tam made clear it was a political decision with no clinical grounds **(CJMW6/042 – INQ000073290)**.

Safety

6.43 Almost no active drug, vaccine or medical procedure is without risk- and indeed some (such as major surgery or chemotherapy) carry substantial risks. The practical question, which is central to all of medicine, is: "is having the drug, vaccine or procedure safer than not having it?". In the case of COVID-19 vaccines this initially meant- "was being vaccinated safer than being unvaccinated with a high chance of acquiring infection in a completely immune-naïve state?". Many of the risks of

vaccination which emerged such as myocarditis were more common, and often much more common, in people who had COVID-19 infection than due to vaccination (albeit they were relatively rare in occurrence- but more common than with vaccination). The correct risk analysis is therefore not "is the vaccine/drug risk free in absolute terms?" (almost none are) but rather "is having it more risky than not having it in the context of this very common, and sometimes life-threatening, disease?".

6.44 Vaccine safety relative to infection of unvaccinated people, and the question of whether to offer the vaccine to a particular group were matters for the MHRA (regulatory) and the JCVI (clinical deployment advice). There were only very limited exceptions, but an issue on which the OCMO did advise was the question of whether to offer the vaccine to 12 to 15-year-olds who did not have underlying health conditions that put them at increased risk from severe COVID-19. This was on the suggestion of JCVI to Ministers.

6.45 In its advice of 2 December 2020, the JCVI said the following:

"Following infection, almost all children will have asymptomatic infection or mild disease. There is very limited data on vaccination in adolescents, with no data on vaccination in younger children, at this time. The committee advises that only those children at very high risk of exposure and serious outcomes, such as older children with severe neuro-disabilities that require residential care, should be offered vaccination.

Clinicians should discuss the risks and benefits of vaccination with a person with parental responsibility, who should be told about the paucity of safety data for the vaccine in children aged under 16 years. More detail on vaccination in children is set out in the Green Book – Immunisation Against Infectious Disease." **(CJMW6/028 – INQ000234638)**.

6.46 Phase two of the vaccine rollout continued to prioritise people by age, with the next groups called to receive the vaccine being all those aged 40 to 49 years, followed by all those aged 30 to 39 years, and lastly all those aged 18 to 29 years.

6.47 At the beginning of June 2021, the MHRA authorised the Pfizer/BioNTech vaccine for use in 12 to 15-year-olds, making it the only vaccine authorised for use in that age group in the UK at the time **(CJMW6/043 – INQ000416177)**. This, by definition, meant their technical assessment was that benefits of vaccination exceeded risks at an individual level in this age group (Moderna was authorised for this group on 17 August 2021).

6.48 On 4 August 2021, the JCVI published a *statement on COVID-19 vaccination of children and young people aged 12 to 17 years.* The JCVI's statement made the following observations and conclusions:

*"**Introduction***

The Joint Committee on Vaccination and Immunisation (JCVI) has previously advised COVID-19 vaccination of all adults aged 18 years and over in the UK, and vaccination of some specific groups under the age of 18 years. The COVID-19 immunisation programme has been highly successful, with rapid delivery and high uptake. The programme has already substantially reduced the risk from severe COVID-19 in the UK population and is estimated to have averted approximately 22 million infections and 60,000 deaths to date. JCVI developed initial advice on vaccination of children and young people on 2 July 2021. Following consideration by policy makers, that advice was published on 19 July 2021. In view of the progress in offering COVID-19 vaccination to all adults and recent changes to the epidemiology of COVID-19 in the UK, the UK Chief Medical Officers requested JCVI to accelerate its planned review of advice for children and young people.

On 29 July 2021, JCVI deliberated on the potential harms and benefits of vaccinating persons aged 12 to 17- years-old, taking into consideration the latest available data pertaining to children and young people, including:

- *the incidence and severity of suspected adverse events following vaccination*
- *the potential impacts of COVID-19 vaccination on the delivery of other school-based immunisations*
- *the potential protection provided by vaccination against severe COVID-19 (hospitalisations and deaths), Paediatric Inflammatory Multisystem Syndrome temporally associated with SARS-CoV-2 (PIMS-TS) and post-COVID-19 syndrome*
- *the mental health and educational impacts of COVID-19*
- *the seroprevalence of SARS-CoV-2 infection in the UK*
- *mathematical models of the impact of COVID-19 vaccination on the epidemiology of the pandemic*

- *the differential impacts of potential harms and benefits on children and young people from more disadvantaged or deprived backgrounds*

When formulating advice in relation to childhood immunisations, JCVI has consistently held that the main focus of its decision should be the benefit to children and young people themselves, weighed against any potential harms from vaccination to children and young people. In providing its advice, JCVI also recognises that in relation to childhood immunisation programmes, the UK public places a higher relative value on safety compared to benefits[footnote 1].

Vaccine choice

At this time, the Pfizer-BioNTech BNT162b2 vaccine is the only vaccine authorised for persons aged 12 to 17 years in the UK. The Conditional Marketing Authorisation for Pfizer-BioNTech BNT162b2 came into effect on 9 July 2021, with approval previously being provided under Regulation 174. JCVI advises that only UK authorised COVID-19 vaccines should be offered to those aged less than 18 years.

Vaccine safety

The Pfizer-BioNTech BNT162b2 vaccine is administered via intramuscular injection, usually in the upper arm. The most frequent adverse reactions following vaccination in persons aged 12 to 17 years are injection site pain, fever and headache. These reactions are generally mild, self-limiting and short-lived, typically lasting 1 to 2 days[footnote 2].

In recent weeks, reports have been submitted in the UK and other countries of the extremely rare occurrence of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the membrane around the heart), following the use of Pfizer-BioNTech BNT162b2 and Moderna mRNA- 1273 vaccines[footnote 3]. These extremely rare adverse reactions have been more frequent shortly after the second dose, and in younger individuals and males; data from the United States indicate about 60 reported cases per million second doses in younger males, with reporting rates after the first dose being 6 to 7-fold lower[footnote 4]. The mechanism of action underlying these rare events is not currently known. Israel and the United States have reported most of the cases and experience from these countries indicate that the reported cases of myocarditis following mRNA vaccination are of a 'milder phenotype' with the vast majority of persons recovering swiftly from the acute episode, compared to more typical cases of myocarditis (which are mostly viral or idiopathic in aetiology). Follow

up of reported cases in Israel and the United States is on-going. These reports will continue to be closely evaluated by MHRA and JCVI. See MHRA reports on COVID-19 vaccines.

Benefits of vaccination

COVID-19 disease in children is typically mild or asymptomatic. Using serological markers as a measure of prior SARS-CoV2 infection, provisional data from the most recent round of testing in secondary school-aged children in England (early July) indicate the proportion of students testing antibody positive is approximately 40%[footnote 5].

The incidence of severe outcomes from COVID-19 in children and young people is very low. In England, between February 2020 and March 2021 inclusive, fewer than 30 persons aged less than 18 years died because of COVID-19, corresponding to a mortality rate of 2 deaths per million. During the second wave of the pandemic in the UK, the hospitalisation rate in children and young people was 100 to 400 per million. Children and young people at higher risk of severe COVID-19 include those with severe neuro-disabilities, Down's Syndrome, underlying conditions resulting in immunosuppression, profound and multiple learning disabilities (PMLD), severe learning disabilities or who are on the learning disability register. The data source for this is from OpenSAFELY.

Efficacy of the Pfizer-BNT162b2 vaccine against symptomatic COVID-19 was 100% in the clinical trial involving persons aged 12 to 15 years. The trial was too small to assess the efficacy against severe COVID-19 in 12 to 15 year olds[footnote 2].

Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-COV2 infection (PIMS-TS), also called Multisystem Inflammatory Syndrome in Children (MIS-C), is a rare inflammatory disorder occurring after recent SARS-CoV2 infection. In the UK, between March 2020 and July 2020, there were 449 cases of PIMS-TS in persons aged <16 years. Forty-four percent were admitted to paediatric intensive care and the overall case fatality ratio was 1.1%[footnote 6]. Much remains unknown regarding the epidemiology of PIM-TS and its underlying cause. There are no clinical trial data of vaccine efficacy against PIMS-TS, nor any real-world estimates of vaccine effectiveness.

Post-COVID-19 syndrome (often called 'long COVID') has been reported in children and young people. Existing studies suggest that longer term (≥8 weeks) symptoms

following SARS-CoV2 infection occur in about <1% to 10% of persons after COVID-19, with controlled studies generally reporting rates at the lower end of this range[footnote 7]. As vaccination protects against COVID-19, it is expected that vaccination will also provide some protection against the development of post-COVID-19 syndrome, although estimates of vaccine effectiveness are not available.

Mental health and educational impacts of COVID-19 on children and young people are widely recognised. Some school-based isolation measures have had a disproportionate impact on education, and may also affect mental health. National advice regarding school-based isolation measures is currently under review although JCVI recognises that there will be heterogeneity in the individual responses of children, parents, head teachers and schools to any advice. The extent to which vaccination may mitigate the mental health and educational impacts of COVID-19 on children and young people is difficult to quantify.

Modelling from the University of Warwick[footnote 8] and from Public Health England[footnote 9] indicate that vaccinating children and young people could have some impact on hospitalisations and deaths in older adults. The extent of such benefits is highly uncertain. By autumn 2021, all eligible adults should have been offered 2 doses of COVID-19 vaccine. A successful adult COVID-19 immunisation programme would mean that education staff and adult household members of pupils and students should have been vaccinated, reducing the risk of onward transmission from children to adults in school or at home, respectively.

Wider health implications and operational considerations

Following disruptions in routine immunisation programmes because of the pandemic, there is an urgent need to catch-up on non-COVID-19 school immunisations such as human papillomavirus (HPV) and meningitis (MenACWY) vaccinations, and there may be a need to offer other routine vaccines (such as mumps, measles and rubella (MMR)) in the school setting as part of overall recovery. In addition, for 2021 to 2022, the childhood influenza programme has been extended in the expectation that influenza activity may be earlier and more pronounced this year. The health benefits from these various non-COVID-19 school-based immunisation programmes are well established, and some may provide the last effective opportunity to complete an individual's immunisation course and provide timely and/or lifelong protection. Further deferral of the delivery of these immunisation programmes may be associated with permanent decreases in uptake of these vaccines in affected school age cohorts.

Delivery of a COVID-19 vaccine programme for children and young people is likely to be disruptive to education in the short-term, particularly if school premises are used for vaccination. Adverse reactions to vaccination (such as fevers) may also lead to time away from education for some individuals.

Considerable additional resource will be required to minimise the operational impacts of a COVID-19 vaccine programme on the wider health of children and young people.

Current advice

For adults aged 18 years and over, JCVI considers that the potential benefits of vaccination with Pfizer-BNT162b2 continue to outweigh potential harms.

For persons aged <18 years old who do not have underlying health conditions that put them at higher risk of severe COVID-19, there is more uncertainty in the precision of the harm-benefit balance when considering the impacts on children and young people themselves. As with adults, age has a strong influence. In general, older children are more likely to benefit from vaccination compared to younger children.

At this time, JCVI advises that all 16 to 17-year-olds should be offered a first dose of Pfizer-BNT162b2 vaccine. This is in addition to the existing offer of 2 doses of vaccine to 16 to 17-year-olds who are in 'at-risk' groups. Pending further evidence on effectiveness and safety in this age group, a second vaccine dose is anticipated to be offered later to increase the level of protection and contribute towards longer term protection. Further data and the potential availability of alternative vaccine options will inform exact details which will be provided in a subsequent update of this advice before second doses are due at approximately 12 weeks after the first dose.

As previously advised by JCVI, persons aged 12 to 15 years with specific underlying health conditions that put them at risk of severe COVID-19, should be offered 2 doses of Pfizer-BNT162b2 vaccine with an interval of 8 weeks between doses. This currently includes children with severe neuro-disabilities, Down's Syndrome, underlying conditions resulting in immunosuppression, profound and multiple learning disabilities (PMLD), severe learning disabilities or who are on the learning disability register. Details regarding additional person-groups with underlying health conditions to be offered vaccination will be provided as updates in the Green Book.

Children and young people aged 12 years and over who are household contacts of persons (adults or children) who are immunosuppressed should be offered 2 doses of

Pfizer-BNT162b2 vaccine on the understanding that the main benefits from vaccination are related to the potential for indirect protection of their household contact who is immunosuppressed. The offer of vaccination may help to alleviate stress and anxiety experienced by the children and young people living in these difficult circumstances. This advice is provided recognising that persons who are immunosuppressed are at higher risk of serious disease from COVID-19 and may not generate a full immune response to vaccination themselves[footnote 10].

Further data and experience relevant to the vaccination of otherwise healthy persons aged 12 to 15 years are accumulating. The current epidemiology of COVID-19 in the UK is also changing rapidly. JCVI considers these factors important in determining the overall harm-benefit balance related to the vaccination of healthy 12 to 15 year olds. JCVI will continue to review emerging data and provide further advice in a timely manner.

In all instances, the offer of vaccination to children and young people must be accompanied by appropriate information to enable children and young people, and those with parental responsibility, to be adequately appraised of the potential harms and benefits of vaccination as part of informed consent prior to vaccination.

Future advice

Clinical trials are underway in pre-school and primary-school aged students. Vaccines are only likely to be approved for use in these age groups after summer 2021. JCVI will continue to update its advice as new data emerge." **(CJMW6/044 – INQ000401363)**

6.49 This matter was kept under continual review and on 3 September 2021, the JCVI issued further advice. Its assessment was that "*the benefits from vaccination are marginally greater than the potential known harms (tables 1 to 4) but ... there is considerable uncertainty regarding the magnitude of the potential harms. The margin of benefit, based primarily on a health perspective, is considered too small to support advice on a universal programme of vaccination of otherwise healthy 12 to 15-year-old children at this time*". The JCVI went on however to suggest that given wider societal impacts of vaccination, including educational benefits, were beyond its remit, the Government may wish to seek further views from the UK CMOs **(CJMW6/045 – INQ000257024)**. In other words, the JCVI considered there was net benefit, was equivocal on the question of the size of clinical risk-benefit but thought it small, but recognised there might be broader public health factors that could tip the balance

towards deployment. Having concluded this, it became appropriate in their view for the UK CMOs to advise on those broader public health factors and their impact on the overall risk-benefit balance.

6.50 On 3 September 2021, following this JCVI advice, the four UK Health Ministers wrote to the UK CMOs to request advice on the question of whether to offer the vaccine to this group **(CJMW6/046 – INQ000235157)**.

6.51 On 7 September 2021, I convened a meeting of the UK CMOs to discuss the matter at the request of Ministers advised by the JCVI. The UK CMOs' task was not to retrace the ground that the MHRA and the JCVI had already covered on clinical risk-benefit (both bodies having concluded that there was greater benefit than harm at an individual level in this age group). We took all previous advice from the MHRA and the JCVI as read. Rather the CMOs were to consider any wider issues that are relevant to the public health of children and young people aged 12 to 15-years-old, including education, operational and mental health issues. Our Terms of Reference were published and are exhibited to this statement **(CJMW6/047 – INQ000066871)**.

6.52 The UK CMOs' final advice on this issue was sent to Ministers and published on 13 September 2021 **(CJMW6/048 – INQ000257035)**. Our advice was as follows:

"Dear Secretary of State, Cabinet Secretary and ministers,

Universal vaccination of children and young people aged 12 to 15 years against COVID-19

Background

The Joint Committee on Vaccination and Immunisation (JCVI) in their advice to you on 2 September 2021 on this subject said:

"Overall, the committee is of the opinion that the benefits from vaccination are marginally greater than the potential known harms… but acknowledges that there is considerable uncertainty regarding the magnitude of the potential harms. The margin of benefit, based primarily on a health perspective, is considered too small to support advice on a universal programme of vaccination of otherwise healthy 12 to 15-year-old children at this time….JCVI is constituted with expertise to allow consideration of the health benefits and risks of vaccination and it is not within its remit to incorporate in-depth considerations on wider societal impacts, including educational benefits. The government may wish to seek further views on the wider societal and educational

impacts from the Chief Medical Officers of the 4 nations, with representation from JCVI in these subsequent discussions."

Their full advice to you is appended in JCVI statement, September 2021: COVID-19 vaccination of children aged 12 to 15 years.

You accepted this recommendation from JCVI, and wrote to us on 2 September 2021 stating "We agree with the approach suggested by JCVI, and so we are writing to request that you take forward work (drawing on experts as you see fit) to consider the matter from a broader perspective, as suggested by the JCVI."

The terms of reference (ToR) of this request, which the UK CMOs agreed, can be found in Terms of reference for UK CMO advice on universal vaccination of children and young people aged 12 to 15 years against COVID-19

In doing so we have been fortunate to have been informed by the independent expertise of leaders of the clinical and public health profession from across the UK. This has included Presidents and Chairs or their representative of:

- *Royal College of Paediatrics and Child Health*
- *Royal College of General Practice*
- *Royal College of Psychiatry*
- *Faculty of Public Health*
- *Academy of Medical Royal Colleges representing all the other Royal Colleges and Faculties*
- *Association of Directors of Public Health*
- *Regional Directors of Public Health*
- *national public health specialists*
- *experts in data and modelling*

We are very grateful to them for taking considerable time and effort to consult their own colleagues in all 4 nations at short notice to get a comprehensive view of the balance of informed medical opinion and experience across the UK.

In addition, we have examined data from the Office for National Statistics as well as published data on the impact of COVID-19 on education, and other relevant published sources. We attach key published inputs in Key published inputs to the UK CMOs advice on universal vaccination of children and young people aged 12 to 15 years against COVID-19.

The UK's independent regulator of medicines and vaccines the Medicines and Healthcare products Regulatory Agency (MHRA) is in law the appropriate body to determine whether, based on risk-benefit grounds, a vaccine is safe and effective to use and so grant a licence. They have done so for children and young people aged over 12 years for two vaccines against COVID-19, those manufactured by Pfizer and Moderna. Their assessment is that benefits exceed risks on an individual basis. We take their independent opinion as read. The MHRA position on mRNA vaccines is similar to the relevant regulatory approvals granted in the same age groups in multiple other jurisdictions including but not limited to the USA, the European Union, and Canada.

The independent JCVI is the proper body to give advice on how to deploy a vaccine which has a prior favourable risk-benefit decision and authorisation from MHRA including whether it has a sufficiently large benefit to be worth deploying on a larger, population scale. Like MHRA they consider the benefits of vaccination in this age group exceed the risks (i.e. it is better to be vaccinated than not vaccinated in this age group). They balanced the risk of COVID-19 against the risks of vaccination, including myocarditis. When forming its advice, the JCVI considered vaccine use according to clinical risk groups, thus identifying different groups according to their potential to benefit from vaccination.

For 12 to 15 year olds who do not have underlying health conditions that place them at higher risk from severe COVID-19, the JCVI considered that the size of both the risk and the benefit are at an individual level very small, and the overall advantage for vaccination, whilst present, is therefore not sufficiently large to recommend universal vaccination on their usual criteria. They deemed the extent to which vaccination might mitigate the impacts of COVID-19 on education was beyond the usual remit of the JCVI. They recognised however that given the substantial scale of the impact of COVID-19 on all children and young people, which goes beyond normal clinical benefit and risk, wider issues could, exceptionally, be relevant hence their suggestion to consult UK CMOs.

The JCVI have already recommended that children and young people aged 12 to 17 with specific underlying health conditions, and children and young people who are aged 12 years and over who are household contacts of persons who are immunocompromised are offered two doses of a vaccine, normally Pfizer BioNTech BNT162b2. They have recommended all young people 16 to 17 are offered an initial first dose of vaccine.

The UK has benefited from having data from the USA, Canada and Israel, which have already offered vaccines universally to children and young people aged 12 to 15.

The UK CMOs start from the position that the MHRA and JCVI set out on individual benefit-risk calculations for this age group, and have not revisited this. We accept that at an individual level benefit exceeds risk but this advantage is small, and we have taken the JCVI figures as the UK current position on this question.

The Chair of the JCVI Prof. Lim has been a member of our group to ensure that there is no duplication of effort or conflict between the views of UK CMOs and the JCVI. We have been fortunate to have been joined also by the lead Deputy Chief Medical Officers for vaccines Prof. Van Tam (England), Prof. Steedman (Scotland) and Dr. Chada (Northern Ireland) and the DHSC Chief Scientific Adviser, Prof. Chappell. The final advice is that of the Chief Medical Officers, but informed by independent senior clinical and public health input from across the UK.

UK CMOs have decided in their ToR that we will only consider benefits and disbenefits to those aged 12 to 15 from vaccinating this age group, including indirect benefits. Whilst there may be benefits to other age groups, these have not been considered in our advice below.

Issues of vaccine supply were not factors considered in decision making.

The UK CMOs are aware of the extensive range of non-clinical views but this UK CMOs advice is purely clinical and public health derived and has not taken issues outside their clinical and public health remit into account. There is a subsequent political process where wider societal issues may be considered by ministers in deciding how they respond to this advice.

Advice

All drugs, vaccines and surgical procedures have both risks and benefits. If the risks exceed benefits the drug, vaccine or procedure should not be advised, and a drug or

vaccine will not be authorised by MHRA. If benefits exceed risks then medical practitioners may advise the drug or vaccine, but the strength of their advice will depend on the degree of benefit over risk.

At an individual level, the view of the MHRA, the JCVI and international regulators is that there is an advantage to someone aged 12 to 15 of being vaccinated over being unvaccinated. The COVID-19 Delta variant is highly infectious and very common, so the great majority of the unvaccinated will get COVID-19. In those aged 12 to 15, COVID-19 rarely, but occasionally, leads to serious illness, hospitalisation and even less commonly death. The risks of vaccination (mainly myocarditis) are also very rare. The absolute advantage to being vaccinated in this age group is therefore small ('marginal') in the view of the JCVI. On its own the view of the JCVI is that this advantage, whilst present, is insufficient to justify a universal offer in this age group. Accepting this advice, UK CMOs looked at wider public health benefits and risks of universal vaccination in this age group to determine if this shifts the risk-benefit either way.

Of these, the most important in this age group was impact on education. UK CMOs also considered impact on mental health and operational issues such as any possible negative impact on other vaccine programmes, noting that influenza vaccination and other immunisations of children and young people are well-established, important, and that the annual flu vaccine deployment programme commences imminently.

The UK CMOs, in common with the clinical and wider public health community, consider education one of the most important drivers of improved public health and mental health, and have laid this out in their advice to parents and teachers in a previous joint statement. Evidence from clinical and public health colleagues, general practice, child health and mental health consistently makes clear the massive impact that absent, or disrupted, face-to-face education has had on the welfare and mental health of many children and young people. This is despite remarkable efforts by parents and teachers to maintain education in the face of disruption.

The negative impact has been especially great in areas of relative deprivation which have been particularly badly affected by COVID-19. The effects of missed or disrupted education are even more apparent and enduring in these areas. The effects of disrupted education, or uncertainty, on mental health are well recognised. There can be lifelong effects on health if extended disruption to education leads to reduced life chances.

Whilst full closures of schools due to lockdowns is much less likely to be necessary in the next stages of the COVID-19 epidemic, UK CMOs expect the epidemic to continue to be prolonged and unpredictable. Local surges of infection, including in schools, should be anticipated for some time. Where they occur, they are likely to be disruptive.

Every effort should be taken to minimise school disruption in policy decisions and local actions. Vaccination, if deployed, should only be seen as an adjunct to other actions to maintain children and young people in secondary school and minimise further education disruption and therefore medium and longer term public health harm.

On balance however, UK CMOs judge that it is likely vaccination will help reduce transmission of COVID-19 in schools which are attended by children and young people aged 12 to 15 years. COVID-19 is a disease which can be very effectively transmitted by mass spreading events, especially with Delta variant. Having a significant proportion of pupils vaccinated is likely to reduce the probability of such events which are likely to cause local outbreaks in, or associated with, schools. They will also reduce the chance an individual child gets COVID-19. This means vaccination is likely to reduce (but not eliminate) education disruption.

Set against this there are operational risks that COVID-19 vaccination could interfere with other, important, vaccination programmes in schools including flu vaccines.

Overall however the view of the UK CMOs is that the additional likely benefits of reducing educational disruption, and the consequent reduction in public health harm from educational disruption, on balance provide sufficient extra advantage in addition to the marginal advantage at an individual level identified by the JCVI to recommend in favour of vaccinating this group. They therefore recommend on public health grounds that ministers extend the offer of universal vaccination with a first dose of Pfizer-BioNTech COVID-19 vaccine to all children and young people aged 12 to 15 not already covered by existing JCVI advice.

If ministers accept this advice, UK CMOs would want the JCVI to give a view on whether, and what, second doses to give to children and young people aged 12 to 15 once more data on second doses in this age group has accrued internationally. This will not be before the spring term.

In recommending this to ministers, UK CMOs recognise that the overwhelming benefits of vaccination for adults, where risk-benefit is very strongly in favour of vaccination for almost all groups, are not as clear-cut for children and young people aged 12 to 15.

Children, young people and their parents will need to understand potential benefits, potential side effects and the balance between them.

If ministers accept this advice, issues of consent need to take this much more balanced risk-benefit into account. UK CMOs recommend that the Royal Colleges and other professional groups are consulted in how best to present the risk-benefit decisions in a way that is accessible to children and young people as well as their parents. A child-centred approach to communication and deployment of the vaccine should be the primary objective.

If ministers accept this advice, it is essential that children and young people aged 12 to 15 and their parents are supported in their decisions, whatever decisions they take, and are not stigmatised either for accepting, or not accepting, the vaccination offer. Individual choice should be respected."

6.53 This advice was accepted by the Secretary of State for Health and Social Care in England and consequently those in the 12 to 15 age bracket who had not yet been offered the vaccine were offered a first dose of the Pfizer/BioNTech vaccine. The same decision was made by Ministers in Wales, Scotland and Northern Ireland.

6.54 As the foregoing makes clear, and contrary to some reporting at the time and subsequently, this was certainly not a case of the UK CMOs "overruling" JCVI advice that the vaccine should not be offered to 12 to 15-year-olds. The JCVI concluded that vaccination did offer an overall clinical benefit in this age group, but that it was probably too small to recommend universal vaccination on their criteria and this was a finely balanced decision. The JCVI itself therefore suggested to Ministers that the UK CMOs consider the wider public health factors and form a view on whether those factors weighed in favour of offering vaccination or not. That is what we did, at their request, with the help of the medical and public health professions across the UK.

6.55 At the time there was already reasonably strong evidence from several studies that there was a reduction in transmission as a result of vaccination, especially in those who had never had infection previously. This was made up of two components: reducing the likelihood someone gets infected (as if you are not infected you cannot pass on infection) and slightly weaker additional data showing that even if infected a vaccinated person is less infectious. This was never complete, and contemporaneous estimates before the CMO report were that this reduction was in the order of 35-50% reduction in transmission over and above the reduction in getting infected- see for

example this report from PHE **(CJMW6/048a – INQ000497999)**. There was no good reason to think this effect would be absent in children, although exact data were not available (by definition as they were not being vaccinated) and it was possible it would be smaller. Current data show the reduction in transmission was higher for the original Wuhan and Alpha variants of COVID-19 than it was for Delta and is lower and shorter-lasting for Omicron (which emerged in November 2021, after this report) but still occurs **CJMW6/048b – INQ000497996**). Subsequent modelling data (post the CMO letter) internationally support the idea that vaccination reduced transmission also in children- for example **(CJMW6/048c – INQ000497998)**.

Dosing interval

6.56 Another area in which the UK CMOs and DCMOs contributed to vaccine advice and decision making was in relation to the interval between the first and second doses of the vaccine.

6.57 When the MHRA initially approved the Pfizer/BioNTech vaccine for use in the UK, a condition of the license was that the vaccine be administered in two doses at a minimum of 21 days apart. The minimum interval for the Oxford/AstraZeneca vaccine was set at 28 days.

6.58 The JCVI considered the dosing interval in the context of managing vaccine supply at its meeting of 29 November 2020. The minutes of that meeting record as follows:

"It was noted that people invited for vaccination would be offered two appointments, one for each dose of vaccine. It was noted that one option would be to hold back 50% of available vaccine from each batch received to ensure supply for the second dose of vaccine. Members noted that very high efficacy was seen after a single dose of the Pfizer-BioNTech vaccine. This could allow more people to be offered the first dose, which would have a larger public health impact. It was noted that a decision had previously been taken to vaccinate a larger number of individuals with a single dose in the childhood influenza vaccination programme.

It was noted that the arrival of future batches of the vaccine could not be guaranteed in a specific timeframe, and this could leave a long interval between doses. It was agreed this was a complex issue and would be considered further at the next meeting of the committee." **(CJMW6/049 – INQ000416147)**

6.59 The question of extending the interval between the first and second doses was considered again by the JCVI at its next meeting the following day. The minutes of that meeting record as follows:

"24. Modelling on the potential benefits of extended intervals between doses was considered. An extended interval would result in double the number of people vaccinated with one dose in the short term. A key variable was the time over which protection from the first dose waned. The longer the protection from the first dose, the greater the benefit from an extended schedule. Evidence indicated more deaths would be prevented with high first dose efficacy and an extended schedule. The risk profile by age would need to be considered further.

25. Members considered the risk of missed second doses with an extended schedule. The practical issues around this would need to be carefully considered.

26. Given the current epidemiology and the potential legal implication of advising a schedule outside of the anticipated authorisation parameters, the Committee agreed a two-dose schedule with a 28-day interval. It was agreed that commentary on the efficacy of a single dose should be included in the statement, to provide reassurance in the case of supply delays forcing an extended interval between doses.

27. The Committee agreed that this could be revisited in the future once the final text in the authorisation for supply was known, or in response to any substantial change in the epidemiology." **(CJMW6/050 – INQ000416148)**

6.60 On 1 December 2020, the JCVI met twice to discuss the MHRA's authorisation of the Pfizer/BioNTech vaccine. At the second meeting the Committee reiterated its agreement with a 28-day dosing interval **(CJMW6/051 – INQ000416146)**.

6.61 On 21 December 2020, officials from DHSC and No.10 separately contacted Professor Van-Tam asking for advice on the possibility of prioritising the roll-out of first doses and delaying the second **(CJMW6/052 & 053 – INQ000153517 & INQ000153518)**. Professor Van-Tam explained that this was already being explored as an option and he was leading that work. He noted that the JCVI would be considering the issue at its meeting the following day and explained as follows,

"I do think the much more transmissible variant is a material change that warrants looking again [at the dosing interval]. *I am working with Julie to get a letter to the MHRA (tonight) asking this to be considered for Pfizer and AZ. But to note the technical ask*

is not to switch to a one-dose regimen but defer the second dose for 12-16 weeks. It amounts to a one-dose protection for twice as many people in the short-term… To proceed we need JCVI comfort and MHRA top cover".

Professor Van-Tam had discussed the matter with me previously and I was supportive of it being considered as the public health logic was strong. I was however aware that it would not be popular with all, including the relevant pharmaceutical companies.

6.62 At its meeting of 22 December 2020, the JCVI considered a possible extension to the dosing interval for both the Pfizer/BioNTech and Oxford/AstraZeneca vaccines. Having considered the potential benefits of extending the dosing schedule, the Committee concluded that: i) the Pfizer/BioNTech vaccine could be offered with an interval of between three and twelve weeks; and ii) the Oxford/AstraZeneca vaccine could be offered with an interval of between four and twelve weeks **(CJMW6/054 – INQ000416152)**.

6.63 On 22 December 2020, Professor Van-Tam and Antonia Williams (the Director for Covid-19 Vaccine Deployment in DHSC) wrote to Dr Raine on behalf of DHSC to request that the MHRA and the CHM consider whether the dosing interval for both vaccines could be extended **(CJMW6/055-057 – INQ000416130, INQ000416131 & INQ000416132)**.

6.64 On 29 December 2020, MHRA sent a submission to Lord Bethell recommending increasing the interval between first and second dose to enable more people to receive a first dose with the limited supply available. OCMO was supportive of this recommendation. Lord Bethell agreed with this recommendation (**CJMW6/057a – INQ000059390 CJMW6/057b – INQ000497989**).

6.65 Professor Van-Tam and I spoke to Pfizer with colleagues at 9.30pm on 29 December. At 10.00pm Professor Van-Tam joined a call with Astrazeneca **(CJMW6/057c – INQ000504723)**. The Inquiry has asked in follow-up questions about a call with Pfizer. With the passage of time I cannot recall the details on this but the broad overview was that they understood the public health case for the proposed change in the dosing schedule but could not endorse the recommendation (likely including having no internal data to support this); therefore they would not comment publicly. An informal note of a call with the UK CMOs on the same day refers to zero-sum game; what was meant by this was that the amount of vaccine was fixed and limited at this time, so a second vaccine for one person inevitably meant there would not be a first vaccine for

another at this point in time. The Inquiry asked about a comment made by 'Scotland'; I cannot recall this point at all but was confident we moved on this on a four nations basis. It was normal (and in my view right) that clinicians and scientists from the four nations tested one another's thinking before coming to a joint view.

6.66 At 9.00pm and 10.30pm on 29 December 2020, the UK CMOs and lead DCMOs for vaccination met to discuss the proposed extension to the dosing interval. A contemporaneous note of that discussion is exhibited to this statement **(CJMW6/058 – INQ000072276)**. The CMOs agreed the proposal and published their joint clinical advice on 30 December 2020. That advice was as follows:

"The 4 UK Chief Medical Officers agree with the JCVI that at this stage of the pandemic prioritising the first doses of vaccine for as many people as possible on the priority list will protect the greatest number of at risk people overall in the shortest possible time and will have the greatest impact on reducing mortality, severe disease and hospitalisations and in protecting the NHS and equivalent health services. Operationally this will mean that second doses of both vaccines will be administered towards the end of the recommended vaccine dosing schedule of 12 weeks. This will maximise the number of people getting vaccine [sic] *and therefore receiving protection in the next 12 weeks"* **(CJMW6/059– INQ000203969)**.

6.67 On 30 December 2020, the MHRA announced the regulatory approval of the Oxford/AstraZeneca vaccine. It confirmed that the vaccine had been approved for use in people aged 18 years or older and that the second dose could be administered between four and twelve weeks after the first. At the same time, it announced that CHM had reviewed further data for the Pfizer/BioNTech vaccine and the advice had been updated to say that the second dose should be given at least twenty-one days after the first **(CJMW6/060 – INQ000309616)**. On the same day, I joined a call with the Prime Minister and Sir Pascal Soriot (AstraZeneca's Chief Executive Officer) and Dame Louise Richardson (then Vice-Chancellor of the University of Oxford).

6.68 On 31 December 2020, the UK CMOs and Professor Van-Tam issued a letter to the medical profession that set out the scientific and public health rationale for the revised dosing schedule as it was at this stage very controversial **(CJMW6/061 – INQ000305156)**:

"Dear colleagues,

Thank you for your remarkable commitment to the health of our nation in the most difficult of circumstances; the COVID-19 pandemic is undoubtedly the biggest health crisis in a generation, and certainly in our professional lifetimes. We are at a critical point in the pandemic as the emergence of a novel variant of SARS-CoV-2 with a markedly higher growth rate is rapidly shifting the epidemiological curve in the wrong direction across much of the UK in the middle of winter.

Authorisation of first the Pfizer and now the AZ vaccine (AZD1222) for use is incredibly welcome. Both are highly effective vaccines from clinical trial data and are anticipated to have sizeable effects on preventing severe disease and hospitalisation. Getting vaccines deployed as rapidly as possible into as many older, clinically vulnerable patients, and also frontline health and social care workers is essential. The Joint Committee on Vaccination and Immunisation (JCVI) has put forward a prioritisation scheme, attached, of which you will all be aware.

We wanted to lay out to you the scientific and public health rationale for the dosing schedule for the AZ vaccine and the change to the dosing schedule for the second dose of the Pfizer vaccine. As with all decisions during this pandemic it is about balance of risks and benefits.

1. *We have to ensure that we maximise the number of eligible people who receive the vaccine. Currently the main barrier to this is vaccine availability, a global issue, and this will remain the case for several months and, importantly, through the critical winter period. The availability of the AZ vaccine reduces, but does not remove, this major problem. Vaccine shortage is a reality that cannot be wished away.*

2. *We are confident that based on publicly available data as well as data available to the JCVI, the statutory independent body, that the first dose of either Pfizer or AZ vaccine provides substantial protection within 2-3 weeks of vaccination for clinical disease, and in particular severe COVID disease. The JCVI has issued a new evidence statement today.[footnote 1]*

3. *The second vaccine dose is likely to be very important for duration of protection, and at an appropriate dose interval may further increase vaccine efficacy. In the short term, the additional increase of vaccine efficacy from the second dose is likely to be modest; the great majority of the initial protection from clinical disease is after the first dose of vaccine.[footnote 2]*

4. *In terms of protecting priority groups, a model where we can vaccinate twice the number of people in the next 2 to 3 months is obviously much more preferable in public health terms than one where we vaccinate half the number but with only slightly greater protection.*

5. *This is why the JCVI has recommended that first doses of vaccine are prioritised for as many people as possible on the Phase 1 JCVI priority list, in advance of second doses which will subsequently provide more assured longer-term protection. It is a classic public health approach centred on doing as much good for as many people in the shortest possible timeframe, within the available vaccine supplies, against a background of immediate disease activity and still high population sero-susceptibility (despite the disease burden seen).*

6. *The JCVI is confident 12 weeks is a reasonable dosing interval to achieve good longer-term protection.*

7. *The position is strongly supported by the UK Chief Medical Officers on public health grounds of maximising benefit.*

We recognise that the request to re-schedule second appointments is operationally very difficult, especially at short notice, and will distress patients who were looking forward to being fully immunised. However, we are all conscious that for every 1000 people boosted with a second dose of COVID-19 vaccine in January (who will as a result gain marginally on protection from severe disease), 1000 new people can't have substantial initial protection which is in most cases likely to raise them from 0% protected to at least 70% protected. Whilst the NHS, through all of your work, has so far vaccinated over 1 million UK patients with a first dose, approximately 30 million UK patients and health and social care workers eligible for vaccination in Phase 1 remain totally unprotected and many are distressed or anxious about the wait for their turn. These unvaccinated people are far more likely to end up severely ill, hospitalised on in some cases dying without vaccine. Halving the number vaccinated over the next 2-3 months because of giving two vaccines in quick succession rather than with a delay of 12 weeks does not provide optimal public health impact.

We have to follow public health principles and act at speed if we are to beat this pandemic which is running rampant in our communities and we believe the public will understand and thank us for this decisive action. We hope this has your support.

We attach a statement from the JCVI laying out their thinking in more detail.

Once again, many thanks."

6.69 This was not a universally popular decision and the OCMO came under pressure to change the advice (see for example, **CJMW6/062-065 – INQ000416149, INQ000400438, INQ000416133 & INQ000416134**). The OCMO and JCVI advice did not change. Studies later showed this decision reduced hospitalisations and deaths (see for example, **CJMW6/066 – INQ000354602**).

Monitoring the rollout

6.70 The OCMO had no direct involvement in the monitoring of the vaccine rollout but Professor Van-Tam or I were present at many of the meetings that Dame Emily Lawson and her team from NHSE had with No.10 and Ministers to provide a clinical perspective when needed. Our collective OCMO view was that Dame Emily and her team did a remarkable job in the vaccine rollout.

Public messaging

6.71 Public messaging in relation to vaccination is a highly complex matter, not least because it is a subject that has been plagued by misinformation since the time Dr Edward Jenner started vaccination against smallpox in the 1790s. The messaging around COVID-19 vaccination was no exception. As the Government's public-facing principal medical adviser I had a significant role to play, along with the DCMOs, in providing clear and accurate information to the public about the vaccine programme. We did this through press conferences, social media, reviewing and commenting on Government publications and vaccine campaign materials, authoring Op-Eds for national newspapers and the vaccine technical briefings.

6.72 Professor Van-Tam played a prominent, and often the leading, role in communicating with the public about COVID-19 vaccination. I consider that the UK was extremely fortunate to have, in Professor Van-Tam, a DCMO who combined significant technical vaccine experience and expertise with excellent communication skills. One of the primary public messaging challenges in relation to vaccines is striking a balance between delivering the messages in a way that is accessible for a broad audience and not diluting the important technical aspects of the information. Like all medical interventions there is a risk-benefit to be communicated. We worked with the Winton Centre on ways to accurately present information on statistical risk **(CJMW6/066a – INQ000497993)**. In the specific vaccine briefings Professor Van-Tam gave, usually

with Dr Raine, Professor Lim and Professor Pirmohamed, Professor Van-Tam was able to go into more in-depth scientific detail than was possible in the regular 10 Downing Street briefings but in all cases he and all the OCMO clinicians tried to ensure people understood what was known contemporaneously about both efficacy and significant side effects.

6.73 The Inquiry has asked specifically about relative and absolute risks; I would stress these are only useful if also presented alongside benefits. Generally relative risks can be misleading in communication to non-experts if the effect size is very rare - for example a 50% increased risk of a side effect that occurs in one in a million people is still a very rare risk. The same is true for efficacy: 50% protection against a disease that only kills one in a million is a small increase in protection. This does not mean that they should not be used, but they should be put in context. The key point here is that consideration of the risks and benefits should be seen as a balance exercise.

6.74 Professor Van-Tam acted as the OCMO's primary interlocutor between the Government's technical advisory bodies (the JCVI and the MHRA), Ministers and the general public. These long-form briefings were held without Ministers present as the advice was entirely scientific and technical. Key messages were then amplified by Professor Van-Tam, Professor Harries and me for OCMO or by other clinicians including the GCSA and Professor Powis at the regular Ministerial briefings to the public.

6.75 I gave long-form information for members of the public who wanted more detail about vaccines, for example a Gresham lecture on vaccination given on 10 February 2021 **(CJMW6/067 – INQ000203927)**.

6.76 We were very mindful that the majority of those who were uncertain about vaccines were not "anti-vax" but had legitimate concerns to which they wanted answers. In my view, there are four things that need to be addressed in order to provide relevant information to those who are uncertain about vaccines:

i. that the disease poses a health risk sufficient to warrant a vaccine;

ii. that the vaccine is effective against the disease, either preventing it or reducing its severity significantly;

iii. that the vaccine is safe relative to infection; and

iv. that the vaccine is easy to obtain.

These four factors are therefore vital in directing public messaging. By the time a COVID-19 vaccine was available, the first of these factors was abundantly clear to the vast majority of people. The technical briefings and comments from the clinicians and scientists in Ministerial briefings were designed to address the more challenging second (efficacy) and third (safety relative to infection) factors. It was then up to the Government, particularly the VTF, and the health system as a whole (particularly NHSE and PHE) to make sure that the vaccine was as easy to obtain as possible.

6.77 There is always more that can be done to improve public communications and increase vaccine uptake. However, this is primarily a matter for Government departments and their communications experts, of which there are many. The OCMO's role was to try to ensure that when we were consulted that information contained in Government communications was scientifically and medically accurate. Our collective approach in the OCMO was wherever possible simply to give accurate information rather than directly countering (and thus potentially amplifying) deliberate or accidental disinformation.

6.78 I am asked by the Inquiry about vaccine hesitancy and public messaging in relation to vaccination of specific groups. I address this below.

Pregnant/breastfeeding women

6.79 There were specific challenges around communicating the JCVI's advice in relation to pregnant and breastfeeding women. This was particularly so given that this group has historically been hesitant in coming forward for vaccination when advised to do so due to understandable concerns about minimising exposure to their unborn, or newborn, baby of any drugs or vaccines that are not needed. The JCVI's initial advice (on 2 December 2020) in relation to pregnant women was that there are no safety data in pregnancy and given the lack of evidence, a precautionary approach was preferred. It therefore advised that pregnant women or women planning a pregnancy within three months of the first dose should not come forward for vaccination **(CJMW6/028 – INQ000234638)**. On 30 December 2020, the JCVI published updated advice for this group. That advice stated that there was no known risk associated with giving non-live vaccines during pregnancy or while breastfeeding. In relation to pregnant women, JCVI maintained its precautionary stance. It advised as follows:

"Although the available data does not indicate any safety concern or harm to pregnancy, there is insufficient evidence to recommend routine use of COVID-19 vaccines during pregnancy.

JCVI advises that, for women who are offered vaccination with the Pfizer-BioNTech or AstraZeneca COVID-19 vaccines, vaccination in pregnancy should be considered where the risk of exposure to Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV2) infection is high and cannot be avoided, or where the woman has underlying conditions that put them at very high risk of serious complications of COVID-19. In these circumstances, clinicians should discuss the risks and benefits of vaccination with the woman, who should be told about the absence of safety data for the vaccine in pregnant women." **(CJMW6/029 – INQ000256950)**.

In respect of women who are breastfeeding, the JCVI advised that they could be offered vaccination with either the Pfizer/BioNTech or Oxford/AstraZeneca vaccines.

6.80 By mid-April 2021, the accumulation of data on vaccination of pregnant women, primarily with mRNA vaccines (i.e. Pfizer/BioNTech and Moderna), meant that the JCVI felt comfortable in modifying its advice. On 15 April, Professor Van-Tam advised on the wording of a press release announcing the new JCVI advice **(CJMW6/068 – INQ000416160)**. On 16 April 2021, the JCVI published its advice that pregnant women should be offered vaccination, with a preference for the Pfizer/BioNTech or Moderna vaccines where available **(CJMW6/069 – INQ000376222)**. By this stage it was already apparent that some pregnant women had bad outcomes for their age if they had COVID-19 infections, especially in the later stages of their pregnancy.

6.81 The transition from not actively recommending vaccination because of a lack of data to actively recommending vaccination because more data was available was of course perfectly logical, but nevertheless required sensitive handling. Pregnant women and their healthcare advisers have entirely understandable caution when it comes to accepting drugs and vaccines whilst pregnant in case of harm to their baby. The announcement was accompanied by statements from Professor Lim, Dr Mary Ramsay (Head of Immunisation at PHE) and Dr Edward Morris (President of the Royal College of Obstetricians and Gynaecologists). Professor Lim also addressed the matter at the next technical briefing on 7 May 2021.

6.82 Professor Lucy Chappell, who became Chief Scientific Adviser to DHSC in August 2021 and is by background a distinguished obstetrician and scientist, took the lead on

public messaging around pregnancy and COVID-19 vaccination. She made a number of public statements aimed at reassuring pregnant women about the safety of the vaccines relative to the risks of COVID-19 and encouraging uptake.

6.83 As the rollout continued, vaccine uptake in this group was carefully monitored. For example, PHE (and then UKHSA) produced weekly surveillance reports that summarised vaccine effectiveness and population impact. As part of the weekly report published on 25 November 2021, UKHSA also published substantial data on vaccination in pregnant women **(CJMW6/070 – INQ000354625)**. That data showed that *"COVID-19 vaccine coverage in women before they give birth has increased as more women have become eligible for vaccination. In May 2021, only 2.8% of women giving birth had received at least 1 dose of vaccine. This increased to 9.8% of women who gave birth in June, 16.0% in July and 22.2% in August 2021"*.

6.84 Around the same time as the release of this report, I was involved in efforts to improve vaccine uptake in this group through public messaging. For example, on 15 November 2021, at a No.10 press briefing, I encouraged pregnant women or women who were intending to become pregnant to come forward for vaccination. I explained that there was a major concern around unvaccinated pregnant women being admitted to hospital and ICU with COVID-19, noting that *"from 1 February to 30 September… 1,714 pregnant women were admitted to hospital with COVID. Of those, 1,681… had not been vaccinated and… of 235 women admitted to ICU, 232 of them, over 98%, had not been vaccinated"* **(CJMW6/071 – INQ000416163)**. I said that *"these are preventable admissions to ICU"* and that *"all the medical opinion is really clear, that the benefits of vaccination far outweigh the risks"*. I reiterated this point on 18 November in the following message, jointly tweeted with the Chief Nursing Officer and the Chief Midwifery Officer, *"Almost all pregnant women admitted to hospital, including ICU, with COVID are unvaccinated. This is a risk to you and your baby. It's safer to be vaccinated"* **(CJMW6/072 – INQ000203954)**.

Children

6.85 The clinical risk-benefit equation for vaccination in most adults (and particularly older adults) was unequivocal. As explained above, that was not the case for children and that meant public messaging was more complicated when the decision to offer vaccination to 12 to 15-year-olds was made in September 2021. The OCMO's involvement in that decision (outlined above at paragraphs 6.50 to 6.53) meant that it also had a prominent role to play in explaining it to the public.

6.86 On 13 September 2021, I led a press briefing with Professor Lim, Dr Raine and the CMOs for Wales, Scotland and Northern Ireland. Over the course of almost an hour, we explained the advice that was already in place for people aged 12 to 17, the new advice in respect of 12 to 15-year-olds and the rationale for it, and fielded questions from members of the press **(CJMW6/073 – INQ000416164)**.

6.87 On 22 September 2021, Professor Van-Tam and I appeared before the Education Select Committee alongside Professor Lim, Professor Willett and Dr Camilla Kingdon (President of the Royal College of Paediatrics and Child Health) to answer questions from MPs on the matter. The evidence we gave was widely reported across national news outlets.

Other specific age groups

6.88 The public messaging for most adults was relatively straightforward in the sense that the benefits of vaccination were much greater than the risks for the great majority of groups. No vaccines or drugs are without risk, the question is whether the benefits exceed the risks. The risks to adults, and especially older or medically vulnerable adults from COVID-19 infection, if they had no prior immunity from vaccination or prior infection were significant. The messaging centred around the four factors I have outlined above: disease risk, vaccine efficacy, vaccine safety relative to risk and vaccine accessibility.

6.89 One area of complexity that I would highlight relates to the third of these factors and the very rare instances of vaccine-induced immune thrombocytopenia (low blood platelets) and thrombosis (blood clots) in under 40s associated in particular with the Oxford/AstraZeneca vaccine.

6.90 On 18 March 2021, the MHRA responded to reports of blood clots with suspected association with the Oxford/AstraZeneca vaccine and the suspension of the use of that vaccine by certain countries. It said that following a rigorous scientific review of the available data, the evidence to that point in time did not suggest that blood clots in veins (venous thromboembolism) were caused by the Oxford/AstraZeneca vaccine. It explained that the CHM had reached the same conclusion having reviewed the available data to date and that its advice remained that the benefits of the vaccines outweighed any risks. The MHRA also explained that a further detailed review into five UK reports of a very rare type of blood clot in the cerebral veins (sinus vein thrombosis)

("CVST") occurring together with thrombocytopenia was ongoing **(CJMW6/075 – INQ000408457)**.

6.91 On 31 March 2021 there was a meeting called 'AZ Progress to Date' which involved vaccine policy colleagues, Professor Lim, Professor Pirmohamed, Dr Raine, myself and Prof Van-Tam which discussed the AZ vaccine ahead of the JCVI meeting on 1 April 2021. We have not found any minutes from the meeting but it would most likely have been an overview of the situation which the JCVI reviewed the following day.

6.92 On 1 April 2021, Professor Lim wrote to the Secretary of State for Health and Social Care on the issue, copying in Dr Raine, Dr Ramsay and the JCVI Scientific Secretariat, who then forwarded the letter to Professor Van-Tam and others **(CJMW6/076 & 077 – INQ000416155 & INQ000416156)**. Professor Lim's letter explained that the CHM and the JCVI had met to review the latest evidence from the MHRA and PHE on reported adverse events related to the Oxford/AstraZeneca vaccine. It noted as follows,

"JCVI recognised that there was growing evidence to support a safety signal related to the AstraZeneca vaccine specifically. JCVI considered that the benefits of vaccination with the AstraZeneca vaccine far outweigh any risks for individuals in Phase 1 of the programme.

[…]

In support of openness and transparency, JCVI felt strongly that individuals offered the vaccine should be fully informed about the benefits and risks of vaccination and that dissemination of this information should occur a timely [sic] *manner, such as to maximise public trust and confidence in the vaccine programme. The communications should include clear information on the rare adverse event of thrombosis with thrombocytopenia, how to monitor for symptoms related to the adverse event, and what action should be taken. It was acknowledged that given the availability of COVID-19 vaccines in the UK, patient choice of vaccine is not possible at this time.*

It was also recognised that:

- *to our understanding, the MHRA would not be publishing their advice until Tuesday 6 April;*
- *whilst adequately coordinated communications from JCVI, MHRA, PHE and DHSC would be much preferred, this was unlikely to be possible till Tuesday 6 April; and*

- *the advice to JCVI from communications experts was that an independent public statement from JCVI over the Easter bank holiday weekend could send the wrong message to the public, leading to greater harm than benefit.*

It was therefore with substantial discomfort that JCVI came to the decision not to release an independent public statement immediately. At the same time, we agreed that silence at this difficult time could lead to media speculation and false reporting. Decisions taken by JCVI's equivalents in Canada and Germany to suspend the use of AstraZeneca vaccine in younger age groups have been reported in the UK press, and there is currently a vacuum of information on the UK position. Members of the committee may therefore set out our thinking over the next few days in response to media requests. This is to provide the public with appropriate and reassuring messages about the benefits and potential risks associated with vaccination.

JCVI will continue to monitor the situation carefully through regular updates from the MHRA regarding their investigation."

6.93 Professor Van-Tam and I shared the discomfort of JCVI, but also had concerns that the significant risks that a poorly communicated or coordinated release of data of this rare side effect could cause over the Easter weekend. There were essentially no good options on timings of communications, in retrospect having this just before a major holiday was not ideal and I would recommend except in emergency situations, meetings that report issues of public interest just as a major holiday begins are likely to cause avoidable difficulties. Module 3 of this Inquiry has heard about the confusion a change of PPE guidance released on a Friday caused to clinicians so this is not a theoretical point. Prior to the JCVI meeting we held informal meetings with MHRA, JCVI Chair, PHE and NHSE to ensure all present were aware of the issues and had knowledge of the practical issues to be resolved. We have not located any minutes but it would have been an information-sharing rather than a decision-making meeting as it preceded JCVI.

6.94 On 2 April 2021, the OCMO advised on a response from the Secretary of State. On the point about communicating this issue to the public, the Secretary of State's response stated as follows:

"I recognise and respect that some have argued for a further communication earlier than 6 April, and have taken advice from the Chief Medical Officer and others on this point. I agree with the judgment that you came to that the balance of the public interest

in this instance is in favour of the approach that was agreed yesterday. That decision was taken on the balance of the risk, considering how a rushed and incomplete message, as we go into the Easter Bank Holiday weekend, could cause confusion or undermine public confidence, while we are still in Phase 1 of the programme and have not yet opened the cohorts for which you have not yet provided final advice. Thus, patients eligible for vaccine this Easter weekend are from cohorts 1-9 where your advice on the balance of risks is unchanged. I agree with the view you came to that clear and complete information from JCVI, MHRA, CHM, DHSC, NHSEI and UKHSA should be coordinated and issued early next week." **(CJMW6/078 – INQ000416158)**.

6.95 Professor Van Tam sets out and exhibits relevant correspondence with JCVI at paragraphs 2.54-2.57 in his Module 4 Personal Statement.

6.96 On the specific point of the interval between JCVI's initial letter on 1 April 2020 and the public briefings on 7 April – it is important to note that at this time the UK's vaccination programme was open to cohorts 1-9, that is persons aged 50 and older (see para 6.38) **(CJMW6/078a – INQ000411678)**. This meant that the issue being discussed by the MHRA and later JCVI, the safety of the AZ vaccine in the under 40s did not in the main apply to those being vaccinated at that time. The exception was health and social care workers who were in cohort 2 and so were likely already vaccinated or partially vaccinated by this point.

6.97 On 3 and 4 April 2021, Professor Van-Tam and I had calls with Dr Raine, Professor Pirmohamed, Sir Menelas Pangalos (Global Head of BioPharmaceuticals Research & Development at AstraZeneca), Sir Pascal Soriot (CEO of AstraZeneca), Dr Richard Marshall (Global Head of Respiratory & Immunology Development at AstraZeneca) and Christine Elaine Jones (Vice President for Regulatory Affairs at AstraZeneca), to discuss the matter. Whilst these were discussions not decision meetings, and so as far as we can tell no minutes were taken, this included discussion of data from PHE and a data offer from Professor Cathie Sudlow, Director of the BHF Data Science Centre, to analyse data from multiple linked datasets.

6.98 On 7 April 2021, the MHRA published the findings of its review of instances of CVST, which concluded that there was a possible link with the Oxford/AstraZeneca vaccine. It did not recommend age restrictions for use of the vaccine but did advise that administration in people of any age who are at higher risk of blood clots should be considered only if benefits from the protection from COVID-19 infection outweigh potential risks **(CJMW6/079 – INQ000408453)**.

6.99 On the same day, the JCVI issued a statement that Professor Van-Tam helped to prepare. That statement explained as follows:

"There have been reports of an extremely rare adverse event of concurrent thrombosis (blood clots) and thrombocytopenia (low platelet count) following vaccination with the first dose of AstraZeneca ChAdOx1 nCoV-19 vaccine (AZD1222)… Given the very low numbers of events reported overall, there is currently a high level of uncertainty in estimates of the incidence of this extremely rare adverse event by age group. However, the available data do suggest there may be a trend for increasing incidence of this adverse event with decreasing age, with a slightly higher incidence reported in the younger adult age groups… JCVI has weighed the relative balance of benefits and risks and advise that the benefits of prompt vaccination with AstraZeneca COVID-19 vaccine far outweigh the risk of adverse events for individuals 30 years of age and over and those who have underlying health conditions which put them at higher risk of severe COVID-19 disease. JCVI currently advises that it is preferable for adults aged <30 years without underlying health conditions that put them at higher risk of severe COVID-19 disease, to be offered an alternative COVID-19 vaccine, if available." **(CJMW6/080 – INQ000234852)**.

6.100 Also on 7 April, Professor Van-Tam led a press briefing on the subject alongside Dr Raine, Professor Lim and Professor Pirmohamed. A readout of the questions and answers from this briefing is exhibited **(CJMW6/081 – INQ000416159)**. The OCMO also provided advice to DHSC on a public-facing Q&A on the matter **(CJMW6/082 – INQ000073127)**.

6.101 On 13 April 2021, JCVI published a statement on Phase two of the vaccine rollout, including details of prioritisation. As part of that statement, JCVI reiterated its advice on vaccination of under 30s with the Oxford/AstraZeneca vaccine, stating: *"it is preferable for adults aged 18 to 29 years without underlying health conditions that put them at higher risk of severe COVID-19 disease, to be offered an alternative to the AstraZeneca COVID-19 vaccine, if available. People may make an informed choice to receive the AstraZeneca COVID-19 vaccine to receive earlier protection"* **(CJMW6/083 – INQ000416165)**.

6.102 Data on these extremely rare adverse events continued to be carefully monitored. On 7 May 2021, the JCVI updated its advice in light of further evidence and advice from the MHRA. From 7 May, the JCVI advised that adults aged under 40 should be offered a vaccine other than the Oxford/AstraZeneca vaccine where possible. The Committee

reiterated that adverse events following the Oxford/AstraZeneca vaccine were extremely rare and, for the vast majority of people, the benefits of preventing serious illness and death far outweighed any risks **(CJMW6/084 – INQ000111089)**.

6.103 One of the difficult aspects of communicating this changing advice was that the Oxford/AstraZeneca vaccine was still considered safe for use in the under 40s relative to the risk of infection. The risks associated with it were extremely small, but at the same time we also had access to other effective vaccines for which the risks were even smaller. Those under 40, unless they had underlying medical conditions, were also at much lower risk of mortality from COVID-19 than those in older age groups, so the risk-benefit was more finely balanced. In those circumstances, it made sense to advise a preference for using the mRNA vaccines in this age group where possible, but that is not the same as saying the Oxford/AstraZeneca vaccine was unsafe relative to infection. If the UK had only had access to the Oxford/AstraZeneca vaccine the advice would have been to use it in the under 40 age group as benefit would have exceeded risk in the absence of an alternative. Communicating that nuance to the public (and some professional colleagues) was not always easy.

Religious and minority ethnic groups

6.104 Historically there has been lower vaccine uptake amongst some religious and minority ethnic groups. Unfortunately, this again proved to be the case with the COVID-19 vaccine. In general, work to improve vaccine uptake in specific groups was carried out by Cabinet Office, NHSE and PHE/UKHSA. However, the OCMO did have a role to play in communicating with members of the public. For example, Professor Van-Tam appeared on televised Q&A specials on ITV News (2 December 2020 and 10 February 2021), Channel 4 News (27 January 2021), Sky News (24 February 2021), Channel 5 News (24 February 2021) and BBC News (29 July 2021). At each of these, he answered questions from the public about the vaccines and specifically addressed the problem of vaccine concerns in certain groups. He emphasised that the virus does not discriminate by race or religion and that high uptake of the vaccine was vital in all groups.

6.105 On 25 January 2021, I convened a meeting between the OCMO and the Directors of Public Health ("DsPH") to discuss the issue of vaccine uptake in BAME communities. Following that meeting, Professor Aliko Ahmed (Regional Director of Public Health for the East of England) agreed to take forward work that would aim to improve uptake in these communities **(CJMW6/085 – INQ000153670)**. I was updated on the progress of

this work via the Silver Local Action Committee meetings as well as further specific meetings with the DsPH.

6.106 On 15 February 2021, I hosted (and Professor Ahmed moderated) an engagement session with BAME health professional networks. The session was attended by 180 participants including leaders from across the health and care system. Professor Ahmed and his team produced a detailed insight report **(CJMW6/086 – INQ000236420)** and a summary report **(CJMW6/087 – INQ000236421)** in response to the session.

6.107 On 29 March 2021, I wrote to Dr Kanani, Professors Ahmed, Powis and Fenton as follows:

"Aliko is kindly leading on some work on ways NHS and public health professionals can help improve vaccine confidence, especially in ethnic minority groups. Ethnic minority health professionals have a very important role, and many groups are highly engaged. In a meeting Aliko arranged one thing that came up repeatedly was that doctors, nurses and other health professionals who volunteered to help address issues of confidence had to do so almost entirely in their own time. A request was that where this is a legitimate activity it might be considered part of their professional role. Whilst this will not always be appropriate, often it will, at least in part.

I attach a letter which makes this point, I hope without being in any way directive. It did seem a legitimate request, as there is a danger that, say, a Somali heritage British health professional will always be expected to do work extra to support the Somali British community which an equivalent health professional would not" **(CJMW6/088 & 089 – INQ000073080 & INQ000073081)**.

6.108 In future pandemics and epidemics where a vaccine is available we need from the outset to consider several aspects which related to specific ethnic minority and religious groups and are important reasons they may be less able, or willing, to take up vaccination. These include: identifying existing lower vaccine takeup groups and engaging early and repeatedly with community leaders (including healthcare workers from these groups); ensuring information is available in all major languages spoken in the UK; considering the particular concerns such as pork or beef or human cell lines that are important to some religious faiths and traditions; being aware of vaccine information from social media and overseas media. We should also recognise that some of the lower uptake is typical of more deprived groups who are less able to

access services or who are relatively distrustful of, or disengaged from, the State rather than principally driven by ethnicity.

Vaccines and Long Covid

6.109 As the importance of the group of syndromes known as Long Covid became more widely recognised there was an important question about whether, and if so the extent to which, vaccination protected against Long Covid. This initially had two components: i) the ability of vaccines to prevent COVID-19 infection at all; and ii) whether in vaccinated individuals Long Covid was less likely, or less severe than in unvaccinated (or alternatively where prior vaccination makes it worse). The answer to the first of these questions was highly likely to be positive. If you do not get COVID-19 you will not get Long Covid. So as vaccines did reduce COVID-19 incidence, vaccination of an individual is likely to reduce the likelihood of them suffering from Long Covid, and vaccination of their contacts may do as well. On the second question, the data took much longer to emerge but the balance of evidence showed that overall vaccination reduces the chances of, or severity of, Long Covid in those who become infected post vaccination (see for example, **CJMW6/090 & 091 – INQ000238554 & INQ000416172**).

Four nations

6.110 The UK CMOs and DCMOs in England, Scotland, Wales and Northern Ireland worked very closely together throughout the pandemic including on medical countermeasures, and we had and have great respect for the professionalism and expertise of the CMOs and DCMOs of the other three nations. The four UK CMOs had regular meetings where we discussed technical issues, and where possible aligned the advice we were giving. In the period January 2020-June 2022 the UK CMOs met as a specific group around 286 times, initially often at short notice when there were new developments, including discussing issues around vaccines and therapeutics. The UK CMOs sometimes gave advice collectively. This was to provide a basis for cross-UK decision-making, to give clarity across the four nations, to add strength of weight to the clinical advice or to make a clear public statement reflecting a collective clinical view. Examples relevant to this Module include joint advice on:

i. Clinical trials for treatments to NHS colleagues (1 April 2020) **(CJMW6/012 – INQ000068589)**.

ii. Dosing schedule for vaccination: advice to healthcare professionals (31 December 2020) **(CJMW6/059 & 061 – INQ000203969 & INQ000305156)**.

iii. Vaccination of 12 to 15-year-olds: advice to Ministers (13 September 2021) **(CJMW6/048 – INQ000257035)**.

iv. 15-minute wait after mRNA vaccines (12 December 2021) **(CJMW6/017 – INQ000438682)**.

6.111 The devolved nations were kept abreast of JCVI advice by their representatives who attended meetings. For example, clinicians from Public Health Scotland, Public Health Wales and Northern Ireland's Public Health Agency and policy teams regularly attended meetings as observers. In addition, Professor Van-Tam regularly briefed the UK CMOs on updates from the JCVI. There were some examples of where the operational side of vaccine delivery varied across the four nations. For example, England made greater use of large vaccination hubs, while Scotland chose to put more emphasis on vaccinating through its GP network. That difference was an example of each country adopting an approach that best suited its geography and health systems. When it came to key decisions around who to offer the vaccine to and at what times, the four nations were aligned in accepting the JCVI's advice.

6.112 The procurement and regulatory approval of vaccines was approached on a four nations basis. Professor Van-Tam tried to ensure that the UK CMOs and DCMOs leading on vaccines were kept updated throughout the process, without sharing commercially sensitive data where that was not necessary to the public health decision.

Additional follow up questions from the Inquiry on vaccines (August 2024),

6.113 The Inquiry have asked specifically about a WhatsApp exchange between me and the then Secretary of State (SofS) for Health and Social Care, the Rt Hon Matt Hancock MP, on 9 November 2020 **(INQ000129569)**. The exchange was:

"CMO: Pfizer vaccine readout positive.

SofS: Yes, esp on efficacy- what do you make of what they've said on safety.

SofS: We are playing down in public as it's still weeks to rollout.

CMO: Agree. We need to see the final data. But a) if this works I think others will and b) I think it deprioritises mass testing as it may become a distraction. We need to get the safety data. But my view is that spring 2021 looks brighter is on track-medical science is great.

SofS: yes!"

6.114 The exchange only makes sense if read after reading the press release from Pfizer and Biontech dates that day on which it is based **(CJMW6/091a – INQ000421407**. The exchange above was mainly on efficacy with the press release saying 90% efficacy - remarkable news at the time and the most encouraging information to date on vaccine efficacy. What the press release said on safety was "*no serious safety concerns have been observed*" and *"Safety and additional efficacy data continue to be collected. Pfizer and BioNTech are continuing to accumulate safety data and currently estimate that a median of two months of safety data following the second (and final) dose of the vaccine candidate – the amount of safety data specified by the FDA in its guidance for potential Emergency Use Authorization – will be available by the third week of November. Additionally, participants will continue to be monitored for long-term protection and safety for an additional two years after their second dose. Along with the efficacy data generated from the clinical trial, Pfizer and BioNTech are working to prepare the necessary safety and manufacturing data to submit to the FDA to demonstrate the safety and quality of the vaccine product produced."*

6.115 The downplaying the Secretary of State was referring to I took to mean we should not go in too hard on the efficacy data, exciting as it was, as this was early data and a press release. I agreed (and still agree this was right; excess excitement from initial press releases from companies or academic groups is often very misleading compared to the finally published data). On safety data this was not sufficient to make any judgement until full data were released and I did not think it sensible for the Secretary of State, or indeed anyone else, to make statements on safety based on these data alone (he agreed); he could not downplay the safety data as there were no adverse data to downplay.

6.116 The Inquiry has asked about a further WhatsApp exchange between me and the Secretary of State dated 9th January 2021 **(INQ000129666)** as follows:

"SofS: How strong is our pharmacovigilance system to check events post roll-out? I was told we were doing it but I worry that the details will be shonky.

CMO: Reasonable but needs to get better.

CMO: There will be cases.

SofS: Who is best to talk to to improve the operationalisation of it?

CMO: JVT and Susan Hopkins leading."

6.117 In understanding this exchange it is important to be aware that there are multiple ways side effects, including serious side effects, are identified. The initial trials are very exhaustive and will generally pick up all side effects that are common, whether serious or more minor. Even large trials however often do not pick up very rare but severe side effects. For example the licensure trial for Pfizer/BioNTech, which informed the licence from MHRA included 46,331 patients. By definition this would be unlikely to detect a severe side effect at a population level of 1:50,000 or rarer, or in particular populations such as by age or ethnicity or pregnancy. These are usually identified by astute clinicians seeing odd outcomes (for example haematologists reporting on thromboses), or through the yellow-card system in the UK where doctors report unexpected side effects to MHRA. The companies themselves also accumulate international data. Generally this combination of reporting works well, but the speed of roll-out of the vaccines, which was essential given the severity of the pandemic, was going to put pressure on the normal processes. This issue was well recognised by clinicians, regulators and epidemiologists at the time, including by MHRA, and by Professors Van-Tam and Hopkins as indicated in the WhatsApp exchange.

6.118 The Inquiry has asked about our involvement in decisions on mandatory vaccination of social care workers. Although we were present in meetings on this ours was not the leading voice for what was, and should always be, a political decision by elected leaders. The clinical aspects of the decision are largely factual; the societal choice balancing the risk to older and vulnerable people being cared for with the choices and employment rights of those who have chosen not to be protected by vaccination are much more complex. The clinical facts were: that COVID-19 was of high risk to adults in care, in particular older and medically vulnerable people; that there was evidence vaccination reduced transmission, so all other things being equal the higher the rate of vaccination in those caring the lower the risk to those needing social care; that no vaccine is without side effects, including rare but serious side effects. Additionally for medical staff it is a long-established principle of professional medical practice that doctors should not through their actions or inactions put people at risk including by

maintaining their immunisation against infections, and this is laid out by the General Medical Council in the standard work on the responsibilities of doctors *Good Medical Practice: "You should be immunised against common serious communicable diseases (unless contraindicated)"* **(CJMW6/091b – INQ000474398)**. I have always been more cautious of mandatory vaccination in any situation, including COVID-19, and in particular I was keen that political leaders understood that rare side effects can and do occur prior to taking a decision. Professor Van Tam, whilst sharing my concerns, has been slightly more favourable, having in the past studied the evidence on the effectiveness of mandatory vaccination against influenza for healthcare workers, mainly in US settings, as part of his contribution to work for WHO. However, OCMO was clear that mandation represented a political choice and was not a clinical imperative and aware it is a complex and vexed issue. This is covered more fully in Professor Van-Tam's personal statement for Module 4. This was not a decision driven by OCMO.

Section 7: Therapeutics

Research

Existing repurposed medications

7.1 At various points, particularly early in the pandemic, some senior decision-makers and their senior advisers (and also some senior political figures not in Government, and internationally) thought that given the seriousness of the situation, it was appropriate to deploy particular medical countermeasures (drugs in the main) then being promoted in some part of the press or social media, in advance of any trial or clinical evidence that they worked.

7.2 I and the DCMOs were very firmly against this, whilst fully accepting the good faith of most of those promoting these interventions. All effective drugs and medical interventions come with side effects and unintended consequences. Proper, unbiased and ideally randomised trials are usually the only way to work out whether the balance of risk and benefit are favourable. An early example is chloroquine, with other examples including ivermectin and Vitamin D. So far none of the interventions that were being pushed as appropriate for immediate deployment early in the pandemic have proved to have significant efficacy in clinical trials, and unsurprisingly some have been associated with net harm (see for example **CJMW6/092 – INQ000399345)**. On

the other hand, several interventions which were not widely predicted to work have proved to do so, in particular dexamethasone and other immunomodulatory drugs. Trials are the way to give the best treatment to people which properly balances risk and benefit based on evidence and it goes without saying that I am strongly supportive of any recommendation that recognises the importance of clinical trials (see 8.4 below for more detail on this). It was perfectly reasonable to trial the interventions that were in vogue, and for example major trials of chloroquine, ivermectin and Vitamin D were undertaken in the UK and elsewhere, and I supported this, but there has to be a very strong justification for deploying a drug widely in advance of trial or other equally robust evidence. Fortunately, the UK system is very effective in its ability to undertake late-stage clinical trials (the ones relevant to repurposed drugs) to a very high standard as was demonstrated during COVID-19.

7.3 The OCMO played a role in ensuring there was this emphasis on confining treatments to proven treatments or clinical trials, rather than going to emergency use with unproven therapies. The UK CMOs wrote to colleagues to urge enrolment in clinical trials and supported this approach internally in Government (1 April 2020 – **CJMW6/012 — INQ000068589**, 6 May 2020 – **CJMW6/013 – INQ000069095)**.

"While it is for every individual clinician to make prescribing decisions, we strongly discourage the use of off-licence treatments outside of a trial, where participation in a trial is possible. Use of treatments outside of a trial, where participation was possible, is a wasted opportunity to create information that will benefit others. The evidence will be used to inform treatment decisions and benefit patients in the immediate future."

7.4 The speed of action in setting up early research meant that results were delivered earlier than they otherwise would have been. Because the RECOVERY clinical trials platform was set up ahead of the first wave it was able to recruit at large scale by international standards and showed by June 2020 that dexamethasone reduced COVID-19 mortality, reducing deaths by about one-third in ventilated patients and by one fifth in other patients receiving oxygen only. This was the first drug shown to do so. The speed of that discovery saved substantial numbers of lives in the UK and internationally. Dexamethasone had the advantages of being well known to all clinicians, relatively safe, widely available and cheap, giving global applicability.

7.5 On 25 February 2020, Professor Van-Tam wrote to Professor Peter Horby (Chair of NERVTAG) to request the establishment of a NERVTAG COVID-19 Therapeutics Sub-

Committee. He outlined the proposed purpose and structure of the Sub-Committee, noting as follows:

"Timing: soonest

Purpose: to advise CMO on the subjects and outlines of a range of key national clinical trials that might need to be activated for Covid-19

Likely interventions to consider: (but not necessarily limited to): chloroquine/ hydroxychloroquine, lopinavir/ritonavir, interferons, antibiotics, oxygen therapy…" **(CJMW6/093 – INQ000151510)**.

7.6 The NERVTAG COVID-19 Therapeutics Sub-Committee met for the first time on 27 February 2020 and Professor Van-Tam provided an introduction and an initial steer on the work that needed to be done **(CJMW6/094 – INQ000221982)**. The Sub-Committee agreed to distribute the work across three subgroups that would look at: i) drugs; ii) supportive care; and iii) endpoints and populations. The drugs subgroup met on 2 March. The supportive care and endpoints and populations subgroups met on 3 March. The discussions and recommendations are set out in the respective minutes **(CJMW6/095-097 – INQ000221962, INQ000221964 & INQ000416126)**. On 9 March, the Sub-Committee reconvened for a meeting that was attended by Professor Van-Tam. The minutes of that meeting summarise the Sub-Committee's overarching recommendations to DHSC as follows:

"1. Support a clinical trial evaluating chloroquine in mildly ill out-patients with COVID-19 at risk of complications.

2. Support a platform trial in moderately ill inpatients with COVID-19. The interventions to prioritise will need to consider data on efficacy in betacoronaviruses, safety data, and availability. The committee consider the current order of priorities to be:

- Remdesivir

- Lopinavir/ritonavir

- Interferon

- Low dose corticosteroids

- Chloroquine

3. Review the viral domain of the REMAP-CAP (Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia) study and potential burden of the study for ICU staff. This review would inform a decision whether to support scaling up the trial to include patients with COVID-19.

4. Support a clinical trial of standard oxygen therapy vs. non-invasive ventilation in patients with a ceiling of care (I.e. not for intubation and mechanical ventilation).

5. Consider the most appropriate mechanism for ongoing surveillance of emerging evidence on therapeutic agents for COVID-19 which could be evaluated." **(CJMW6/098 – INQ000221978)**.

7.7 The NERVTAG COVID-19 Therapeutics Sub-Committee therefore provided the initial recommendations for inclusion in the RECOVERY trial, including low dose corticosteroids, of which dexamethasone was chosen as the specific corticosteroid. Its recommendations provided a steer to research on therapeutics which lasted over a considerable period of time. Its minutes provide a good contemporaneous record of the drugs which were being considered at this early stage of the pandemic. At the beginning of April 2020, the Therapeutics Taskforce ("TTF") was set up within DHSC with the remit of coordinating the Government's efforts to deliver safe and effective treatments for COVID-19 as quickly as possible.

7.8 The TTF Executive Board (April 2020 – March 2021), met 17 times and was chaired by Professor Van-Tam. It focused on strategic decisions on procurement of therapeutics. These decisions were supported by reviewing evidence from trial outcomes and input from advisory groups. It eventually evolved into the Therapeutics Taskforce Oversight Board chaired by Lord Bethell (May 2021 – September 2021) and Clara Swinson (December 2021 to February 2022)

7.9 A TTF Programme Board (October 2020 – March 2022) met to review progress, resolve problems and escalate significant risks. The membership of this board included senior Government officials including Professor Van-Tam, as well as representatives from the arms-length bodies to DHSC and the devolved administrations.

7.10 An externally facing Engagement Board met regularly to ensure a steady exchange of information between Government, patient representative groups and industry partners.

7.11 In August 2020, the TTF Executive Board, decided that an independent panel should be established to recommend promising therapeutics for prioritisation in clinical trials.

TTF, working with NIHR and UKRI, set up the independent COVID-19 Therapeutic Advisory Panel ("UK-CTAP") to advise on which candidate therapeutics should be included in clinical trials. UK-CTAP was formed by a group of independent experts and chaired by Professor Patrick Chinnery. The final decision on which drugs would be included in a particular trial would be taken by the chief investigators, with my input where relevant. Prioritisation was based on several factors, including:

i. Scientific rationale (well defined modality of action relevant to pathophysiology of COVID-19 based on in vitro, pre-clinical and clinical data).

ii. Pharmacokinetics and pharmacodynamics (to establish whether therapeutically relevant drug concentrations would be plausible and at what dose and regimen).

iii. Safety and possible drug interactions.

iv. Availability and supply, including cost.

v. Emerging evidence in human studies globally.

vi. Practicalities of giving treatment (for example, intravenous drugs can be potentially useful but impractical at scale).

7.12 In giving advice relevant to the NHS, where possible, I and the DCMOs relied on research evidence. In some cases this was only available in pre-print form. Normally it is best practice to use published evidence that has been through peer review, ideally synthesised through a systematic review, and when that was available that is what we used. Given the speed of the pandemic however we were frequently reliant on pre-prints or even early descriptions of data. If I or the DCMOs considered this was sufficiently strong and it was better to present data early than wait for further peer review we did so, but this was taken on a case-by-case basis and the default was that we would not. An example where we did was when the initial data from the RECOVERY trial were given to us showing a roughly one third decrease in mortality in those on ventilation and around one-fifth reduction in those on oxygen when given steroids. My risk-benefit judgement was that the trial was large and well done, the size of the mortality effect was sufficiently large that it was very unlikely to be overturned in reanalysis, the drug (dexamethasone) was very well known, widely available and generally well tolerated in terms of side effects in short-term use, and the risks of delaying, with people untreated, were greater than the risks of proceeding. On 16 June 2020, I therefore wrote out to the NHS recommending it be used:

"Dexamethasone has been demonstrated to have a clear place in the management of hospitalised patients with COVID-19. There were no excess harms identified in using this dose of dexamethasone in this patient population. Dexamethasone was not used in pregnant women. Clinicians should therefore consider dexamethasone for the management of hospitalised patients with COVID-19 who require oxygen or ventilation. Out of hospital treatment is not appropriate. There is no current or anticipated constraint on supply of the medicine in the UK." **(CJMW6/014 – INQ000069714)**.

7.13 This use of unpublished data should not be seen as normal good practice and was only appropriate in the context of this major and fast-moving emergency, a well-known drug and a substantial mortality benefit.

7.14 There were people who expressed concern about dexamethasone being part of RECOVERY (see for example, **CJMW6/099 – INQ000070662**), others thought that the recommendation on 16 June 2020 was premature. Studies estimated that dexamethasone saved a substantial number of lives in the UK in the six months that followed and more globally (see for example, **CJMW6/100 – INQ000408156**).

7.15 The Inquiry has also requested that I comment on the rapid expert review shortlisting meeting that occurred on 3 April 2020.

7.16 In late March and early April 2020, I was copied into correspondence with the Director of Strategy at the Wellcome Trust, Mr Edward Whiting, who was organising a rapid expert review shortlisting meeting on potential therapeutic candidates. On 3 April 2020, a shortlisting meeting was held, organised by Mr Whiting **(CJMW6/100a – INQ000497950**). An update about the same was provided in an email on 8 April 2020 to Therapeutics Taskforce members, myself included, in which Mr Whiting stated that, following a call with the ACCORD group that day, they were moving forward with a proposal to create a 'core' group and then to pull in experts from a wider pool, to facilitate discussion about specific drugs candidates (**CJMW6/100b – INQ000497952**).

New therapeutics

7.17 Therapeutic drugs can be used in multiple ways: to reduce mortality in the severely ill (generally in ICUs); to reduce the probability of hospitalised patients becoming severely ill; to reduce the chances a mildly ill person will need to be hospitalised; to act as a prophylactic preventive drug; to reduce infectiousness; or to shorten illness

without changing eventual clinical outcome. Generally, data are first available on reducing mortality from severe disease.

7.18 It was our expectation in OCMO that it would take some time for drugs, probably antivirals, specifically designed for COVID-19 to be developed. In the intervening period it would be necessary to test and use repurposed drugs (drugs which have a licence for another indication). These have the advantage that their side effect profile is usually known, and some or all clinicians are used to using them. They are also available and licenced. It is common practice to use drugs 'off licence' (i.e. outside the terms of their UK licence or without a licence for use in the UK) where there is good trial evidence to support this practice although the prescribing clinician takes responsibility for its off-licence use.

7.19 Whilst the development and testing of novel drugs specifically for COVID-19 was always likely to be predominantly done in industry initially (although often using data from publicly funded basic research), the testing of older drugs, and especially those which are off-patent, was always likely to be predominantly done in the public sector through a combination of academic and NHS work. Since these older drugs were likely to be quicker to be deployed, and less likely to be pursued by industry because many were already off-patent and available in cheaper generic formulations, this is where we put our initial efforts around research.

7.20 As the pandemic progressed, focus shifted from repurposed disease-modifying therapeutics (largely with impact on the immune system) to specific antiviral treatments and prophylaxis such as monoclonal antibodies against the virus and directly acting antiviral drugs. These were not available earlier in the pandemic. The OCMO (Professor Van-Tam and I) were involved in many of the discussions but were not driving the decisions on individual drugs to progress, which were mainly made by expert committees.

7.21 The Inquiry has asked specifically about prophylactic drugs. It was my view that prophylactic drugs had the potential to be important for a number of specific situations. These might include in particular higher-vulnerability individuals going into high-risk environments (e.g. a cancer patient going to hospital) or being visited by their family or undertaking social activities, for health or social-care workers in important but high-risk environments and where people from low-prevalence areas were visiting high-risk ones to reduce the risk of transmission over epidemiological boundaries. On the other hand, effective prophylactic drugs must have a number of essential properties. They

will have to have good antiviral activity; they have to be long-duration (unlike treatment) to cover the period at risk; they have to have very good safety profile as the person taking them does not have disease.

7.22 Because of these advantages, in an email dated 10 June 2020, I sought the expertise of a number of individuals, including Professor David Lalloo of the Liverpool School of Tropical Medicine, on what more we could do on prophylaxis for COVID-19, aiming to establish if there were any existing drugs, such as antivirals, which might be used for prophylaxis and how we could assess their effectiveness for preventing COVID-19 **(CJMW6/100c – INQ000497956)**.

7.23 A Prophylaxis Group Meeting was then held on 7 August 2020, the minutes of which state that as a 'next step', a Prophylaxis Study Design Group would be established with Professor Lalloo as the Chair **(CJMW6/100d & 100e – INQ000497957 & INQ000497545**.

7.24 By 15 September 2020, Professor Lalloo was the Chair of the newly-formed Prophylaxis Oversight Group, which had been set up with the broad purpose of determining which drug candidates may be suitable for COVID-19 prophylaxis **(CJMW6/100f – INQ000497960)**.

7.25 Once it became apparent that there was a good vaccine with high efficacy, and that effective antivirals were slow to be developed, the relative importance of prophylactic drugs receded. There was a remaining concern that people who could not mount an immune response might need prophylactic drugs, but in the absence of any good, long-acting and safe antiviral drugs this became less important in practice. Most people even with some immune paresis mounted a response to vaccines, but not all, although repeated vaccination increased this likelihood. With antibody-based drugs (like Evusheld) every time there was a major genetic shift in the virus (such as from Alpha to Delta) the previously assessed efficacy could not be assumed as the antigens to which the antibodies are targeted may have changed in a clinically relevant way. Professor Van-Tam was the primarily lead for OCMO in this area and provides detail in his personal statement at 3.36 – 3.38 on Evusheld. On 11 December 2020, I responded to Nick Elliott, Director General of the Vaccine Taskforce, outlining that Evusheld would not be available until after spring 2021 when the UK will have been rolling out a highly effective vaccine which would significantly change the landscape of the pandemic. I stated I could not recommend buying at scale for the reasons given above and "*at this stage there is too much uncertainty to recommend from a clinical*

perspective that government purchase any monoclonal antibody in advance of those [trial] results" but "*if there remains political appetite to buy on an at risk, precautionary basis the amounts bought should remain low. I would suggest under 50,000 doses.*" **(CJMW6/100g – INQ000507423)**. This would have been for particularly high risk individuals.

7.26 New treatments under development by pharmaceutical companies since the start of the pandemic were approved in the second year of the pandemic after demonstrating safety and efficacy in clinical trials. These included:

i. Ronapreve – a novel monoclonal antibody combination product for use in the preventing and treatment of hospitalised patients.[2]

ii. Sotrovimab – a monoclonal antibody for high-risk, non-hospitalised people and those with hospital-onset COVID-19.

7.27 Collectively, these drugs reduced hospitalisations, had mortality advantage and reduced pressures on the NHS, although to date none with as large an effect as dexamethasone.

7.28 It is important to recognise that much of the improvement in therapeutics seen in the first year of the pandemic was by doctors and other clinicians learning and sharing that learning with colleagues. Clinical trials were essential for identifying which repurposed, and subsequently more targeted, drugs were effective. Many of the therapeutic improvements, such as proning in ICU, best use of anticoagulants, or a switch from mechanical ventilation to non-invasive high-flow oxygen were the normal operation of the practice of medicine developing. We lay this out in more detail in the Technical Report **(CJMW6/001 – INQ000203933)**, especially Chapters 3, 9 and 10.

7.29 Alongside facilitating clinical research, a substantial part of the OCMO's role was to help avoid a situation in which unproven drugs were deployed without proper testing or strong clinical data to support them. It is very easy in an emergency to fall into the false syllogism: "something must be done; this is something; therefore we should do it".

[2] Subsequent variants were increasingly resistant to Ronapreve and by the time this was commercially available its efficacy against newer variants was much poorer than in the original trials data.

Procurement

7.30 Procurement of therapeutics was coordinated by the TTF and led by Steve Oldfield (DHSC Chief Commercial Officer). Professor Van-Tam, and I to a lesser extent, were involved in providing clinical advice to Ministers and other officials on what drugs to procure and in what quantities. By way of example:

i. On 31 January 2020, Professor Van-Tam advised Steve Oldfield, Sara McAleer (Principal Pharmacist, Medicine Supply Team, DHSC) and others in relation to the procurement of Remdesivir, Kaletra (lopinavir/ ritonavir) and Clarithromycin **(CJMW6/101 – INQ000151398)**.

ii. On 19 February 2020, Professor Van-Tam provided a combined DCMO and CMO view on the procurement of Kaletra and chloroquine/ hydroxychloroquine to Steve Oldfield, Kathryn Glover (Deputy Director, EU Exit & Medicines Supply, DHSC) and others **(CJMW6/102 – INQ000151493)**.

iii. On 2 April 2020, Professor Van-Tam advised Dr Helen Lovell (Deputy Director, Medicine Supply and Contingency Planning, DHSC) and others on joint procurement of various therapeutics with the EU and proposed quantities **(CJMW6/103 – INQ000068647)**.

iv. On 30 April 2020, Professor Van-Tam provided a note on Remdesivir (including a discrete section on procurement) to the Prime Minister **(CJMW6/104 & 105 – INQ000069025 & INQ000069026)**.

v. On 8 October 2020, Professor Van-Tam and Charlotte Taylor (Acting Director, TTF, DHSC) provided an update note on therapeutics to the Prime Minister **(CJMW6/106 & 107 – INQ000071054 & INQ000071055)**.

7.31 In April 2021, the Antivirals Taskforce ("ATF") was established along similar lines to the VTF and the TTF. The aim of the ATF was to ensure that the UK had access to at least two effective antiviral treatments by the winter of 2021 that could be used in the community. Molnupiravir and Paxlovid were purchased. The 'Antivirals Taskforce Proposition' document, outlining the purpose of and plans for the ATF is exhibited to this statement **(CJMW6/108 – INQ000416154)**. Professor Van-Tam helped establish the ATF and was a member.

7.32 In April 2022, the ATF and the TTF were merged to create the Antivirals and Therapeutics Taskforce ("ATTF"). A paper that was prepared for me and the DHSC CSA outlines the decision to merge the ATF and the TTF and consolidate their activities under the single ATTF **(CJMW6/109 – INQ000340353)**.

Approval

7.33 The OCMO did not have a role in the approvals process for therapeutics, which was independently conducted by the MHRA and the CHM. Ethical approvals for research were given by the HRA, also independently.

7.34 In respect of any innovations that were introduced to speed up the approval of new therapeutics, as intimated above, treatments that were trialled under UPH badging were prioritised for MHRA consideration and expedited through the MHRA process.

Delivery

7.35 The DHSC Therapeutics Clinical Review Panel was formed of senior clinicians from the four nations and determined which at-risk patient cohorts could be eligible for COVID-19 therapies. The panel provided advice on the definition and revision of eligible cohorts for new COVID-19 therapeutics from December 2021 to March 2023. Endorsed by Professor Powis, it provided advice to the UK CMOs for agreement of the UK clinical policy.

7.36 The practical delivery of therapeutics once they had been approved for use was a matter for NHSE. The OCMO's role was limited to the above and providing information to the medical profession through CAS alerts. For example, in mid-December 2020, OCMO issued a CAS alert along with the MHRA advising that results from the RECOVERY trial had indicated no significant clinical benefit of azithromycin in patients hospitalised with COVID-19 and that it therefore should not be used in the management of such patients unless there are additional indications for which its use remains appropriate **(CJMW6/110 – INQ000416174)**.

7.37 In contrast to vaccines there was no particular need for the CMOs and DCMOs to lay out risk-benefit to the public in respect of therapeutics. Risk-benefit discussions on drugs should be, and were, done on an individual risk-benefit basis by the attending clinician for a patient based on their particular circumstances. Usually this would be by a hospital doctor or general practitioner for someone who was unwell. The OCMO

therefore took a much less prominent role in the communication to the public around therapeutics, although we sometimes flagged that new trial evidence was available for example via the CMO Twitter account.

7.38 The COVID-19 Neutralising Monoclonal Antibodies (nMABs) and Antivirals Access Independent Advisory Group was established in late 2021 to identify a set of patient cohorts who were deemed to be at the very highest risk of an adverse COVID-19 outcome, namely hospitalisation and/or death.

7.39 In early June 2021, Professor Van-Tam was approached by Professor Anthony Kessel (NHSE&I), asking for his thoughts on the establishment of a national expert group to develop the process and clinical policy for nMABs **(CJMW6/110a – INQ000497961)**. A meeting was arranged for 17 June **(CJMW6/110b – INQ000497962)**. The first meeting of the nMABs IAG took place on 29 June 2021. Professor Van-Tam was not a member of the group; however he was informed about the first meeting, including its list of initial members **(CJMW6/110c – INQ000497963)**.

7.40 Professor Van-Tam was sent a copy of an interim draft report of the nMABs IAG, dated 19 November 2021 **(CJMW6/111 – INQ000067910)**. The group considered the use of nMABs and antiviral drugs in highest risk clinical subgroups upon community infection with SARS-CoV-2. A call was arranged later that afternoon to discuss the contents of the report with Professor Van-Tam. We agreed with the group's recommendations, which was fed back to the UK CMOs and DHSC colleagues **(CJMW6/111a & 111b – INQ000504731 & INQ000504733)**.

7.41 I am asked about the relationship between the nMABs IAG and the Therapeutics Clinical Review Panel (TCRP). I have no understanding of the relationship between the two groups as this was not a major part of OCMO activity.

Four nations

7.42 As with vaccinations, there was close engagement between the UK CMOs on therapeutics and the four nations collectively received advice from the Therapeutics Clinical Review Panel.

Additional points raised by the Inquiry in August 2024 relating to therapeutics.

7.43 The Inquiry has asked about a statement in the Technical Report the '*Generally, the UK was stronger on phase 3 and 4 trials than phases 1 and 2*' **(CJMW6/001 –**

INQ000203933 p314**)**. This was true in COVID-19 but this also in my view reflects strengths going into the pandemic. The UK has historically been one of the global leaders in methodology for phase 3 and 4 trials, including the design, running and statistical analysis of these including more complex methodologies such as platform trials and cluster-randomised trials, and in particular non-industry (academic or charity) led trials. Alongside this there is a centralised NHS (most health services are more fragmented), a strong tradition of evidence-based medicine in clinical training, existing trials support structures through the NIHR and respected regulators in the HRA and MHRA. UK patients and citizens more widely have a strong tradition of volunteering for trials. The relatively centralised decision-making allowed for rapid decision-making. Very few other countries have all of these, so it was unsurprising (to me and the DCMOs at least) that the UK had some of fastest, largest and most productive Phase 3 and 4 studies in COVID-19.

7.44 Phase 1 and 2 trials tend to have to be more industry driven and include much smaller numbers and the relative advantage of the UK is therefore smaller in an emergency. The UK conducts many Phase 1 and 2 trials, but so do other countries **(CJMW6/111c & 111d – INQ000497992 & INQ000497991)**.

7.45 The inquiry has asked whether the rapid development of new drugs or repurposed medications was prioritised over vaccines or vice versa. There was initially no strategic prioritisation and indeed to do so would have been unwise- at the start of the pandemic we did not know whether new vaccines, new antivirals (as with for example HIV), or repurposed drugs would be effective, and in which combination. We therefore set out to start all of them running in parallel. In general studies of drugs and vaccines did not compete as they are developed by different science teams and trialled in different groups **(CJMW6/111e – INQ000497994)**. It was possible to start phase 3/4 trials on repurposed drugs straight away whilst the basic and preclinical work was undertaken for novel antivirals and vaccines. Most therapeutic drug trials are in already infected patients (so in the NHS) whilst vaccine trials are in the community (pre infection). The difficult prioritisation was between the drugs or vaccines in class: generally vaccine studies did not compete with drugs because different people were being enrolled, but vaccine trials competed with one another, and drug trials in severely ill patients (or in primary care) competed with one another so a prioritisation was needed, and was set up.

7.46 On procurement more widely OCMO was relatively peripherally involved, but clinical prioritisation was on the basis of efficacy data and likely impact on the pandemic in the main.

Section 8: Lessons learned

8.1 There are several lessons relevant to this Module in the Technical Report. I therefore only make some key ones here.

8.2 In all pandemics the principal aim is to move from social measures (also known as non-pharmaceutical interventions (NPIs)) to medical interventions as soon as is practically possible. NPIs are, of necessity, blunt instruments which can cause significant social harm and are relatively less effective. All pandemics and major epidemics have been tackled that way since modern medical science became established in the 1850s.

8.3 To do this however requires a major international scientific effort. COVID-19 demonstrated this, and also demonstrated that the UK remains one of the leading countries able to undertake this kind of research, and at speed. In particular the global development of one of the major vaccines deployed, and the testing of multiple repurposed drugs was much faster than if the UK had not had the capacity to respond very fast. This in turn depends on steady investment and an integrated system of science and medicine in advance of the emergency; it cannot be created from scratch in the time needed. It is always easier to build out from or repurpose existing structures than create new ones.

8.4 Central to this is the ability to conduct clinical trials, and especially late-stage clinical trials. Through its public funding bodies such as NIHR, and the NHS, the UK has particular advantages for these kinds of study. This has to be invested in.

8.5 The most important starting point is that drugs, vaccines and diagnostics should be tested in rigorous randomised trials. Unless there is overwhelming evidence from indirect means that a new intervention is effective, and safe relative to efficacy, it should not in our view be used outside a trial except on an exceptional basis. The temptation in an emergency to say some variant of 'something must be done, this is something, therefore we should do it' is strong, and we came under considerable pressure to deploy treatments in advance of evidence. In COVID-19, as in the rest of medicine, treatments and vaccines for which there was strong theoretical or popular

support proved not to work, others were more effective than anticipated, and some important side effects were unexpected. Only by trials and proper follow up can the actual benefit and risk be quantified.

8.6 The prioritisation of a small number of studies was essential. Several countries started many more studies than the UK, but these failed to reach statistically or clinically meaningful outcomes, either at all, or in time, because the effort was diffused over too many studies at the same time with competition for resources, clinical scientists and above all volunteers. The centralised system in the UK (with the CMO as the final point of agreement) was effective and allowed for prioritisation at speed.

8.7 The remarkable volunteer spirit of the UK public to benefit others in the future was very apparent. Over 1 million people took part in studies.

8.8 Simplicity of study design was essential. Any additional detail leads to complexity and delay, and this is particularly important in a fast-moving emergency when all staff are very stretched.

8.9 There was however a price to be paid in non-COVID research. The UK, and England specifically, pivoted its resources in medical research over to COVID-19 research probably faster and harder than any comparable country. This achieved remarkable results for COVID-19, but at the cost of many studies on other diseases. The UK therefore took longer to get non-COVID research back on track after the greatest danger was passed and took longer than we initially anticipated. This was, in the view of the OCMO, a price worth paying given the size of the global emergency. But it was a high price.

8.10 Only by being transparent is it possible to maintain trust in scientific advice on drugs and vaccines. Giving balanced advice that also made clear the major advantages of drugs and vaccines but acknowledged side effects and uncertainties was not always easy in the compressed timeframes of press conferences and public statements. I, the DCMOs and other scientists spent a lot of time trying to work out how to do this in a way that had a reasonable chance of working for people starting with many different levels of scientific understanding. This will be true for any future infectious emergency.

Statement of Truth

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

Signed:

Dated: 7 October 2024