UK COVID-19 INQUIRY
MODULE 4: VACCINES AND THERAPEUTICS

CLOSING STATEMENT ON BEHALF OF THE OFFICE OF THE CHIEF MEDICAL OFFICER

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1. This brief written closing statement is filed on behalf of the Office of the Chief Medical Officer ("**OCMO**") at the conclusion of the hearings in Module 4 of the UK Covid-19 Inquiry.

2. The Inquiry has heard a great deal of evidence demonstrating the remarkable scientific effort and the volunteering spirit of UK citizens which helped to achieve significant success in the matters that were addressed in Module 4. As Professor Whitty set out in his sixth witness statement[1]:

> *"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."*

3. The CMO and DCMOs would like to take this opportunity to thank again all of those who responded so remarkably to address the threat posed by Covid-19, including in the field of vaccines and therapeutics.

4. However, it goes without saying that there are always lessons to be learned and individuals and communities who could be better served in any future epidemic, pandemic or other national health emergency. A clear example that has emerged in the evidence before the Inquiry (and in The Sudlow Review[2]) concerns the fragmentation of data. There will no doubt be more. The OCMO looks forward to receiving the Chair's report and recommendations which follow this Module.

5. There is one area on which OCMO wishes to address the Chair, namely the decision of DHSC not to procure Evusheld, in order to ensure that that the Inquiry does not take a wrong turn in the understandable desire to improve the lives of those who are immunocompromised and at increased risk of severe Covid-19 outcomes.

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[1] **[INQ000474401_0003]** at §1.4
[2] **[INQ000474861]**

6. **First**, OCMO asks the Inquiry to closely consider the timeline in respect of Evusheld. It was not until 17 March 2022 that Evusheld was given conditional marketing authorisation by the Medicines and Healthcare products Regulatory Agency. It was therefore not possible to use Evusheld before that date. By this point most of the population was vaccinated, and high risk individuals were vaccinated multiple times; shielding had ended many months before; and Omicron had become the dominant variant and was evolving rapidly in a direction which did not favour the drug. The trial evidence was on previous variants of Covid-19, in unvaccinated populations. In OCMO's submission, those witnesses who suggest that procuring Evusheld would in fact have made a difference to the lives of high risk individuals do not sufficiently acknowledge this timeline.

7. **Second** (and related to the above) it is important to bear in mind that there are a great many, and based on recent data probably the great majority, of patients who are immunocompromised for whom the solution is vaccination. The position is not a binary one between vaccination for the general population and therapeutics for the immunocompromised[3]. The academic literature overwhelmingly demonstrates that Covid-19 vaccines are protective against severe Covid-19 outcomes in this vulnerable population and show a similar safety profile in immunocompromised individuals and the general population[4]. As Professor Whitty observed: "*very good data subsequent to this decision has demonstrated that most of the people we were worried would not respond to the vaccine in fact did*"[5].

8. That subsequent academic research is in line with the initial view of OCMO when it was asked to provide advice in respect of Evusheld in late 2020. In his letter to the UK Vaccine Taskforce of 11 December 2020[6], Professor Whitty observed that the earliest Evusheld (AZD4722) "*would become available for use is after spring 2021, so after the UK intends to have rolled out the vaccination programme quite significantly*". Professor Whitty observed that the landscape had changed by that stage "*since we have vaccines which seem highly effective in use or under review*".

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[3] Professor Van Tam, Transcript of 20 January 2025 at **[5/182/18]**
[4] See, for example, *Uptake, effectiveness and safety of COVID-19 vaccines in individuals at clinical risk due to immunosuppressive drug therapy or transplantation procedures: a population based cohort study in England*, Chen et al in BMC Medicine (2024) 22:237 **[INQ000572004]** and *Effectiveness and safety of COVID-19 vaccination in people with blood cancer*, Copeland et al in European Journal of Cancer (2024) vol 201 **[INQ000572003]**. See also Professor Van Tam, Transcript of 20 January 2025 at **[5/179/15]**
[5] Professor Whitty, Transcript of 20 January 2025 at **[5/114/7]**
[6] **[INQ000507423]**

9. Professor Van Tam similarly noted on 10 February 2021 that "*the UK vaccination programme is advancing at pace*"[7] and stated that a key priority at that stage was therefore collecting data on vaccine effectiveness in those who were immunocompromised. Identifying the correct cohorts who might receive relevant therapeutics (such as those with unpredictable, low or no antibody response) would be essential. Like Professor Whitty, Professor Van Tam noted that Evusheld was "*unlikely to produce trial data or obtain regulatory approvals until the end of 2021, if not later*". As it happens, both of these time estimates for Evusheld were overly optimistic and it was not in fact given conditional marketing authorisation until 17 March 2022 as noted above.

10. In short, the vaccine programme was progressing at pace and ultimately working for a great many immunocompromised patients whilst Evusheld was still in its early stages of testing and approval.

11. **Third**, it was well established that monoclonal antibodies such as Evusheld carry significant disadvantages to vaccines. In particular, the latter can deal with the evolution of a virus to a much greater extent. This was explained contemporaneously by Professor Van Tam in his letter of 10 February 2021 in which he observed: "*DHSC will also want to understand the impact of Covid-mutations, recognising that current antibody therapies may need replacement as the virus evolves".*

12. The Rapid C-19 Oversight Group ('the Group") considered the evidence base for Evusheld from February 2021. By December 2021 its recommendation to the CMO stated that "*there is a risk associated with introducing a partially or minimally effective therapy and [we] do not currently recommend routine use of this treatment until more data on efficacy against Omnicom is available*"[8] By May 2022 the Group had observed that "*because of the difficulties in extrapolating non-clinical data to conclusions about clinical effectiveness, there is no certainty that…[Evusheld] would prevent symptomatic COVID-19 caused by the Omicron variants in the vulnerable population*" and "*the risks of proceeding to…access are considered to outweigh the risks of not providing the treatment*".[9] The Group had the benefit of input from the Prophylaxis Oversight Group ("POG").[10] As Helen Knight observed in her oral evidence to the Inquiry:

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[7] **[INQ000072735]**
[8] **[INQ000479901_0016]**
[9] **[INQ000479901_0010]**
[10] **[INQ000494606]**; Helen Knight statement, **[INQ474611_0053]**

> *"we were very aware that we were discussing a prophylactic medicine for patients who had a high unmet need but we were also very clinically vulnerable and shielding at the time. And so we felt…these were people that weren't infected with the virus and…we wanted to make sure that we had a high confidence that the treatment would protect this clinically vulnerable group because…we wanted to be confident that the protection would continue and we didn't see the evidence to say that it would".*[11]

13. Professor David Lalloo, chair of POG, was also a member of a National Expert Group convened to discuss the suitability of Evusheld.[12] He explained that following a meeting on 19 May 2022 there "*was unanimous agreement from the National Expert Group that Evusheld could not progress to deployment as PrEP against COVID-19. The group's recommendation not to proceed with Evusheld was shared with the CMO.*"[13] The briefing to the CMO reiterated the need to generate "*meaningful clinical data"* suggesting this could be in the form of a "*pragmatic clinical trial*".[14] Professor Lalloo agreed with the Inquiry's proposition that further clinical research evidence could have been obtained explaining that this was why there was "*a concerted effort to get Evusheld into PROTECT-V, however there was reluctance from AstraZeneca to participate which meant that no further research was done".*[15]

14. In the absence of trial data, which might have demonstrated Evusheld's efficacy against Omicron, or being able to extrapolate laboratory data into conclusions on clinical effectiveness, the Group was asked to consider real world data (i.e observational) from countries which had deployed Evusheld. It considered this evidence on 17 and 24 August 2022.[16] At its meeting on 24 August 2022 the Group observed:

> *"Overall, RAPID C-19 considers that the quality of the data is insufficient to warrant action to progress to consideration of an access policy as an interim measure before NICE technology appraisals (see proposed actions). There is uncertainty that tixagevimab plus cilgavimab would prevent symptomatic COVID-19 caused by the current Omnicron variants in the vulnerable population who would potentially be eligible for this treatment. There is insufficient evidence to proceed to patient access in the current pandemic context".*[17]

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[11] Helen Knight, Transcript of 30 January 2025 at **[12/55/11]**
[12] **[INQ000474625_0016]**
[13] **[INQ000474625_0017]**
[14] **[INQ000414472]**
[15] **[INQ0000474625_0017]**
[16] **[INQ000474611_0054]**
[17] **[INQ000479901_0006]**

15. These observations from the multi-agency expert initiative were consistent with the position as set out by the CMO and DCMO in early 2021, in particular that there was too much uncertainty to recommend Evusheld in advance of licencing but that it should be kept under review. Had Evusheld acquired a licence before the evolution of Omicron and the population was multiply vaccinated the situation would very possibly have been different, but it did not.

16. The Rapid C-19 Oversight Group reports are important in the overall consideration of the Evusheld issue because, as Helen Knight made clear, the Group "*never considered the cost, particularly with Evusheld…at no point were we thinking about the cost or cost effectiveness*"[18]. Similarly, Professor Lalloo emphasised that "*cost considerations did not influence decision making around Evusheld … by the POG*." In those circumstances, any suggestion that cost was the driving factor in the advice concerning the proposed procurement of Evusheld (either in 2022 or earlier in 2021) is without any evidential foundation. Cost was, in the words of Professor Whitty, only a "*third order question*" for OCMO[19]. If a drug is not considered effective, its cost is irrelevant as it would not be prescribed.

17. Whilst OCMO acknowledges that there may well be legitimate debate as to whether public money should be spent on therapeutics on a precautionary basis irrespective of matters such as likely effectiveness vis-à-vis vaccinations, it is respectfully submitted that Evusheld is a poor example on which to properly consider this issue in light of the timing of its approval and inadequate information as to its effectiveness in particular in respect of the evolution of the virus.

Bilal Rawat
Julian Blake

12 February 2025

[18] Helen Knight, Transcript of 30 January 2025 at **[12/66/23]**
[19] Professor Whitty, Transcript of 20 January 2025 at **[5/114/11]**