THE UK COVID-19 INQUIRY

MODULE 4

OPENING STATEMENT ON BEHALF OF
THE MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY

Introduction

1. This written opening statement is made on behalf of the Medicines and Healthcare products Regulatory Agency ("MHRA").

2. The MHRA welcomes the opportunity to take part in Module 4 of the UK Covid-19 Inquiry to ensure that its role and actions are fully understood and to play its part in supporting the Inquiry to make findings and recommendations which will ensure that the United Kingdom and global community are better prepared for future pandemics.

3. At the outset of these submissions, the MHRA wishes to record its condolences and sympathies to all those who were affected by the Covid-19 pandemic. In particular, and in the immediate context of Module 4 of this Inquiry, the MHRA wishes to publicly acknowledge its profound regret that anyone should have suffered adverse effects in association with receiving a Covid-19 vaccine or therapeutic. The MHRA recognises the serious suffering faced by those who now live with long-term injuries, and by their families. No vaccine or medicine is without risk, and the MHRA is committed to finding out as much as possible about those risks and to ensuring that no effort will be spared to further strengthen its systems to identify and act to minimise risks however rare.

4. It is important to acknowledge the many deaths that were prevented as a result of the Covid-19 vaccination programme. It has been estimated that from 1 January to 8 December 2021, Covid-19 vaccines prevented between 14.4 million and 19.8 million deaths from Covid-19 in 185 countries and territories, and by September 2021 it was estimated that the UK vaccination programme had prevented over 20 million infections and over 100,000 deaths.

5. The Inquiry will also have in mind the extraordinary context in which unprecedented decisions and actions were taken. The authorisation and subsequent rapid and widescale deployment of Covid-19 vaccines prevented the loss of many thousands

of lives and allowed the UK and the global community to return to some degree of normalcy more quickly.

The role and functions of the MHRA

6. The MHRA is the United Kingdom's regulator of medicines (including vaccines and therapeutics), medical devices, and blood components for transfusion. The MHRA is responsible for ensuring their safety, quality and efficacy. Its mission is to enhance and improve the health of millions of people in the UK every day through the effective regulation of medicines and medical devices, underpinned by science and research.

7. The MHRA is an executive agency of the Department of Health and Social Care. It was formed in 2003. Although it is legally indistinguishable from the Secretary of State, it is operationally independent.

8. In September 2020 the MHRA agreed with the then Secretary of State that licensing decisions on Covid-19 medicinal products were exceptional by nature and therefore the MHRA should not take its usual delegated action. It was decided instead that the 'Licensing Minister' who took advice from the MHRA and the independent scientific advisory body, the Commission of Human Medicines, would take all licencing decisions.

9. The MHRA's primary responsibilities are:
    a. Ensuring that medicines, medical devices and blood components for transfusion meet applicable standards of safety, quality and effectiveness;
    b. Ensuring that the supply chain for medicines, medical devices and blood components is safe and secure;
    c. Promoting international standardisation and harmonisation to assure the safety, quality and effectiveness of all medicines;
    d. Helping to educate and inform the public and healthcare professionals about the risks and benefits of medicines, medical devices and blood components, leading to safer and more effective use;
    e. Supporting innovation and research and development that are beneficial to public health; and
    f. Influencing UK and international regulatory frameworks so that they are risk-proportionate and effective at protecting public health.

10. The Inquiry will hear from the MHRA's Chief Executive, Dame June Raine CBE who has provided a detailed witness statement. In summary, and by reference to the Provisional List of Issues for Module 4, the MHRA was involved in:

    a. The development of Covid-19 vaccines, including through the authorisation of clinical trials;

    b. The authorisation of Covid-19 vaccines;

    c. Post-marketing surveillance of those vaccines and communication of the results of that surveillance to clinicians, the public and others; and

    d. The development, clinical trials and authorisation of therapeutics.

11. Throughout the pandemic the MHRA benefited from independent expert advice from several advisory committees. In particular, the MHRA sought the advice of the Commission on Human Medicines ("CHM") and its Expert Working Groups.

12. The MHRA is not responsible for procurement or deployment decisions. In respect of the latter, decisions on which vaccines and medicines were deployed and who might receive those vaccines and medicines were taken by the Joint Committee on Vaccination and Immunisation ("JCVI") or the devolved health authorities.

13. The JCVI's decision-making processes and remit are entirely distinct from those of the MHRA. Therefore, while the JCVI is made aware of the advice of the MHRA and the CHM, the JCVI is not involved in decisions concerning the authorisation of vaccines or medicines and has no influence on them. Similarly, the MHRA does not take part in formulating UK vaccine policy recommendations, such as whether to procure and deploy a vaccine for a particular group, or at all. Such decisions are within the remit of the JCVI alone. There is advantage in having the two approaches of separate regulatory and deployment decisions, side by side but taking into account different criteria. The regulatory approach is strictly focussed on safety, quality and effectiveness, and provides the terms and measures which support effective and safe use, while the health authority's deployment advice can prioritise different products depending on wider factors including availability of vaccines, changing disease pattern and considerations for vulnerable groups.

A flexible and enabling regulator

14. The Covid-19 pandemic was a profoundly challenging time for everyone, including for those public servants who were at the forefront of the national response effort. Traditional ways of working were adapted, including by the MHRA. It did so by adapting and enhancing its established scientific and regulatory advice service to put patients first, becoming a truly world-leading, enabling regulator and protecting public health through excellence in regulation and science.

15. The MHRA collaborated with Government departments, industry and academia to support the development and approval of new medicines. At all times the MHRA protected and preserved its independence whilst at the same time supporting the efforts to find vaccines and therapeutics which would save lives.

16. As is well-known, the Pfizer/BioNTech (Comirnaty) vaccine was the first vaccine for Covid-19 that was authorised for use by the MHRA and was the first vaccine against Covid-19 authorised worldwide. In subsequent weeks regulators in other jurisdictions followed suit, with no significant differences in the terms of their approvals. It was first administered in UK on the morning of 8 December 2020 in Coventry, England. This was a pivotal moment: the start of mass Covid-19 vaccination programmes worldwide.

17. As of December 2023, the MHRA had authorised nine vaccines for use against Covid-19 with a further four strain-adapted vaccines. Six new medicines were authorised for Covid-19 with two previously authorised therapeutics approved by the MHRA for use to treat Covid-19.

18. The MHRA adopted a number of regulatory flexibilities that were crucial in facilitating these approvals. This included the use of the 'rolling review' processes which ensured that medicinal products were made available in the shortest possible time once benefit risk was found to be positive from the perspective of safety, quality and effectiveness. The use of the accelerated rolling review procedure meant that the MHRA authorised not only vaccines, but also some Covid-19 therapeutics significantly sooner. For example: Paxlovid (nirmatrelvir with ritonavir) was authorised in 37 days, Lagevrio (molnupiravir) was authorised in 127 days, and Xevudy (sotrovimab) was authorised in 134 days.

19. Whilst outside the scope of Module 4, it is also material to note that simultaneously the MHRA played a leading role in securing access to medical devices through, for example, the 'Ventilator Challenge' (which will be explored in Module 5 of the Inquiry).

20. Following 1 January 2021, the MHRA was able to grant national licences for Great Britain as it was no longer subject to the European Medicines Agency's regulatory processes. However, even prior to 1 January 2021, utilising regulation 174 – and later regulation 174A – of the Human Medicines Regulations 2012, the MHRA was able to take action and ensure that medicinal products were available for use earlier than would otherwise have been the case. This was in line with Article 5.2 of Directive 2001/83/EC.

21. None of those flexibilities compromised the rigour of scientific scrutiny of the evidence of safety, quality and efficacy. The MHRA's scientific standards remained unchanged and were in line with international standards.

Benefit risk decision-making by MHRA

22. An understandable focus of much of the evidence in Module 4 will be on the safety of Covid-19 medicinal products. The MHRA's first priority is safety, with a core focus at all times on the balance of benefits and risks of a medicinal product or vaccine. As already stated, no medical product is completely risk-free: all have the potential to cause side effects.

23. The MHRA is responsible for regulating medical products, including vaccines, medicines, and devices in the UK by ensuring that they work and are acceptably safe. In this context, 'acceptably safe' means that based on the assessment of the MHRA, the benefits, or expected benefits, associated with a particular product are considered to outweigh any risks associated with that product, at a population level, and that the risks are acceptable in the context of the expected benefits.

24. The MHRA adopts a qualitative approach to benefit risk analysis which is best described as 'critical appraisal': weighing all the available evidence on efficacy and safety when used in a particular indication, taking into account the disease and the patient population in question and the current treatment options. Increasingly, the

views of patients with lived experience of a condition are involved in MHRA benefit risk decision-making.

25. In practice, in order to make an assessment of the benefit risk of a medicinal product for authorisation, the MHRA considers all evidence from the pre-clinical studies and clinical trials on how well a given medical product works and its safety profile. Clinical trials generally only study a finite number of patients over a defined period which means that understanding of benefit risk is necessarily provisional. The MHRA therefore puts in place a risk management plan which comprises what is known about a medicine's safety profile, how any risks will be prevented or minimised in patients, any plans for studies or other activities to gain more knowledge about the medicinal product in areas of knowledge gaps (for example use in pregnancy), and the plans to evaluate the effectiveness of any risk minimisation measures.

26. In studies of whether available therapeutic agents were effective in the treatment of Covid-19, the MHRA demonstrated flexibility in supporting the design of the protocol for the RECOVERY trial, which was an 'Adaptive Platform Trial' embedded in clinical care that allowed multiple therapies to be evaluated simultaneously under a master protocol. This led to results which could promptly inform clinical care of patients with Covid-19 and early recommendations for Covid-19 therapeutic treatments. For example, the positive outcome of the RECOVERY trial on the use of dexamethasone in the treatment of hospitalised Covid-19 patients was introduced into standard of care for patients with Covid-19 who had been admitted to hospital and who required oxygen therapy, on the day the results became available.

Post-marketing surveillance and safety monitoring

27. Importantly, medicinal products are authorised by the MHRA with a requirement that manufacturers operate a robust post-authorisation surveillance system through which the benefit risk balance can be revised as real-world data becomes available and as clinical usage expands.

28. Cognisant of the likely mass roll-out of Covid-19 vaccines, well in advance of licensing the MHRA developed a comprehensive vigilance strategy to monitor safety in as close to real-time as possible. There were four 'pillars' to the MHRA's Covid-19 surveillance strategy which combined to address the relative strengths and

weaknesses of each form of vigilance and build the most comprehensive strategy capable of providing close to real-time vigilance. Those four 'pillars' were:

a. Enhanced passive surveillance ('observed versus expected' analysis);
b. Targeted active monitoring through the Yellow Card Vaccine Monitor;
c. Rapid Cycle Analysis and Ecological analysis; and
d. Formal epidemiological studies.

29. The Yellow Card Scheme is the method through which healthcare professionals and members of the public can report suspected side effects or adverse drug reactions associated with any medicines or vaccines (as well as medical device incidents). These reports are evaluated by MHRA scientists and clinicians, together with other data, to identify any new safety signals of changing or emerging side effects. During the pandemic roughly 500,000 reports of suspected adverse reactions were received. The MHRA operated with unprecedented transparency and openness as the safety profile of the Covid-19 vaccines and therapeutics used in the UK population evolved, publishing fortnightly summaries of Yellow Card data.

30. The Inquiry will hear evidence about the Yellow Card Scheme and the understanding of the adverse reactions associated with particular vaccines. The Inquiry will consider, in particular, how the MHRA detected, evaluated and responded to the risk of thrombosis with thrombocytopenia syndrome associated with the AstraZeneca vaccine and the risk of myocarditis / pericarditis associated in particular with mRNA vaccines (Pfizer/BioNTech and Moderna).

31. Thrombosis with thrombocytopenia syndrome was a new and very rare specific syndrome which was identified and characterised following the rollout of the Covid-19 vaccination programme. The MHRA first received Yellow Card reports of suspected thrombosis and associated thrombocytopenia connected with the AstraZeneca (Vaxzevria) vaccine in February 2021. In the following days and weeks, the MHRA sought expert advice on the investigation of the risk, its impact on the benefit risk of the vaccine, and on appropriate regulatory action including communication from the Covid-19 Vaccines Benefit Risk Expert Working Group of the Commission on Human Medicines and from the Commission itself.

32. As the Inquiry will hear, the MHRA provided updated guidance to healthcare professionals and the public. However, it did not withdraw the marketing authorisation for the AstraZeneca (Vaxzevria) vaccine in line with all other regulatory authorities worldwide as the overall balance of benefits and risks remained favourable. The JCVI did alter its recommendations as to the use of the vaccine.

33. Similarly, the licences for mRNA vaccines were updated to include risks known about myocarditis and pericarditis as evidence became available. The first update to product information regarding the risk of myocarditis and pericarditis was made on 25 June 2021, with further updates to product information and to the public from the close monitoring of mRNA vaccines particularly with the deployment of further doses.

Conclusion

34. The MHRA seeks to be an organisation which learns and improves through that learning. It recognises the importance of external scrutiny, especially in the context of vaccination where misunderstanding, misinformation or disinformation are prevalent. Little could be more corrosive to public confidence in vaccines and other medicinal products as secrecy or obfuscation. To that end, during the pandemic the MHRA sought to be open and transparent about its decision-making on the benefit risk of Covid-19 vaccines and therapeutics. The MHRA comes to this Inquiry with a willingness to continue to assist in establishing the facts and to enable lessons to be learnt, so that it can continue to strengthen its systems and processes, particularly in the likely event of a future pandemic.