Witness Name: Darius Hughes
Statement No.: 1
Exhibits: DH/1 – DH/59
Dated: 22 October 2024

UK COVID-19 INQUIRY

WITNESS STATEMENT OF DARIUS HUGHES

I, Darius Hughes of Moderna Biotech UK Limited, 54 Portland Place, London, England, W1B 1DY, will say as follows: -

1. I joined Moderna Biotech UK Limited in July 2021 as General Manager for the UK. I am responding to the UK COVID-19 Inquiry's (the "**Inquiry**") Request for Evidence under Rule 9 of the Inquiry Rules 2006, received by way of the letter dated 18 September 2023 (the "**Inquiry's letter**"). In this statement I refer to Moderna Biotech UK Limited as "MBUK" ("**MBUK**") rather than "Moderna", as used in the Inquiry's letter, to avoid confusion with references to other Moderna entities operating and based outside the UK including ModernaTx, Inc., Moderna Switzerland GmbH and Moderna Biotech Spain, S.L. Individuals and teams within those two entities and other companies within the Moderna group outside the UK undertook tasks relevant to the development, regulatory approval, and supply of vaccines to the UK as noted further below.

2. I refer to the "Moderna business" or "Moderna group" or "Moderna team" when speaking more generally about activities relevant to Moderna's COVID-19 vaccine and when my comments are not specific only to one entity. I note that the Inquiry's letter refers to the Moderna COVID-19 vaccine as Spikevax and I generally adopt that approach.

3. I make this written statement to the best of my knowledge and belief, based upon the information available to me in my role as General Manager, UK and Ireland at MBUK, and from facts within my own knowledge. I have also consulted widely with colleagues in the UK, Europe, and the USA in order to be able to answer the Inquiry's questions as completely as possible. In addressing some questions, I am relying on the memory of others based outside the UK regarding events which happened over four years ago in a fast paced and challenging working environment. However, I have tried to verify information and where the facts stated are not within my own knowledge, I believe them to be true.

4. I am conscious of the significance and the importance of the Inquiry's work and, as someone who lived and worked through the pandemic in the UK, I understand the need to help explain to the UK public how vaccines were developed, approved, and regulated and then supplied to the UK and in particular the role played by MBUK.

5. MBUK values the opportunity to participate in this Inquiry and to address the role that vaccines have played in preventing severe illness and death throughout the COVID-19 pandemic. The COVID-19 pandemic has claimed an estimated 7 million lives worldwide. These deaths are not simply statistics, they represent far-reaching loss and suffering for much loved family members, friends and colleagues. Moderna recognises that the impacts of the pandemic, at its outset and still today, continue to have profound and long-term impacts on families and communities.

6. The Inquiry's letter includes a request for a witness statement, relevant to the Module 4 Provisional Outline of Scope, and identifies a number of individual questions under ten topic headings as set out in Annex A of the Inquiry's letter. I provide below MBUK's comments in relation to each of the ten topics identified in the Inquiry's letter. I have tried to address the specific questions under each of those headings but have found that in some instances it made sense to answer several questions together in one answer in order to avoid repetition and to provide a more coherent and complete answer.

7. As proposed in Annex A of the Inquiry's letter, the subject matter of this statement relates primarily to matters that occurred between 30 January 2020 – the date upon which the first case of COVID-19 was confirmed within the UK – and 28 June 2022

("**the date range**"). However, where I believe that further context is helpful, I have also referenced matters outside the date range.

8. As requested, I exhibit key documents to this witness statement.

9. This statement is structured as follows:

Section	Subject	Paragraphs
A.	**Structure, Role, People and Processes**	**10 - 19**
B.	**Key decisions, actions and documents**	**20**
C.	**Vaccine preparedness**	**21 - 25**
D.	**Development of COVID-19 vaccines**	**26 – 90**
E.	**Approval process**	**91-104**
F.	**Vaccine delivery and prioritisation**	**105-121**
G.	**Vaccine safety**	**122- 200**
H.	**UK Vaccine Damage Payment Scheme**	**201**
I.	**Lessons learned and preparing for a future pandemic**	**202-210**

A. STRUCTURE, ROLE, PEOPLE AND PROCESSES

10. In this section, I provide a brief overview of MBUK and its relationship with other Moderna group companies and an outline of MBUK's recent history in relation to the subject matter of Module 4.

Moderna Biotech UK Limited, Moderna Switzerland GmbH, Moderna Biotech Spain S.L., ModernaTx, Inc. and Moderna, Inc.

11. MBUK is a private company limited by shares that was incorporated as "ModernaTX Ltd" on 10 May 2019. The company name was changed to Moderna Biotech UK Limited on 17 June 2020. MBUK's current registered address is 54 Portland Place, London, England, W1B 1DY. It is a wholly owned subsidiary of ModernaTx, Inc. When I joined MBUK in July 2021 I was only the second employee. I recruited the initial UK team. Since 2021 when I joined the company, UK Moderna operations have developed significantly. In June 2022, two new legal entities were formed: Moderna Biotech Distributor UK Ltd, and Moderna Biotech Manufacturing UK Ltd. As of October 2024, Moderna companies in the UK now currently employ over 100 people.

12. As the Inquiry can see, MBUK is a relatively young company which was established during the pandemic. Given that context it may be helpful for me to briefly explain the history of the Moderna group further.

13. The first Moderna company was founded in 2010 by scientists as a biotechnology "start-up" company and a pioneer in the development of messenger RNA (**"mRNA"**) vaccines and therapeutics. The founders of the first Moderna business wanted to find ways of developing mRNA technology to treat and prevent diseases **[DH1/1 - INQ000398086]**. The "Moderna" name reflects this founding principle combining the words "modified" and "RNA".

14. Since the Moderna business was first founded, it has developed an industry leading mRNA platform that builds on continuous advances in basic and applied mRNA science, technology, and manufacturing. The focus is creating a new generation of medicines based on mRNA technology to pave the way for clinical development of therapeutics and vaccines for infectious diseases, immuno-oncology and rare diseases **[DH1/3 – INQ000502012].**

15. The Moderna group of companies has become a global business of which the UK company that I represent, MBUK, is one company.

16. The ultimate group parent company is Moderna, Inc. Both ModernaTx, Inc. and Moderna, Inc. are headquartered in Massachusetts, USA, Moderna Switzerland GmbH was established during the pandemic in June 2020 as the international headquarters

of the Moderna business outside of the US. It was the central resource in Europe to manage the Moderna group's interactions with international governments and agencies outside of the US particularly during the early phase of the pandemic. When the UK Government sought an agreement for the supply of the Moderna COVID-19 vaccine, Moderna Switzerland GmbH, the main group company in Europe, was the contracting party.

17. When the Moderna COVID-19 vaccine was authorised by the European Medicines Agency (**"EMA"**) and then the Medicines and Healthcare products Regulatory Agency (**"MHRA"**), Moderna Biotech Spain S.L. was the group company in Europe that held the marketing authorisation for the vaccine in both the European Union and the UK. That remains the case today. (See **[DH1/2 - INQ000398087]**).

18. In response to the Inquiry's request for the identification of key individuals and decision makers within the Moderna business, I have provided a list of individuals, identified to date, who I think are relevant to the matters in the Provisional Outline of Scope for Module 4.

19. In compiling this list of "Moderna" individuals I have tried to identify people I think played an important role rather than list everyone at each Moderna company who played a part in vaccine development, delivery and supply to the UK. It was a huge effort undertaken by numerous people within the Moderna business. The list also notes the key individuals within the Vaccine Taskforce (**"VTF"**) and MHRA with whom the Moderna business had contact.

B. KEY DECISIONS, ACTIONS AND DOCUMENTS

20. A chronology of key events and actions is exhibited to assist the Inquiry's understanding of MBUK and the Moderna group's role in relation to matters within Provisional Outline of Scope for Module 4 (see **[DH1/4 - INQ000398088]**).

C. VACCINE PREPAREDNESS

21. Following the declaration of COVID-19 as a global pandemic by the World Health Organization in March 2020, developing vaccines was the top priority of governments, medical researchers, and the wider global community, because it was promptly recognised that control of the pandemic would require safe and efficacious vaccines.

The Moderna group dedicated its expertise and resources to COVID-19 vaccine development from January 2020.

22. Worldwide, it is estimated by the World Health Organization (**"WHO"**) that over 13 billion COVID-19 vaccine doses have been administered, and more than 70% of the world's population have received at least one dose. Moderna have supplied approximately 1.5 billion COVID-19 vaccines to date. I explain further below how Moderna's Spikevax vaccine was developed, tested, approved, and supplied to the UK.

23. I cannot comment on what others had learnt from previous epidemics or pandemics, but when the COVID-19 pandemic arose, ModernaTx, Inc. had been doing foundational research in the field of mRNA-based drugs, in particular on other coronaviruses including Middle East respiratory syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS), for a number of years. Before developing mRNA-1273, ModernaTx, Inc. had already established a close relationship with the US National Institute of Health (**"NIH"**) as a result of its previous work on an mRNA vaccine for MERS.

24. Through this partnership ModernaTx, Inc. and the NIH developed and tested mRNA vaccination strategies aimed at prevention of MERS. This work alongside other ModernaTx, Inc. research targeting influenza viruses had clearly demonstrated that the mRNA technology was effective **[DH1/5 - INQ000398089].**

25. When it came to responding to the COVID-19 pandemic ModernaTx, Inc. leveraged its existing expertise in developing mRNA vaccines, encoded for the viral spike protein to respond to MERS and SARS infections, to identify a potential vaccine candidate that could be effective against COVID-19.

D. DEVELOPMENT OF COVID-19 VACCINES

26. The Inquiry has asked for a chronological overview of the key stages of the development, manufacture, procurement and approval of the vaccine which I have tried to describe in summary below breaking up the chronological account in stages to reflect the different work which was undertaken.

Response to the COVID-19 pandemic with mRNA-1273: vaccine development

27. The development of the initial Moderna COVID-19 vaccine, including all clinical trials, was undertaken in the United States. As a result, the history of the initial Moderna vaccine development is focused largely in the United States.

28. On 11 January 2020, the Chinese authorities shared the genetic sequence of the novel coronavirus. Shortly after, ModernaTx, Inc. began discussions with the NIH, the Federal Drug Administration (**"FDA"**) and other US agencies to discuss clinical development collaborations, funding options and potential regulatory pathways for a vaccine candidate.

29. ModernaTx, Inc.'s, SARS-CoV-2 vaccine was developed with in-kind support from the NIH and funding support from the Biomedical Advanced Research and Development Authority ("**BARDA**"). Moderna's vaccine was one of a handful of vaccine programs to which BARDA provided funding, and across the vaccine portfolio supported a systematic evaluation of the efficacy, immunogenicity, and safety of the vaccine candidates. ModernaTx, Inc. and the NIH had previously conducted preclinical research against a number of pathogens with pandemic potential, including MERS and Nipah, and planned to undertake a "proof-of-concept" exercise to explore the speed at which Moderna could deploy a novel vaccine for clinical testing. In early 2020, the NIH and Moderna agreed to redirect their partnership to accelerate a COVID-19 vaccine to Phase 1 clinical testing. ModernaTX, Inc. finalised the composition of mRNA-1273 against SARS-CoV2 by 13 January 2020. The ModernaTx, Inc. team recognised important similarities to the MERS virus and based on that prior experience, decided to encode for the pre-fusion stabilized full-length Spike (S) protein. A detailed account of the development of the vaccine can be found in the briefing document presented to the VBRAC on 17 December 2020 which is exhibited to this statement (see **[DH1/6 - INQ000398090]**) but I have tried to summarise the key milestones below.

Development and clinical trials of the Moderna COVID-19 Vaccine

Phase 1 study in the United States

30. The National Institute of Allergy and Infectious Diseases (**"NIAID"**) disclosed its intent to run a Phase 1 study using the mRNA-1273 vaccine. A Phase 1 study is usually the first time that a drug or treatment is tested in humans. The purpose is to study the drug

or treatment to learn about its efficacy and identify any side effects, that is to assess its benefit/risk profile. On 7 February 2020, ModernaTx, Inc. completed the manufacture of its first batch of mRNA-1273 for human use in clinical trials, which then proceeded to analytical testing prior to release. On 24 February 2020, the vaccines were shipped to the NIH to be used in NIH's Phase 1 study in the United States.

31. On 4 March 2020, the FDA approved the NIH's Investigational New Drug application (**"IND"**) for mRNA-1273 and allowed the Phase 1 clinical trial to proceed. The Phase 1 study was conducted by NIAID under its own IND application in the United States. Following the submission of the IND, ModernaTx, Inc. regularly consulted with the Center for Biologics Evaluation and Research (**"CBER"**) on the clinical development of mRNA-1273 and provided nonclinical and clinical data packages to help assess the benefit-risk profile of mRNA-1273 on an ongoing basis. The clinical development of mRNA-1273 was expedited under Operation Warp Speed ("**OWS**") - the US Government's coordination project to accelerate and facilitate vaccine development - and designed in collaboration with the NIH and BARDA, to support a systematic evaluation of the efficacy, immunogenicity and safety of the candidate vaccine.

32. On 11 March 2020, the WHO declared COVID-19 a global pandemic.

33. On 16 March 2020, the first participant in the NIAID's Phase 1 study of mRNA-1273 was dosed with mRNA-1273.

Phase 2 study in the United States

34. Following standard requirements for vaccine development, on 27 April 2020 ModernaTx, Inc. announced that it had filed an IND with the FDA to evaluate mRNA-1273 in Phase 2 and late-stage studies if supported by safety data from the Phase 1 study led by the NIAID.

35. A summary of that Phase 2 study is set out in **[DH1/6 - INQ000398090]**. A Phase 2 study is used to determine the effectiveness of the drug or treatment and to further study its safety. ModernaTx, Inc. committed to undertake the Phase 2 study, which required investment in large scale manufacture on the basis of promising data from Phase 1, whilst Phase 1 data was still being collected and analysed. Running the studies in parallel rather than in sequence was not usual practice, nevertheless all the usual standards and approvals were required and followed. Conducting the studies

this way meant that the data that was needed to assess safety and efficacy could be collected, processed and analysed within a much shorter timeframe.

36. On 12 May 2020, ModernaTx, Inc. announced that the FDA had granted Fast Track Designation for the vaccine, underscoring the urgent need for a vaccine against coronavirus. The FDA's Fast Track is designed to facilitate the development and expedite the review of therapies and vaccines for serious conditions that address an unmet medical need. Programs with Fast Track designation benefit from early and frequent communication with the FDA, in addition to a rolling submission of the marketing application.

37. On 18 May 2020, ModernaTx, Inc. announced positive interim Phase 1 clinical trial data. By the end of the month, the first participant had been dosed in the Phase 2 study. The Phase 2 study was conducted in the United States across eight sites, in healthy adults over 18 years old **[DH1/7- INQ000398091]**.

38. On 14 July 2020, positive interim Phase 1 data was published in the NEJM **[DH1/8 - INQ000398092]**. The conclusion on the Phase 1 data was that the mRNA-1273 vaccine induced anti-SARS-CoV-2 immune responses in all the participants, with no trial-limiting safety concerns identified.

39. On 28 July 2020, results from a non-human primate preclinical viral challenge study of the Moderna vaccine against Covid-19 were published **[DH1/9 - INQ000398093]**.

Phase 3 study in the United States

40. By 27 July 2020 the Moderna team, in collaboration with the NIH and BARDA, began conducting a Phase 3 trial and dosing participants. The Phase 3 trial would run in parallel with Phase 2. This study, known as the COVE study, enrolled more than 30,000 participants in the U.S. and was conducted in collaboration with NIAID and BARDA under the umbrella of OWS. The Phase 3 trial, like Phases 1 and 2, had to meet exactly the same requirements and approvals as if conducted in any other circumstances (as noted below), but critically it was the primary focus of the regulatory authorities and benefitted from OWS which directed US Government resources and logistics expertise to assist the efforts of vaccine development. In order to quickly scale and implement the Phase 3 trial ModernaTx, Inc. partnered with PPD Inc., a long established and respected global contract research organisation with established

structures and networks with clinical sites in the USA. PPD Inc. had also supported the Phase 2 clinical study.

41. The Phase 3 study protocol followed the FDA guidance on clinical trial design for COVID-19 vaccine studies. The randomized, placebo-controlled trial tested an mRNA-1273 dosage of 100µg **[DH1/10 - INQ000398094]**. The primary endpoint was the prevention of symptomatic COVID-19 disease. Key secondary endpoints included prevention of severe COVID-19 disease (as defined by the need for hospitalization) and prevention of infection by SARS-CoV-2 regardless of symptomology (SARS-CoV-2 is the virus that causes COVID-19).

42. The Moderna team published the un-redacted Phase 3 protocol online to provide free access and complete transparency about the Phase 3 trial to clinicians around the world **[DH1/6 - INQ000398090]**.

43. On 5 August 2020, ModernaTx, Inc. published further research and data from studies conducted on mice relating to the mRNA-1273 vaccine **[DH1/11 - INQ000398095]**. The research showed that mRNA-1273 induced a neutralising antibody response to and protected against SARS-CoV-2 infection in the lungs and noses of mice without evidence of immunopathology.

44. As already noted above the benefit of the Fast Track designation was the frequency of communication with the FDA and the approach that the FDA took to reviewing and assessing data. As the trials were running in parallel the data from Phase 2 and Phase 3 was being shared with the FDA analysed and assessed on a rolling basis. It was this process that enabled the ModernaTx, Inc. to then make a formal submission for Emergency Use Authorisation (**"EUA"**) to the FDA. Approval was granted before the end of December as noted below.

45. On 29 September 2020, the interim results from Older Adult Age Cohorts in the Phase 1 study were published. This was a subsequent data analysis on the data collected from the Phase 1 trial **[DH1/12 - INQ000398096]**.

46. On 30 November 2020, the ModernaTx, Inc. team announced that the Phase 3 trial met the statistical clinical pre-specified endpoint in the study protocol for efficacy, demonstrating a vaccine efficacy of 94.1 percent and, importantly, mRNA-1273's ability

to prevent severe COVID-19 disease. The article reporting the results of the Phase 3 trial was published in December 2020 **[DH1/13 - INQ000408427]**.

47. In February 2021, results from the Phase 2 trial of the vaccine were published **[DH1/7 - INQ000398091]**. The results demonstrated that vaccination with mRNA-1273 resulted in significant immune responses to SARS-CoV-2, with an acceptable safety profile confirming the safety and immunogenicity of 50 and 100 µg mRNA-1273 given as a two dose-regimen.

Manufacturing of Moderna's Covid-19 vaccine

Manufacturing

48. Because of the need to secure manufacturing capacity to enable large scale manufacture of mRNA-1273 globally, ModernaTx, Inc. partnered with the Lonza group (**"Lonza"**) for manufacture of the vaccine in May 2020. This was before the Phase 3 trial had commenced. Lonza had global reach and experience in scaling manufacturing of innovative medicines. Moderna additionally engaged a number of contract manufacturing organisations (CMOs) to support with the filling stage which involves filling vials with the vaccine ready for distribution internationally (including to the UK). This included Labaratorios Farmacéuticos Rovi, S.A. (**"ROVI"**) in Madrid, Spain.

49. When manufacturing the vaccine and in compliance with its manufacturing authorisations, Moderna ensured compliance with all applicable regulatory requirements including the standards of Good Manufacturing Practice (GMP). All Moderna manufacturing sites were inspected and approved by the applicable regulatory authority. For example the Lonza site in Visp, Switzerland was inspected by Swissmedic and the ROVI site in Spain was inspected by The Spanish Agency of Medicines and Medical Devices (**"AEMPS"**). In terms of transitioning from vaccines manufactured for the clinical trials to scaled up production, we adhered to GMP standards approved by the relevant certifying regulatory agencies mentioned above and conducted chemical comparability analysis.

50. All required information, analysis and data regarding Moderna vaccine manufacture was produced to the regulatory authorities and in conformity with GMP. In addition, Section G below describes Moderna's vaccine safety monitoring more specifically.

Supply of the Moderna's COVID-19 Vaccine to the UK

51. The UK Government was aware of the ModernaTx, Inc. vaccine clinical trials underway in the United States and the promising interim results. My understanding is that first negotiations between Moderna Switzerland GmbH and the UK Government's Vaccine Taskforce (**VTF**) for supply of Moderna's COVID-19 vaccine began in October 2020.

52. On 16 November 2020, Moderna Switzerland GmbH and the VTF (acting on behalf of the UK Government) signed a Supply Agreement for Moderna's Covid-19 vaccine (**"the Supply Agreement"**). Supply of the vaccine was to begin on 1 April 2021, subject to approval for use by the MHRA.

53. On 23 November 2020, the VTF (acting on behalf of the UK Government) and Moderna Switzerland GmbH agreed to an Amendment to the Supply Agreement which provided for an additional 2 million doses of the mRNA-1273, a new total of 7 million doses.

54. On 30 December 2020, Moderna Switzerland GmbH agreed to a Second Amendment to the Supply Agreement which provided for an additional 10 million doses (a total of 17 million doses). Since April 2021 and based on figures up to 30 June 2022, Moderna has supplied approximately 27,819,900 vaccines to the UK Government. Moderna does not have data on the number of doses administered but the NHS collects that data across the UK.

Overview of the approval process for the Moderna COVID-19 vaccine

Approval in the United States (provided for context)

55. On 30 November 2020, ModernaTx, Inc. filed for an EUA with the FDA for use of the vaccine to prevent COVID-19 in people ages 18 years and older following rolling review of data by the FDA and ModernaTx, Inc. submission of the required data package and all supporting evidence. The EUA application was approved by the FDA on 18 December 2020.

56. Just over a year later full approval for the Spikevax vaccine was received from the FDA for individuals 18 years and older on 21 January 2022.

Approval process in UK

Initial Approval Under Regulation 174

57. At the end of October 2020 Moderna initiated the submission of mRNA-1273 data for rolling review to the MHRA, following positive results from a preclinical viral challenge study of mRNA-1273, the positive interim analysis of the Phase 1 study of mRNA-1273 in adults (ages 18-55 years) and positive results in older adults (ages 56-70 and 71+) published in the NEJM **[DH1/12 - INQ000398096]**. The rolling review process allowed the MHRA to begin its independent assessment and accept new evidence as it became available until the application was deemed complete. The aim of the rolling review process was to share information which was normally provided in stages periodically over the course of the approval process, at the earliest opportunity, and so reduce time to authorisation.

58. Initial authorisation for Moderna's COVID-19 vaccine was made pursuant to Regulation 174 of the Human Medicines Regulations 2012 (**"Regulation 174"**) following submission of the required data package and assessment by the MHRA. Regulation 174 is a mechanism which allows the MHRA to grant temporary authorisation of an unlicensed medicine in response to public health threats, such as a pandemic.

59. On 8 January 2021, the MHRA authorised the use of Moderna's COVID-19 vaccine under Regulation 174.

60. The UK authorised Moderna's COVID-19 Vaccine Spikevax, following the United States on 18 December 2020, Canada on 23 December 2020, Israel on 4 January 2021 and the European Union on 6 January 2021.

61. However, despite this initial, provisional authorisation, Moderna Switzerland GmbH did not in fact supply to the UK under Regulation 174.

Conditional Marketing Authorisation

62. The Moderna group applied for a Great Britain conditional marketing authorisation (**"CMA"**) through the European Commission Decision Reliance Procedure (**"ECDRP"**) which was a transitional arrangement put into place after the UK voted to leave the EU. The Moderna group and the MHRA agreed that the ECDRP path would be a better and more robust process as it allowed for more flexibility than a Regulation 174

authorisation. The ECDRP allowed the Moderna group to apply for a CMA on the basis that it had received approval for its COVID-19 vaccine from the EMA. Under this approval process, the MHRA could then rely on submissions, including data, already made to the EMA and the EMA's analysis. In practice the MHRA received all the data that was being shared with the EMA on a rolling basis and the MHRA could undertake its assessment of the data in parallel with the EMA.

63. Having assessed the comprehensive data package submitted in support of the Moderna COVID-19 vaccine, the EMA granted conditional marketing authorisation for the COVID-19 vaccine for individuals over 18 years of age on 6 January 2021. The holder of the Moderna vaccine marketing authorisation was Moderna Biotech Spain S.L. Supply pursuant to the Supply Agreement was not due until April 2021.

64. On 31 March 2021, the MHRA adopting the data package which had been submitted to and assessed by the EMA, issued a CMA for the Moderna vaccine, pursuant to the ECDRP process. As I have already remarked the MHRA had been reviewing the data submitted to the EMA on a rolling basis.

Omicron-targeting bivalent vaccines

65. As SARS-CoV-2 continued to evolve, ModernaTx, Inc. continued to develop variant-specific versions, including versions targeting the Beta, Delta and Omicron variants of the virus. Multiple studies supported the development of the vaccine booster, and these were conducted in the United States **[DH1/14 - INQ000398098]**.

Omicron

66. The Omicron-targeting bivalent vaccines were developed primarily in the United States but a Phase 3 study was conducted in the UK.

Clinical trial for Omicron-targeting Bivalent vaccines in the UK

67. In Autumn 2021, ModernaTx, Inc. discussed conducting an Omicron-targeting Bivalent Booster trial in the UK with the MHRA.

68. On 16 February 2022, the Moderna team in conjunction with the National Institute for Health Research (**"NIHR"**) announced a collaboration for a Phase 3 study investigating Omicron-targeting Bivalent vaccine in the UK and the associated Information Sheet

and Consent Form for the study is exhibited **[DH1/15 - INQ000398099]**. The clinical trial developed the adapted COVID-19 Spikevax vaccine that targeted the Omicron variant (i.e., the bivalent Omicron-containing booster candidate (mRNA-1273.214)).

69. The Phase 3 study enrolled 3,557 individuals. The study involved half of the participants receiving an Omicron-targeting Bivalent vaccine (mRNA-1273.529 or mRNA-1273.214) and the other half vaccinated with Moderna's original COVID-19 vaccine Spikevax. The study was completed on 23 June 2023 **[DH1/16 - INQ000502013]**.

Approvals in the UK

70. On 15 August 2022, the approval of the Omicron-targeting Bivalent vaccine was given as a line extension to the CMA of Moderna's original COVID-19 vaccine, which was authorised pursuant to the ECDPR process. This was prior to the approval of the Omicron-targeting Bivalent vaccine by the EMA for use in people aged 12 and above on 1 September 2022.

Approval of the vaccine relating to other cohorts

71. On 17 August 2021, the MHRA granted approval for the CMA to be extended to children aged 12-17 years old. An overview of Moderna's clinical development of mRNA-1273 for adolescents, children, toddlers, and infants is exhibited at **[DH1/17 - INQ000398100]**. The extension followed the approval of the extension of the EMA to the CMA on 23 July 2021. On 14 April 2022, the MHRA approved an update to the CMA allowing Moderna's original COVID-19 vaccine to be used in children aged 6 – 11 years old. The associated Moderna prescribing information document for children aged 6 – 11 years is exhibited at **[DH1/18 - INQ000398101]**. The extension followed the approval of the extension by the EMA to the CMA on 2 March 2022.

Manufacture

72. The Moderna group faced several challenges in relation to rapid development, manufacture, procurement and approval of the vaccine during the pandemic.

73. The Moderna COVID-19 vaccine, as with all mRNA products, is based on novel technologies that are complex and difficult to manufacture. Together with third party manufacturers (e.g., Lonza and ROVI), and along with other pharmaceutical

companies, the Moderna group faced the challenge of shortage of supply of some materials from time to time because of global demand and restrictions on export imposed by some jurisdictions during the pandemic. This was an issue for meeting supply volume requirements. By necessity the supplied volumes and/or delivery frequencies had to be varied from time to time but generally did not result in material supply delays as together with our partners we usually managed to find solutions which were acceptable to the UK VTF.

Initial authorisation under Regulation 174

74. As discussed at paragraphs 57-59, Moderna's COVID-19 vaccine approval was originally made pursuant to Regulation 174 of the Medicines Act 2012. However, it became clear to the MHRA and the Moderna group that this would not be a sustainable solution for vaccine supply in context of the global pandemic.

75. Approval under Regulation 174 did not allow for details to be amended in the Marketing Authorisation or in the manufacturing process. It did not allow for the upscaling of manufacturing or any flexibility in the supply chain. Given all the circumstances, the most efficient pathway for approval of the Moderna vaccine proved to be the ECDRP route which has subsequently been phased out.

Importing and logistics

76. Initially there were other practical hurdles which related to the export of the vaccine which was manufactured in the EU, and which required EU authorisation for export (Implementing Regulation (EU) 2021/111 pursuant to Article 5 of Regulation (EU) 2015/479 and as subsequently amended) and the requirement for authorisation from the UK to allow import of the vaccine into the UK.

77. There was a discussion between the VTF and Moderna Switzerland GmbH about the early supply of the Moderna COVID-19 vaccine before the contracted supply date of 1 April 2021, but that could not be achieved in part because of the import and export requirements and the time it would have taken to resolve them.

78. In addition, in early 2021, Moderna Switzerland GmbH was still a relatively young business and was building a supply chain infrastructure from 'the ground up' to deliver the vaccine from manufacture to a distribution hub in Belgium and then for onward

supply to end markets. This was new and had to be developed with logistics partners at pace.

79. The Inquiry has asked about the Moderna group's relationship with the VTF. I will do my best to answer, noting again that the UK company MBUK was a new company and initial contacts were with colleagues generally working for Moderna companies outside of the UK. It may also be helpful to understand the context for those contacts in relation to the supply of the vaccine to the UK covered at paragraphs 85-88 below.

80. I understand that there was some preliminary contact with the VTF before Moderna Switzerland GmbH and the VTF started negotiations for the Supply Agreement in October 2020. There was contact between the Moderna team and members of the VTF who were tracking the development of the Moderna vaccine, and there was a suggestion that some of the clinical study work for the vaccine could be conducted in the UK. The UK, as a clinical trial location, was appealing to the Moderna group because there was a highly integrated system between the NHS and MHRA. The Moderna team was impressed by how the clinical sites and participants were organised and as I understand submitted a Clinical Trial Authorisation (**"CTA"**) application in the summer of 2020. Given that at this time the number of COVID-19 infections was decreasing over the summer of 2020, ModernaTx, Inc. decided not run a clinical trial in the UK and so the CTA was put on hold.

81. More generally the relationship between the VTF and Moderna Switzerland GmbH was cooperative and collaborative. Before I was at MBUK, initial contact with the VTF was from Switzerland with Dan Staner who was our commercial lead for Europe, Middle East and Africa at the time. Key points of contact at the VTF were Ruth Todd and Steve Glass both Programme Directors at the Vaccine Taskforce. During the initial period of supply Dan and his team were in frequent contact with the VTF. Dan recalls having weekly calls. Other members of the team in Europe who were involved with logistics and manufacture had more regular contact addressing the detailed practicalities of the supply requirements and keeping the VTF updated. It was a good relationship with all involved understanding that they were working to achieve a common goal.

82. Looking ahead, and after initial vaccine delivery, in around the summer of 2021 there were discussions, between the Moderna team and the VTF, focusing on the UK

Government's interest in technologies that could respond to variant viruses. On the basis of the successful delivery of the Moderna mRNA Spikevax vaccine, the UK Government was interested in the adaptability and flexibility of mRNA to respond quickly to new viruses. Colleagues from the Moderna team talked with Sir John Bell (Member of the expert advisory group to the UK Vaccine Taskforce), Sir Richard Sykes (Chair of Vaccine Taskforce), Sir Patrick Vallance (Government Chief Scientific Advisor), Professor Matthew Snape (Oxford Vaccine Group, Chief Investigator) and Adam Finn (Member of Joint Committee on Vaccination and Immunisation) about the potential of the technology and future collaboration.

83. As already explained the Moderna COVID-19 vaccine was developed in the United States and its collaboration with government agencies regarding the vaccine development is described above. The UK Government was supportive in assisting with administrative and practical hurdles in relation to the supply of the vaccine to the UK.

84. They were also supportive in relation to the development of the Covid-19 Omicron Bivalent Booster as noted above.

Overview of contractual arrangements

85. The Inquiry has also asked about contractual arrangements with the UK Government in the relevant period. I was not directly involved in the negotiations of the Supply Agreement of November 2020, negotiated between Moderna Switzerland GmbH and the VTF **[DH1/19 - INQ000503566]**. However, I note the circumstances under which the Supply Agreement was concluded were unprecedented and, given the importance attached to making vaccines available in the UK, both parties were motivated to reach agreement quickly. The Supply Agreement was contracted between The Secretary of State for Business, Energy and Industrial Strategy, acting on behalf of the Crown, and Moderna Switzerland GmBH. The Supply Agreement specified that the VTF would secure, from Moderna Switzerland GmBH, filled and finished mRNA-1273 that had been labelled, released and delivered in accordance with the Supply Agreement. The supply was to begin in April 2021, subject to approval for use by the MHRA.

86. Moderna Switzerland GmbH and the VTF each appointed a Representative to oversee conduct under the Supply Agreement and be responsible for ongoing discussions

relating to supply and there was regular contact between the parties and rolling updates regarding supply.

87. Moderna's Representative was Patrick Bergstedt. The VTF Representative was Ruth Todd.

88. It's important to remember the unique and unprecedented circumstances we were all facing during the height of the pandemic. The world was in urgent need of a solution, and we, at Moderna, were working at an unprecedented pace to provide a safe and effective vaccine. Given these unique circumstances and the UK Government's urgent need for the supply of vaccines, the Supply Agreement provided for an indemnity. At the same time, in March 2021, the UK government extended Vaccine Damage Payment Scheme (**"VDPS"**) to cover COVID-19 vaccines. My understanding is that this extension was made to ensure that individuals could submit a claim in connection with a "severe disability" as defined within the scheme, that might result from receiving a COVID-19 vaccine.

89. These were Moderna's first contracts for vaccine supply in the UK. Given this was a first-time contract, I cannot say how the contract may have differed from standard contractual arrangements for the development, supply or manufacture of other vaccines as we did not have a standard against which to compare. However, I am aware that similar indemnities were provided by governments around the globe in favour of other Covid-vaccine manufacturers and the UK Government's approach was not unusual.

90. In terms of innovations that were introduced during this period in respect of development, I have already mentioned the flexibility, rolling review and collaboration that was adopted by the parties involved. One innovation in respect of manufacturing that was specific to this period was how some tasks were completed. For example, because of travel restrictions there were some approval processes that differed because of restrictions on travel, and inspections of manufacturing locations were conducted virtually. Generally this worked well.

E. Approval Process

91. The Inquiry has asked for an overview of the clinical trials and approval process and how this work ran alongside procurement and manufacture. I have already described

(at paragraphs 30-46) the timeline of clinical trials for the Moderna vaccine and how data was shared with regulators on a rolling basis to help accelerate review and analysis and obtain approval. Alongside this work the UK Government was speaking to vaccine manufacturers including ModernaTx, Inc., and ModernaTx, Inc was trying to secure manufacturing capacity for a vaccine that had not been approved or ordered.

92. In relation to assessment and approval whilst the timeline was compressed, the scrutiny, analysis and approval process did not differ from the usual processes under the ECDPR and extensions of the CMA. The major difference was that tasks were undertaken on a condensed timeline and data was shared and reviewed on a rolling basis.

93. My understanding is that the same steps were taken as would be required under "normal" pre-pandemic conditions but gathering clinical data and submitting data for analysis and approval by regulators, setting up manufacturing operations and logistics was the primary and only focus of all those involved. There were no other competing tasks and that was how it was possible to achieve outcomes in a relatively short period.

94. Another factor was that there was open cooperation between regulators in different jurisdictions in terms of sharing information and agreeing requirements, which made compliance more straightforward both in terms of clinical trial requirements and approval submissions.

95. In terms of regulatory approval, the Moderna group, led by Moderna Biotech Spain S.L., followed the EMA procedure, but also submitted all the required documents and data to the MHRA. This process allowed the MHRA to review in parallel with the EMA, and once EMA approval was granted, the MHRA could quickly make their own decision based on the already available data. This is how the vaccine became available to the UK and was harmonised with the procedure in Europe. It was one product for both the UK and the EU.

Approval process in the UK

96. As I have already described above, the Moderna original Spikevax vaccine was first approved in the United States and then in Europe and the UK. As noted above at paragraph 74, Regulation 174 was a temporary and impracticable solution for the Moderna vaccine because it did not allow for any variations. When this became

apparent the Moderna group discussed the most appropriate approval pathway with the MHRA. In particular, Nadia Assenova from Moderna Switzerland GmbH met with Julian Bonnerjea and his colleagues.

97. One regulatory option was to apply for full marketing approval through a UK national pathway which would require UK specific modules. Having discussed with the MHRA, Moderna decided to pursue approval under the ECDRP. On 31 March 2021 the Moderna vaccine was approved under the ECDRP because the vaccine had already been approved in the EU.

98. The ECDRP pathway allowed for a harmonized process with the EU, which was the faster and more efficient choice.

Clinical trial in the UK for Omicron-targeting Bivalent

99. As mentioned above, there were clinical trials conducted in the UK for Omicron-targeting Bivalent vaccines.

100. The Moderna group was one of several major pharmaceutical companies that participated in a non-competitive environment, sharing clinical trial sites to collect data for Omicron-targeting vaccines. The UK Government encouraged this collaboration, because there were a limited number of sites approved to conduct clinical trials in the UK.

101. It was helpful that the MHRA had a sophisticated framework for oversight of clinical trials. MHRA personnel would prioritise their availability for all matters relating to the vaccine. The MHRA personnel involved to oversee this work were Kirsty Wydenbach an Expert Medical Assessor and Martin O' Kane the then head of the Clinical Trials Unit who were both experienced and were able to answer questions quickly and knowledgeably.

102. We submitted the data package relating to the Omicron-targeting Bivalent vaccine to the MHRA in September 2022.

103. Looking back at the events of the last four years my understanding is that there weren't any significant innovations made in respect of the requirements for the trials and the approval process. All the standard steps and requirements remained the same however the execution was different in some respects. For example, data was shared

on a rolling basis and clinical trial stages were run in parallel rather than sequentially. In addition, and particular to these circumstances, there was the focus of effort and collaboration amongst those involved. Teams worked around the clock to achieve a common goal. There was close cooperation between regulators in different countries which meant that the processes around study design and approval were accelerated. Whilst the same data and detail was still demanded by regulators, they were flexible about the format and timing of data being submitted. The aim was not to delay processes on the basis of administrative or technical details which were not substantive.

104. There are possible lessons that we can learn from the response to the pandemic in terms of vaccine development and approval. For example, formal harmonisation across jurisdictions regarding data requirements from clinical trials would help in trial study design so that the minimum requirements were universal and clear in terms of subjects and exposure **[DH1/20 - INQ000398103]**.

105. Pre-defining a simplified data package structure for submission to regulators for pandemic specific products would also be helpful in terms of preparing the product for market. A pre-defined pandemic approach for product presentation and considering digital labelling could also speed up the process **[DH1/20 - INQ000398103]**.

F. VACCINE DELIVERY AND PRIORITISATION

106. I have already discussed our contacts with the VTF in relation to vaccine supply and delivery under the Supply Agreement. As a young company globally and with limited presence in Europe MBUK did not have a role in advising the UK Government.

107. The objective of the Moderna group was to create a vaccine that would help to save lives in the context of an unprecedented global pandemic. Any vaccine created had to be safe and effective for as many people as possible **[DH1/21 - INQ000398104]**. As noted above, when undertaking early development and designing clinical trials, we sought to develop a vaccine that could be used across diverse populations, ages and genders.

Identifying the suitability of specific vaccines for particular groups

108. The Moderna group considered throughout the development of Spikevax how the

vaccine would work in different groups of individuals. We submitted our findings from clinical trials regarding the suitability of Spikevax for different populations (the results of which are discussed at paragraph 63) when seeking regulatory approval of Spikevax, including to the EMA and the MHRA.

109. The Spikevax EMA Public Assessment Report (the "**PAR**") reflects Moderna Biotech Spain, S.L. submissions to the EMA regarding its findings on the safety of the vaccine in specific populations, including in pregnant and lactating women, elderly subjects and immunocompromised individuals **[DH1/22 - INQ000377508]**. Moderna Biotech Spain, S.L. provided the PAR (and the data and analysis underpinning the PAR) to the MHRA in support of its Spikevax approval submission in the UK initially under Regulation 174 and then under the CMA, the mechanisms which are described above at paragraphs 57-63 (see **[DH1/23 - INQ000502014]** and **[DH1/24 - INQ000398106]**).

110. Further developments in the Moderna group's knowledge and understanding of Spikevax were included in ModernaTx, Inc.'s Risk Management Plans ("**RMPs**"), monthly safety reports, and periodic evaluations of safety data aggregated on a six-monthly basis (see for example RMP **[DH1/25 - INQ000398107]**). Each of these summaries and reports of safety information were provided to the MHRA to help build a picture in relation to the safety data associated with the vaccine and were produced with varying frequency (as explained further below) post the approval of Spikevax.

111. The need for monthly safety reports was initiated by regulators to monitor COVID-19 vaccines and it was not a pre-existing regulatory requirement prior to the COVID-19 pandemic. The requirement to produce monthly safety reports was introduced specifically to address the unprecedented scale with which the COVID-19 vaccines were administered as a result of the active global vaccination campaigns adopted by governments throughout the world. The benefits were the timely provision of safety information to allow a dynamic assessment of safety information. Usually, safety reports would be required by regulators on a 6 monthly basis.

112. As noted above, in respect of the approval of Spikevax, the MHRA thoroughly reviewed and validated the EMA's findings rather than duplicating the work of the EMA **[DH1/26 - INQ000408430]**. Given the scale and urgency of regulatory review this step expediated the approval process of Spikevax in the UK. As a result of this process the UK Government had timely information and data on the efficacy of the vaccine and its

suitability for (in relation to each of the Spikevax vaccines and booster doses) particular groups of individuals.

Prioritisation of the vaccine for particular groups

113. The WHO Prioritization Roadmap identified categories of high priority groups and made clear that such categories of priority also applied to the Spikevax vaccine **[DH1/27 - INQ000398108]**. Individuals identified as groups to be prioritised for receiving the vaccine under the WHO guidance include older adults, persons with moderate to severe immunocompromising conditions and health workers **[DH1/28 - INQ000502016]**.

114. MBUK did not assume any role at all in advising the UK Government, the VTF, or JCVI on vaccine distribution or prioritisation.

Time intervals between doses

115. Available evidence on time intervals between doses at the time of the approval of Spikevax was reflected in the PAR. The data was communicated to the appropriate regulatory bodies throughout the world including, by way of illustration, in the summary presentations provided to the FDA **[DH1/29 - INQ000398109]** and such findings were reflected in the Spikevax Summary of Product Characteristics (the "**SmPC**") (see for example the first SmPC **[DH1/31 - INQ000398111]**).

Vaccination of particular age groups, including children.

116. Data relevant to age profile as discussed above was included in the information shared with the appropriate regulatory bodies, including by way of illustration, to the FDA in the summary presentation **[DH1/32 - INQ000398112]**. Moderna's data and analysis is communicated to the MHRA and reflected in the SmPC (see for example **[DH1/33 - INQ000398113]**).

Vaccination of pregnant and breastfeeding women

117. The need for a vaccine suitable for pregnant women had been canvassed widely, including by the MHRA, and this was taken into account when designing the vaccine development process.

118. The SmPC notes that a large amount of observational data from pregnant women

vaccinated with Spikevax during the second and third trimester has shown no increase in adverse pregnancy outcomes. The SmPC also sets out that since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, Spikevax including the Omicron-targeting vaccine can be used during pregnancy **[DH1/33 - INQ000398113]**.

119. Regarding breastfeeding, the SmPC notes that existing studies showed no effects on the breastfed new-born/infant are anticipated since the systemic exposure of the breastfeeding woman to the vaccine is negligible and that that observational data from women who were breastfeeding after vaccination with Spikevax have not shown a risk for adverse effects in breastfed new-borns/infants **[DH1/33 - INQ000398113]**.

Effectiveness of boosters and timescales for administering boosters relative to first doses.

120. The Moderna group conducted studies (the results of which were communicated to the MHRA and included in its SmPC) looking at the immunogenicity of Spikevax after a booster dose and considered this both in adults as well as in adolescents from 12 through to the age of 17. The Moderna group has also shared data with regulatory bodies as already noted in ModernaTx, Inc.'s findings shared with the FDA **[DH1/29 - INQ000398109]**. Any and all findings of the Moderna group in relation to the safety and effectiveness of Spikevax, including in relation to booster doses, were communicated to the MHRA (and other global regulatory entities) on a rolling basis, including through regular safety updates, as well as being formally included in the SmPC.

121. MBUK weren't involved in advising the UK Government in relation to roll-out procedures or public information campaigns about COVID-19 vaccines.

G. VACCINE SAFETY

122. Approval of a medicine ultimately comes down to a careful assessment of the risk versus the benefit of its use. All medicines carry certain risks of adverse reactions.

123. When deciding whether to grant marketing authorisation for a drug, the regulatory authority examines whether the therapeutic efficacy of the drug has been sufficiently

documented and whether its safety has been proven. The assessment concludes with a benefit-risk analysis for the drug.

124. The benefit-risk balance can be defined as the "assessment of the medicinal product's positive therapeutic effects in relation to its risks, i.e., all risks with regard to the quality, safety and efficacy of the medicinal product in respect of the health of patients or public health".

125. The Inquiry has asked me to identify the risks associated with the Moderna vaccine and to provide a chronological account of when the risks were identified and to whom they were communicated. I explain further below the mechanisms for identifying "safety signals" which are the indicators of a potential risk. In all cases where safety signals were investigated and analysed following that analysis and validation, they were promptly raised with regulatory bodies including the MHRA and the process of making changes to the relevant safety information were implemented with agreement and oversight from the MHRA. In the context of discussing the potential risks it may be helpful to address this subject by explaining:

(a) the systems that were in place to identify potential risks and how those risks were assessed;

(b) the nature of the interactions between the Moderna teams based in the USA, EU and UK and regulators including the MHRA on safety and risk; and

(c) the current risks as noted in the SmPC and PIL.

(a) Systems in place to identify potential risks

126. The Moderna group identified potential risks through a number of mechanisms both during clinical studies and from ongoing post marketing surveillance work. All identified potential risks from whatever sources are included in the RMP, which is a detailed plan (running to several hundred pages).

Clinical Studies

127. Dealing first with risks identified through clinical trial process, as I have already noted, ModernaTx, Inc. published its protocol used in the Spikevax clinical trials. The protocol included definitions for adverse events and reactions, which were assessed on an on-

going basis as part of the clinical trials, as well as explanations of how those risks would be evaluated. For example, "Adverse Reactions" monitored included short term responses like pain at the site of vaccination, fever or fatigue post vaccination, responses which are generally mild and short-lived. The protocol also explains the serious adverse reaction criteria and the relevant definitions of Serious Adverse Reactions ("**SARs**") and Suspected Unexpected Serious Adverse Reaction ("**SUSARs**") which were incorporated into the clinical report forms which were used to collect data and formed the basis of data entered into the Electronic Data Capture system ("**EDC**") used during those studies.

128. I have already described in this statement how the vaccine was developed and approved and the focus and effort of all involved. Though times frames were condensed the same steps were taken as for any clinical trial, the same study documentation was prepared and reviewed, the studies were subject to the same ethical and regulatory standards, participants were recruited and assessed for eligibility on the same basis, and data was collected in the same way and subject to the same rigorous analysis. What was unique was the unprecedented level of focus and prioritisation of all involved. The only significant difference was that regulators accepted the submission of data on a rolling basis.

129. As noted in the protocol for the Baden study Protocol mRNA-1273-P301 **[DH1/10 - INQ000398094]** the aim was to recruit diverse study participants and Moderna enrolled more than 30,000 participants, ages 18 and older, across 99 U.S. study sites. The clinical trial protocol for mRNA-1273-P301 was conducted and monitored by Moderna in accordance with ICH requirements (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) GCP (Good Clinical Practice) standards and US CFR (Code of Federal Regulations), including specific requirements to record and report any adverse reaction (see **[DH1/10 - INQ000398094]** at 6.6 "Safety Analysis").

130. The initial clinical trial Protocol mRNA-1273-P301 noted above recorded the characteristics and eligibility criteria for the trial participants for this study including age sex, race and ethnicity. Children under 18 and pregnant women were excluded. Recognising that COVID-19 had a disproportionate impact on racial and ethnic minority communities, we designed our Phase 3 trial for everyone. We slowed enrolment to ensure representation. In the end, our trial included more than 11,000 participants

from ethnic minority communities, representing 37 percent of the study population. **[DH1/1 - INQ000398086]**. Subsequent studies as noted in the VBRPAC report **[DH1/17 - INQ000398100]** were conducted on younger age groups: Study mRNA-1273-P203, a Phase 2/3, randomized, observer-blind, placebo-controlled study to evaluate mRNA-1273 in participants 12 to 17 years of age and Study mRNA-1273-P204, a Phase 2/3, two-part, open-label, dose-escalation, age de-escalation and randomised, observer-blind, placebo-controlled expansion study to evaluate mRNA-1273 in participants 6 months to 11 years of age were conducted and reported.

131. Again, as noted in the VBRAC report **[DH1/17 - INQ000398100]** PASS non-interventional studies were undertaken to assess the effect on pregnancy notably: Monitoring safety of COVID-19 Vaccine in pregnancy: an observational study using routinely collected health data in five European countries (mRNA-1273-P905); and Moderna mRNA-1273 Observational Pregnancy Outcome Study (mRNA-1273-P902). As noted further below as part of its ongoing safety monitoring Moderna also tracked real world data regarding co-morbidities and immuno-suppression.

132. Modera also evaluated Spikevax in well-controlled HIV+ participants as part of the original mRNA-1273-P301 study. We also performed a small study in immunocompromised participants that included transplant recipients as part of Study mRNA-1273-P304.

133. All relevant information was shared with regulators as part of Moderna's Pharmacovigilance commitments as described for example in the EMA and MHRA Public Assessment Report (see [**DH1/22 - INQ000377508]** and **[DH1/24 - INQ000398106]**).

134. SARs and SUSARs are specific criteria set by international regulation that define the characteristics of a serious adverse reaction as opposed to an adverse reaction. Those criteria are not specific to the COVID-19 vaccine but rather universally applicable to clinical trial testing.

135. The definition of a serious adverse event in the UK is an adverse event that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or consists of

a congenital anomaly or birth defect. This definition is consistent with that of the EMA and FDA **[DH1/34 - INQ000398114]**.

136. In effect the criteria for what constitutes a SAR is the same throughout the world. The ModernaTx, Inc. COVID-19 vaccine protocol provides detail on the SAR criteria and the relevant definitions of SARs and SUSARs were embedded into the clinician forms **[DH1/10 - INQ000398094]**.

137. The EDC is configured to recognise when a SAR or SUSAR is entered. The SAR or SUSAR data would then be fed into Moderna's global safety database.

138. In accordance with regulatory requirements in the UK and the rest of the world, the Moderna group actively monitors, collects, reviews, and assesses safety data for Spikevax accruing from all external sources and this is detailed in the RMP (see Chapter 9 of the Green Book which outlines the process of vaccine safety monitoring in the UK and the reporting of adverse events following immunisation **[DH1/35 - INQ000398115]**). All identified potential risks from whatever source are included in the RMP which is a detailed plan running to several hundred pages. It includes data collected by regulatory authorities such as the MHRA and the EMA. The Moderna pharmacovigilance team download reports generated by the MHRA on the Yellow Card system of adverse reactions including SARs and SUSARs (that have been entered into the system by both healthcare professionals and patients) **[DH1/36 - INQ000502017]**.

139. The Moderna pharmacovigilance team also review and evaluate relevant medical publications and peer reviewed journals for any reports of new developments in data or analysis relating to adverse events associated with both Spikevax and COVID-19 vaccines more generally.

140. The initial RMP for the Moderna COVID-19 vaccine was shared with the MHRA as part of its original CMA submission package or "dossier". The MHRA requires Moderna Biotech Spain S.L. (as the Marketing Authorisation Holder) to update the RMP when a new potential safety risk arises or where there is a new or significant change in the existing pharmacovigilance plan or additional risk minimisation activities (see **[DH1/37 - INQ000502040]** and **[DH1/38 - INQ000502019]**). This would include circumstances where a new safety 'signal' arose. A 'safety signal' is information about an adverse event that may be related to a medicine and requires further investigation. The EMA

together with the regulatory authorities in the EU Member States (and in the UK the MHRA) are responsible for detecting and managing safety signals. Safety signals can be detected from a wide range of sources, such as spontaneous reports, clinical studies and scientific literature. The presence of a safety signal does not mean or imply that there is a causal association between a medicine and the reported adverse event **[DH1/39 - INQ000502020]**.

141. During the pandemic there were various iterations of the RMP because of the global roll-out and simultaneous vaccination programme and consequential very large volume of data being generated. In order to support the processing of global case reports and safety data sources, the Moderna group partnered with IQIVA Inc. with more than 50 years' experience in the field of pharmacovigilance systems and data management.

142. In summary, the RMP sets out the safety related information relevant to clinical trials and post-authorisation studies, the Moderna group's overarching pharmacovigilance plan, including discussion of the weekly signalling processes and responses, as well as identified and potential risks, safety concerns and risk minimisation measures that the Moderna group was, or intended to, implement.

Periodic Benefit-Risk Evaluation

143. Information on safety captured through these systems are assessed and risks are described to the MHRA through summaries of evaluated safety data which was aggregated and provided to the MHRA every six months for the first two years after approval of the vaccine. The safety data updates provided by Moderna to the MHRA summarise and evaluate all the relevant safety data. In particular, the six-monthly updates address the actions taken since the last update, changes to safety information, overall exposure, a summary of significant findings in terms of trial data, summary of safety signals, risk evaluation and benefit evaluation.

(b) Interactions between the Moderna teams based in the US, EU and UK and the MHRA on safety and risk

144. There are existing formal requirements for communicating information on potential risks including a statutory requirement in the UK for pharmaceutical companies to report to the MHRA serious suspected adverse risks associated with their products **[DH1/35 - INQ000398115]**.

145. I have described the RMP and the updates of evaluated safety data that were provided to the MHRA every month and six months above. In addition, any relevant data and analysis as it relates to adverse reactions, including SARs and SUSARs, would also be included in monthly safety reports already discussed. The monthly safety reports summarised the aggregate key medical data and analysis and focused on a summary of potential risks, including SARs and SUSARs, analysis of the existing data and safety signals, as well as a discussion of exposure and incident rates. As noted above, the monthly safety updates were an innovation introduced during the pandemic specifically to address the unprecedented exposure rate of COVID-19 vaccines and to increase the frequency of reporting.

146. Moderna had already shared all relevant data, including safety information, as part of the marketing authorisation process. We are not aware of any mechanism allowing applicants to withhold relevant information. Aside from these mechanisms for communicating information which I have described, the Moderna group was in regular communication with the MHRA from early 2021, often on a daily basis. Safety data from the clinical trials was published by Moderna in the academic papers reporting each trial and Moderna's application for CMA also included extensive safety information. I understand that the pharmacovigilance team had prepared the first monthly safety report and shared that with some regulators in February 2021. They were undertaking signal detection weekly as routine. More generally, and after first delivery of the vaccine in April 2021, the Moderna regulatory team would communicate information about product characteristics and potential adverse events and safety related information at least bi-weekly. However, any potential SAE would be reported to the MHRA on an urgent basis outside regular scheduled meetings.

147. Regarding whether mRNA vaccines should, in addition, be characterised or described as "gene therapies", mRNA medicinal products are designated as "advanced therapies" in accordance with applicable legislation. They cannot be correctly considered as "gene therapies" as they do not change the human genome. The mRNA vaccines do not insert any new genetic information (the product does not enter the cell nucleus where the genetic information is stored). By translation of the mRNA sequence, the cells are given an 'instruction' for synthetizing a specific protein. Various regulatory bodies including the FDA and EMA have indicated that infectious disease vaccines cannot be considered as "gene therapies".

148. In respect of regular meetings, the Moderna team would inform the MHRA of any topics for discussion in virtual meetings and flag matters that the Moderna group intended to include in monthly safety reports. These meetings were organised by the MHRA, who would also set an agenda for topics that they wanted to discuss and generate the meeting minutes.

149. Individuals from different departments within the Moderna group would join the meetings and the exact composition of attendees would vary depending on the subject matter being discussed, but regulatory, pharmacovigilance, and medical team members would often participate.

150. During such meetings the Moderna group would report on observations relating to SARs and SUSARs and the MHRA would similarly provide information on any relevant data or reports that they were aware of **[DH1/36 - INQ000502017]**. For example, we would inform each other of any technical issues that either party was having, including for example regarding the timelines for review of non-serious adverse incidents. The scale and speed of the vaccine roll out was unprecedented and, accordingly, so was the volume of post-vaccination data and the review of non-serious adverse incidents took time.

151. By way of illustration, due to the volume of administrations of the vaccines in a short time period (as I have noted above around 1.5 billion doses of the Moderna vaccine have been supplied worldwide), the Moderna COVID-19 vaccine had generated approximately the same amount of data in less than one year that might be expected from an influenza vaccine in use for 20 years. Because of the unprecedented volume of people being vaccinated there was an unprecedented volume of data being collected including information about adverse events. This huge volume of data allowed a clearer view of the safety profile of the vaccine to be reached more quickly. This large dataset also meant that it was easier to understand the frequency, and possible significance of, reported adverse events.

152. The meetings with the MHRA were collaborative and generally ensured that an open and effective dialogue was maintained throughout the COVID-19 pandemic between the Moderna group and the MHRA and that safety concerns were escalated quickly if necessary and discussed.

153. Moderna group individuals also met with the MHRA safety assessors monthly to discuss safety signals or warnings that were considered important. An example of this was in the summer of 2021 where a safety signal associated with myocarditis and pericarditis was identified. Moderna colleagues met with the MHRA, along with other regulatory bodies throughout the world, to discuss the potential risk and produce a robust action plan in response.

154. The Moderna group's pharmacovigilance work, including discussion of our weekly signalling processes and responses, identified potential risks, safety concerns and the risk minimisation measures that the Moderna group had or intended to implement, was set out in the RMPs. As such, upon identification of a new risk we would disclose a detailed assessment of any such risk to the MHRA through the RMP, alongside other communications, as detailed above.

155. There were also provisions in place to monitor batches and detect whether any batches were associated with higher adverse events rates. The EU RMP and SmPC (see for example **[DH1/57 - INQ000398126]** and **[DH1/33 - INQ000398113])** detail the instructions provided with the vaccine for healthcare professionals to record the name and batch number of the administered vaccine to improve traceability. The vaccine carton labelling also contains a scannable 2D barcode that provides the batch/lot number and expiry date. Moderna has also developed Traceability and Vaccination Reminder cards including batch and lot numbers and a scannable (QR) code (see **[DH1/22 - INQ000377508]**).

156. We continue to assess the safety of and risks associated with Spikevax on an on-going basis. Our review of the data has shown that Spikevax is an effective vaccine with a favourable risk benefit profile **[DH1/1 - INQ000398086]**.

157. Information about Spikevax including risks associated with the Spikevax vaccine are provided within the SmPC and the Patient Information Leaflet (**"PIL**") which collectively comprise the key product labelling information. Both the SmPC and PIL are regulated documents which are reviewed and approved by the relevant regulator as part of the authorisation of any medicine. As I have already explained the Moderna COVID-19 vaccine was primarily authorised by the EMA following the established EU legal framework. Article 8(3)(j) of Directive 2001/83/EC and Article 6(1) of Regulation (EC)

726/2004 require that, in order to obtain a marketing authorisation, a SmPC in accordance with Article 11 of Directive 2001/83/EC must be included in the application.

158. The SmPC is first issued when a drug receives approval by the appropriate regulator, for the UK this is the MHRA (see the first Spikevax SmPC **[DH1/31 - INQ000398111]**). It is a legally controlled and required document and the language is agreed with the regulator. It includes in its Clinical Particulars a section setting out special warnings and precautions for use.

159. More generally the SmPC is a description of a medicinal product's properties and the conditions attached to its use. It explains how to use and prescribe a medicine. It is used by healthcare professionals, such as doctors, nurses and pharmacists. In particular, it includes information on therapeutic indications, i.e. defining the target disease and population for which the medicine is approved; the dose and methodology of administration; the risks of a medicine, including contraindications, special warnings and precautions for use; a summary of the safety profile of the medicine, informing on the most serious and or/most frequently occurring adverse reactions, as well as a tabulated list of all adverse reactions with their respective frequency category; and the benefits of a medicine, including its mechanism of action and the main results of clinical trials supporting the marketing authorisation. It also includes information for individualised care and further pharmaceutical and pharmacological information about the product.

160. The PIL is intended to be read by patients and is available via the QR code on the carton or via the Moderna COVID-19 vaccine webpage (see for example the first PIL **[DH1/40 – INQ000398116]**). Rather than issuing hard copies of the PIL that would become outdated relatively quickly, the EMA agreed that providing a physical PIL, in all the circumstances, was not necessary and it would be more effective to provide the QR code to accompany the vaccine in order that the most current information was readily accessible. This agreement to simplify the packaging requirements was very helpful in streamlining logistics and speeding up vaccine delivery. However, it was my understanding that initially the UK preferred Moderna to provide a physical copy of the PIL (in addition to the QR Code) to accompany the vaccine which could be available at vaccination sites. The information in the PIL (however it is provided) includes identification of the medicine, therapeutic indications, information necessary before taking the medicine, including situations where the medicine should not be used,

precautions and warnings, dosage, description of side effects, and any additional information required.

161. The information in the SmPC is updated over time, with approval from the regulator, if new data emerges **[DH1/41 - INQ000502021]**. The Moderna group periodically assesses and updates the MHRA, and other regulators around the world, on the benefit-risk profile based on a review of the cumulative safety information from worldwide data sources. Like the SmPC, the PIL is also updated on an on-going basis, with approval from the MHRA (see for example the most recent Spikevax PIL **[DH1/42 - INQ000398117]**).

162. A summary of the individual risks as described in the current SmPC are set out below **[DH1/33 - INQ000398113]**. The updates to the SmPC and PIL from when Spikevax was first authorised for use in the UK can be tracked on the MHRA website which records every significant change made to the SmPC and PIL and when those changes were made **[DH1/43 - INQ000502022]**. In addition, I have provided further information below on specific risks, including when potential risks were first identified and how information about risks was communicated.

Hypersensitivity and anaphylaxis

163. Hypersensitivity and anaphylaxis was identified as a potentially adverse reaction that has been reported in individuals who have received Spikevax and this risk was included in the first SmPC dated 1 April 2021 (see **[DH1/44 – INQ000398118]** and **[DH1/31 – INQ000398111]**).

Myocarditis and Pericarditis

164. The increased risk for myocarditis and pericarditis following vaccination with Spikevax was included in an updated version of the SmPC on 25 June 2021 **[DH1/45 – INQ000398119]**. The risk of myocarditis and pericarditis was also monitored as an adverse event within ModernaTx, Inc's clinical trials as described above, but it was not observed despite the very large trial group (30,000). The absence of reported incidents in this group indicates how rare such an event is.

165. The risk of myocarditis and pericarditis (as set out in the SmPC) is very rare, which means that potential occurrence is less than 1 in 10,000. Myocarditis and pericarditis,

when observed is more often after the second dose compared to the first dose, and more often in younger males, although the risk profile appears to be similar for the second and the third dose. Available data suggests that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general **[DH1/33 - INQ000398113]**.

166. In February 2021 the Israeli Ministry of Health received reports of myocarditis post vaccination and initiated active surveillance, requesting that all hospitals report cases of myocarditis, and subsequently published post-authorization safety surveillance studies which identified instances of myocarditis following administration of Pfizer's mRNA COVID-19 vaccine (see **[DH1/46 - INQ000502023]** and **[DH1/47 - INQ000502024]**). A similar study of U.S. military populations was published in the Journal of the American Medicine Association in June 2021 which also identified cases of myocarditis following immunisation with mRNA COVID-19 vaccines **[DH1/48 - INQ000502025]**. In April 2021, in the European Economic Area ("**EEA**") the Pharmacovigilance Risk Assessment Committee (the "**PRAC**") started its review. As of May 2021, there were 19 reported cases of myocarditis among people who received Spikevax and an additional 19 cases of pericarditis out of a total approximately 20 million doses of Spikevax that had been given at that point in time (see **[DH1/49 - INQ000398120]** and **[DH1/50 - INQ000398121]**).

167. On 25 June 2021 the SmPC and PIL were updated to include a warning about the risks of myocarditis and pericarditis. More extensive information was included in the SmPC on 15 June 2023 (see **[DH1/33 - INQ000398113]**) and myocarditis and pericarditis noted as a "very rare" possible side effect in the PIL dated 15 September 2023.

168. In addition, Moderna implemented risk mitigation measures for its mRNA-1273 clinical trials and in respect of post-authorization safety assessment took the following steps:

    (a) Myocarditis/pericarditis continued to be evaluated in signalling activities

    (b) Updates were provided during regularly scheduled meetings with the MHRA

    (c) Detailed reports were provided within monthly comprehensive safety reports

    (d) Moderna published its findings on myocarditis/pericarditis (see below)

    (e) Additional PAS studies were implemented.

169. We have continued to collect and review data on the risk of myocarditis and pericarditis using routine and enhanced surveillance activities. The extent of those findings is reflected in the product information (including the SmPC and PIL) as well as communicated to the regulatory bodies throughout the world.

Thrombocytopenia and coagulation disorders

170. A further identified risk is bleeding or bruising that may occur following an intramuscular administration in individuals who are receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia), although that risk also exists with other intramuscular injections more generally and not just with the Spikevax vaccine.

171. The NIH published an article recording that it had identified 11 reported incidents of patients with thrombocytopenia following vaccination as of May 2021. It was also reported that Venous thromboembolic ("**VTE**") complications have been consistently reported to be increased following COVID-19 vaccinations. As of 11 August 2021, the MHRA had received two reports of thrombosis events with low platelets following vaccination with the Spikevax COVID-19 vaccine and this data was reported back to us **[DH1/51 - INQ000408461]**. The Moderna group took steps to evaluate all reports, clinical trial data, the Pharmacovigilance Database, and performed clinical literature search reviews following their identification of such risks. The Moderna group included this risk in its initial SmPC in 1 April 2021 **[DH1/33 - INQ000398113]**. It continually monitors trial data, its pharmacovigilance database and medical literature to determine if any further safety issue arises relating to thrombocytopenia and coagulation disorders that requires further risk management action or an update to the SmPC.

Capillary leak syndrome flare-ups

172. A few cases of capillary leak syndrome ("**CLS**") flare-ups have been reported in the first days after vaccination with Spikevax.

173. In March 2022, the PRAC begun its assessment of all the available data and cases of CLS reported in the EudraVigilance database after the administration of the Spikevax vaccine. There were a total of 11 reported cases out of an estimated 559 million doses for Spikevax that had been administered worldwide at that time, although the PRAC concluded that there was insufficient evidence to establish a causal association

between Spikevax and the onset of new cases of CLS **[DH1/52 - INQ000502027]**. The Moderna group took steps to update the SmPC on 17 June 2022 to include a warning regarding the risk of flare-ups of CLS in individuals who already have CLS **[DH1/53 - INQ000398122]**.

174. ModernaTx, Inc. provided an updated analysis of the association between Spikevax and CLS, following the PRAC's recommendation, and this was communicated to the MHRA through its safety data evaluation updates the Moderna group took steps to review clinical trial data, the Moderna pharmacovigilance database and perform medical literature study reviews, and it was concluded that findings reviewed with respect to Spikevax do not show convincing evidence of a link to CLS. The Moderna group continues to monitor whether any further risk management steps or updates to product information are required.

Immunocompromised individuals

175. The efficacy of Spikevax and the Omicron BA.4-5 vaccine may be lower in immunocompromised individuals.

176. In general, public health and professional groups recommend COVID-19 vaccination for patients who are immunocompromised. Throughout the course of 2021, real-world studies of immunocompromised populations observed a reduced immune response to COVID-19 vaccines in those individuals compared to the general population. The Moderna group continue to conduct a review of clinical trial data, our pharmacovigilance database and perform clinical literature study reviews into the efficacy of the vaccine in immunocompromised individuals. The results of the Moderna group's analysis are summarised in the safety summaries which are periodically provided to regulators including the MHRA.

177. The extent of the Moderna group's knowledge as it relates to all risks, including in relation to immunocompromised individuals, is communicated to the MHRA, detailed in our RMPs, the evaluations of safety data as provided on a six-monthly basis and reflected in the product information (including the SmPC). This resulted in Moderna's recommendation being incorporated into SmPC that a third booster dose be given to immunocompromised individuals 22 December 2022 **[DH1/54 - INQ000398123]**. This had subsequently been updated to include the most recent recommendation as set out

in the Spikevax SmpC dated 15 September 2023 that a third dose (0.5 mL, 50 micrograms) may be given at least 28 days after the second does in severely immunocompromised children aged 6 years through to 11 years of age of age and that the 0.2 mg/mL strength vial should be used in individuals 12 years of age and older **[DH1/31 - INQ000398111]**.

Other risks

178. The Moderna group has also identified further, more frequently reported mild or moderate adverse reactions, including pain at the injection site, lymphadenopathy, fatigue, headache, dizziness, myalgia, arthralgia, chills, nausea/vomiting, abdominal pain, axillary swelling/tenderness, fever, facial swelling, injection site swelling, rash and redness. These adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination **[DH1/31 - INQ000398111]**.

179. The Inquiry have also asked me to comment on messaging around potential risks which were reported to the MHRA and addressed in the SmPC and PIL. The focus of the Moderna group throughout the COVID-19 pandemic was to develop and provide an effective, immunogenic and efficacious vaccine that was compliant with the requirements set by regulatory bodies throughout the world, including those in EU and the UK. All validated data relating to risks associated with Spikevax that were identified, were communicated clearly and promptly to the appropriate bodies, including to the MHRA. The information was reflected in the vaccine product safety information, including through updated SmPCs and PILs, to ensure that the product information reflected the current state of scientific knowledge (consistent with our regulatory obligations).

180. In the UK there is a general prohibition on the advertising and promotion of specific prescription-only medicines, including vaccines, to the public (though that does not apply to vaccination campaigns approved by UK health ministers). However, beyond sharing information and data promptly with the MHRA and updating product information the Moderna group did not play an active role in public messaging regarding vaccination in the UK.

181. In terms of steps taken to address validated information on potential risks I refer to the information already provided about the pharmacovigilance systems in place,

interactions with the MHRA and the updates to the SmPC and PIL. However, some further steps were taken in respect of risk related to cardiac disorders.

Further additional measures

182. In relation to risks, associated with cardiac disorders such as myocarditis and pericarditis, Moderna Biotech Spain, S.L. prepared a Direct Healthcare Professional Communication (a "**DHPC**") in July 2021. The DHPC was prepared with BioNTech/Pfizer, BioNTech Manufacturing GmbH being a marketing authorisation holder of another mRNA COVID-19 vaccine **[DH1/55 - INQ000398124]**.

183. A DHPC is a communication which is designed to deliver important information for healthcare professionals prescribing, dispensing or administering medicines and is an additional risk minimisation measure. The DHPC provided context to the safety concern, as well including a request that instances of suspected adverse reactions be reported via the channels of national reporting systems in order to assist in assessing additional information. We sought to ensure our effective and timely response to relevant data and provide maximum clarity on the associated risks of Spikevax. My recollection is that Pfizer undertook the distribution of the communication.

184. In addition, the Moderna group also conducted post-authorisation safety studies ("**PASS**") and Post marketing surveillance studies ("**PMS**") for certain risks in order to obtain further information on the safety of Spikevax and to measure the effectiveness of risk-management measures (see the studies listed below).

185. Preliminary analyses of myocarditis and pericarditis were included within the interim report for the US PASS (mRNA-1273-P903) submitted on 31 October 2021 **[DH1/56 - INQ000398125]**. The language in the SmPC and the PIL was updated to more accurately describe the risk in light of our findings. There are also a number of post-market authorisation studies specifically focused on myocarditis including mRNA-1273-P910, mRNA-1273-P911: and others with outcomes including myocarditis such as mRNA-1273-P903 (which is now complete) and mRNA-1273-P904 and mRNA-1273-P920 which are on-going, as outlined in Moderna, Inc.'s RMP **[DH1/57 - INQ000398126]**.

186. In line with the EU's safety monitoring plan for COVID-19 vaccines and national UK requirements, the Moderna COVID-19 Vaccine had mandatory monitoring. Moderna

was initially required to provide monthly safety reports in addition to the regular updates already required and to conduct studies to monitor the safety and effectiveness of the vaccine. There are non-interventional Post Approval Safety Studies and interventional studies described in the EMA Public Assessment Report and MHRA Public Assessment Report (see **[DH1/22 - INQ000377508]** and **[DH1/24 - INQ000398106]**). In total by the end of 2023, Moderna had 16 ongoing or completed studies classified as post authorisation safety studies: 8 interventional and 8 non-interventional.

(a) Interventional studies

(i) 20-0003 Phase I, Open-Label, Dose-Ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (mRNA-1273) in Healthy Adults. Study status: Completed.

(ii) mRNA-1273-P201 Phase 2a, Randomized, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS- CoV-2 Vaccine in Adults ≥18 Years. Study status: Completed.

(iii) mRNA-1273-P203 A Phase 2/3, Randomized, Observer-Blind, Placebo-Controlled Study to Evaluate the Safety, Reactogenicity and Effectiveness of mRNA-1273 SARS-CoV-2 Vaccine in Healthy Adolescents 12 to < 18 years of age. Study status: Ongoing.

(iv) mRNA-1273-P204 A Phase 2/3, two-part, open-label, dose-escalation, age de-escalation and subsequent randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity and effectiveness of mRNA-1273 in healthy children 6 months to less than 12 years of age. Study status: Ongoing.

(v) mRNA-1273-P205 A Phase 2/3 Study to Evaluate the Immunogenicity and Safety of mRNA Vaccine Boosters for SARS-CoV-2. Study status: Ongoing.

(vi) mRNA-1273-P301 Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and

Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older. Study status: Completed.

(vii) mRNA-1273-P304 A Phase 3b, Open-Label, safety and Immunogenicity Study pf SARS- CoV-2 mRNA-1273 Vaccine in Adult Solid Organ Transplant Recipients and Healthy Controls. Study status: Ongoing.

(viii) mRNA-1273-P306 An Open-Label, Phase 3 Study to Evaluate the Safety and Immunogenicity of the mRNA1273.214 Vaccine for SARS-CoV-2 Variants of Concern in Participants Aged 6 Months to <6 years. Study status: Ongoing.

(b) Non-interventional studies

(i) mRNA-1273-P901 Real-world study to evaluate mRNA-1273 effectiveness and long-term effectiveness in the U.S. Study status: Ongoing.

(ii) mRNA-1273-P903 Post-Authorization Safety of SARS-CoV-2 mRNA-1273 Vaccine in the US: Active Surveillance, Signal Refinement and Self-Controlled Risk Interval (SCRI) Signal Evaluation in Health Verity. Study status: Completed.

(iii) mRNA-1273-P904 Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1273 Vaccine in the EU. Study status: Ongoing.

(iv) mRNA-1273-P905 Monitoring safety of COVID-19 Vaccine Moderna in pregnancy: an observational study using routinely collected health data in five European countries. Study status: Ongoing.

(v) mRNA-1273-P910 Natural history and clinical outcomes of vaccine associated myocarditis. Study status: Ongoing.

(vi) mRNA-1273-P911 Long-term outcomes of myocarditis following administration of SPIKEVAX (COVID-19 vaccine mRNA). Study status: Ongoing.

(vii) mRNA-1273-P919 An observational study to assess maternal and infant outcomes following exposure to Spikevax during pregnancy. Study status: Ongoing.

(viii) mRNA-1273-P920, Post-marketing safety of elasomeran/davesomeran and andusomeran vaccines in the United States. Study status: Ongoing.

187. In addition, independent studies of COVID-19 vaccines, including Spikevax, coordinated by EU authorities were also planned to provide more information on the vaccine's long-term safety and benefit in the general population. Many of these studies have resulted in publications, others have been presented at scientific congresses, while others are ongoing.

188. The Inquiry has asked whether any Moderna entity had a financial relationship with the MHRA during the relevant period. I can confirm that there was no such financial relationship other than the required payment of fees charged by the MHRA.

189. During the pandemic the working relationship was collaborative. The MHRA were professional and focused on maintaining an open and productive dialogue and in my experience MHRA individuals were dedicated and diligent.

190. From our dealings with the MHRA, our understanding was that their role was to scrutinise the relevant data and accompanying analysis both in granting the authorisation of Spikevax and monitoring the safety and effectiveness of the vaccine post authorisation. It is my understanding that this remit existed independently of any other concerns or issues outside of their regulatory function and that the MHRA performed their role impartially.

191. The Inquiry have asked me to comment on the Yellow Card system. The Moderna group consider the Yellow Card system to be an efficient means of monitoring and reporting data.

192. In terms of improvements in relation to the data collected and recorded via the Yellow Card system, it may be useful to have more accurate data on the doses administered in order to provide a denominator, which is needed for calculating adverse event rates. Ideally this would also provide anonymized demographic data to allow for calculating

rates in subpopulations (for example as it relates to individuals of a certain age or having a specific comorbidity).

193. I have already described the way in which the Moderna group monitors adverse events and how related information is captured analysed and reviewed.

194. Although the criteria and resultant definition of SAR is consistent throughout different jurisdictions, the specific requirements under the regulations applicable in each jurisdiction, including as it relates to the timeframe for reporting, can differ.

195. By way of example, under the currently applicable regulation in the UK for reporting in clinical trials (the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031)) SUSARs are required to be reported to the MHRA in an expedited timeframe. The Moderna safety database uses pharmacovigilance intelligence to ensure compliance with all different jurisdictions throughout the world, including the MHRA. As detailed above, upon identification of risks, steps were taken to notify authorities, update labelling and produce various types of safety reports explaining the risk.

196. The Inquiry has asked if the monitoring process for the Moderna COVID-19 vaccine was different from other products. I can comment that the process of producing the original submission package for the MHRA when the Moderna group sought UK approval of Spikevax was in all material respects identical to the process that occurs for other vaccines or therapeutics and the documents submitted to the MHRA for their review and approval were the same (as discussed in detail above at paragraphs 62-64). The MHRA did not alter what documentation was required for approval. However, it was clear that in the context of the approval of vaccines there was an awareness amongst all parties that the timeline for approval needed to be accelerated **[DH1/58 - INQ000408436]**.

197. However, post approval of Spikevax, there were notable differences. In particular, there were increased monitoring processes put in place in the form of further reporting obligations. Once the Spikevax vaccine was approved on 18 December 2020 in the US (its International Birth Date ("**IBD**")) we began the process of weekly signal detection.

198. The requirement to engage in signal detection is dependent on the product itself but typically, in the context of other vaccines, it is usually required around once a month. The MHRA, along with other regulatory bodies around the world (including the FDA and EMA), required signal detection to be on a weekly basis.

199. As already noted, there was a very significant amount of data being generated in a short period of time because of the global uptake of the Moderna vaccine. The data was being reviewed on an expediated basis. As already explained the MHRA required monthly safety reports as well as 6 monthly reports **[DH1/59 - INQ000502029]**.

200. Post approval of a vaccine or therapeutic, periodic reports aggregating safety information are required to be produced in the UK every six months for the first two years and then annually (and this requirement also applied to Spikevax post approval).

H. UK Vaccine Damage Payment Scheme

201. The Inquiry has asked for MBUK's views, if any, on the Vaccine Damage Payment Scheme (**"VDPS"**). MBUK is aware of a number of challenges facing the VDPS but we do not have a view on its current scope or potential for reform.

I. Lessons learned and preparing for a future pandemic

202. The COVID-19 pandemic demonstrated the value of close public and private sector collaboration, particularly in the way individuals with private sector experience were recruited to contribute to the public sector response. One example of this synergy is the VTF, which brought together experts from across the health and life sciences spectrum (including from public health, manufacturing and clinical trials).

203. The Moderna Innovation and Technology Centre (**"MITC"**) is an example of how lessons have been learned from the pandemic as to how the public and private sectors complement each other regarding future vaccine development and manufacturing. As the first of its kind in the UK, the MITC will be an innovative vaccine research and manufacturing centre based in Harwell, Oxfordshire. The aim of the partnership is to enhance the UK's resilience against future pandemics and health crises by onshoring the production of mRNA vaccines and therapeutics against COVID-19 and potentially other respiratory infections.

204. The COVID-19 pandemic has underscored the profound value of public-private partnerships in addressing global health crises, as exemplified by the VTF and the MITC. However, challenges such manufacturing capacity shortfall and the need for a future-ready life sciences workforce highlight areas for further collaboration.

205. I have also been asked about the industry's readiness to respond to future pandemics. I can only speak for MBUK and the Moderna group. It is our mission to explore the potential of mRNA science to help create a new generation of medicines for patients.

206. Our industry leading mRNA platform played a critical role during the pandemic enabling the development of an effective vaccine against COVID-19 quickly. This achievement was the result of years of dedicated research into the potential applications of mRNA technology. COVID-19 demonstrated the significant potential of mRNA vaccines, and the worldwide success of the vaccine rollout underscored the transformative potential of mRNA vaccines in revolutionising pandemic preparedness.

207. In response to the lessons learned from the pandemic MBUK signed a contract with the UK Government in December 2022 to establish the MITC in Harwell, Oxfordshire. This was a recognition of mRNA technology's crucial role bolstering the UK's resilience to future pandemics and acknowledging the UK's need for domestic mRNA production infrastructure. The UK Government committed to a 10-year strategic partnership to deliver up to 250 million vaccines annually for COVID-19 and other potential respiratory infections. Once operational in 2025, the facility will be a vital asset in enabling the supply of respiratory vaccines and strengthening the UK's ability to respond rapidly to future health crises.

208. As part of our Global Health Strategy, the Moderna group is also committed to developing our prototype vaccine approach. This platform is in preparation for "Disease X" - a term created by the World Health Organization to represent a hypothetical, unknown pathogen that could cause a future epidemic. We use preliminary versions of vaccines developed against representative viruses, which are rapidly adapted to tackle other related pathogens, to achieve this.

209. Moderna appreciates and supports the proactive steps taken in the UK following the COVID-19 pandemic to bolster future pandemic preparedness. We recognise that

initiatives like the MITC can play a crucial role in ensuring a robust, swift and effective response to any future pandemic.

210. I trust that the information I have been able to provide in this statement is of assistance to the Inquiry.

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 without an honest belief of its truth.

Signed: **Personal Data**

Dated: 22 October 2024